

ROBERT KOCH INSTITUT



125

125 YEARS ROBERT KOCH INSTITUTE

The Public Health Institute

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The Public Health Institute

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125 Years Robert Koch Institute – The Public Health Institute

Originally founded as the Royal Prussian Institute of Infectious Diseases on July 1st 1891 with Robert Koch as its director, the institute has since experienced dramatic changes to achieve its present standing as the German National Public Health Institute. Officially named after Robert Koch in 1912 – 30 years after his ground-breaking discovery that tubercle bacilli are the cause of tuberculosis – the Robert Koch Institute became a pillar of the newly established Federal Health Office in 1952 and, after the dissolution of the Federal Health Office in 1994, became today's independent research institution.

Particularly over the last 25 years, both the tasks as well as the scientific and technical capabilities of the institute have undergone fundamental changes. While research initially concentrated only on infectious diseases, the institute's research agenda substantially broadened from 1994 onwards to include non-transmissible diseases. The integration of the "Institut für Sozialmedizin und Epidemiologie", nowadays the Department of Epidemiology and Health Monitoring, provided the basis for transforming the Robert Koch Institute into a national Public Health Institute. This epidemiological expertise also paved the way to establishing another section – the Department of Infectious Disease Epidemiology. This department represents the largest concentration of Infectious Disease Epidemiology expertise in Germany, optimally complementing the research into infectious diseases carried out by the Department of Infectious Diseases. The major reorganisations recommended in 1998 by the German Council of Science and Humanities – a panel of experts focusing on the institute's research agenda – together with the 2001 release of the Protection against Infection Act further fostered the Robert Koch Institute's leading role in collaborations within the Federal States.

The new millennium saw further expansion with the formation of the Centre for Biological Threats and Special Pathogens in 2002. This centre closes an earlier gap in Germany's ability to appropriately deal with the threat of intentionally released biological agents. Two further important events shaped the Robert Koch Institute into its current form. First, in 2007 a selected team of experts developed the agenda RKI 2010, a concept for the much-needed strengthening and reorganisation of the RKI as a major public health institute. The German Parliament agreed upon a budget to allow the necessary expansion of staff at the RKI, making it possible to better tackle, for example, the new challenges in health protection and prevention of infection posed by our ageing society. A key element of this agenda was the construction of a high containment BSL-4 laboratory facility, which was inaugurated in 2015. Second, our institute has been mandated

since 2008 to continuously perform representative surveys of the population's health. The data generated by such health monitoring, which is available to the public and public health scientists in Germany, forms the basis for developing and evaluating intervention strategies at the national level.

It is important to acknowledge that the history of the Robert Koch Institute is not without its dark periods, and in this context it needs to be mentioned that the institute took critical responsibility for its historic burden by launching a project in which independent researchers investigated its activities during the times of National Socialism. The results of this project, carried out between 2006 and 2008, confirmed that major stakeholders of the institute had indeed then been involved in studies of a reprehensible nature.

Today the institute is part of an international network for public health research and development. It has duties in line with the International Health Regulations (IHR) and communicates with the European Centre for Disease Prevention and Control (ECDC), the European Commission and the World Health Organization (WHO). The institute also has a constant exchange of views with some hundred public health institutes globally as part of the International Association of National Public Health Institutes (IANPHI).

The institute is run by the efforts of its more than 1,100 dedicated employees who, with their over ninety different professions, transform the institute's vision to protect health and explore risks into reality, an excellent basis for providing sound recommendations to political decision makers. The tremendous and ongoing scientific and technological developments in biosciences, such as next generation sequencing, novel imaging technologies, bioinformatics and computational modelling, continuously challenge the experimental capability of the institute and the expertise of its staff. We will always strive to keep pace with scientific and social developments in order to fulfil our duties in the best possible way.

This booklet gives you an insight into the Robert Koch Institute as it stands 125 years after its foundation. Enjoy the tour!

Best regards



Prof. Dr. Lothar H. Wieler
President of the Robert Koch Institute

The Locations of the Robert Koch Institute



At Seestraße, you find the majority of research laboratories including a biosafety level 4 laboratory as well as central facilities such as the IT unit

The RKI has its headquarters and two additional locations in Berlin as well as a branch in Wernigerode. After completion of building works, two sites will remain in Berlin, Nordufer and Seestraße, both in the direct vicinity of the Charité university hospital and other research facilities. The historic site at Nordufer (up) houses the institute's HIV and bioinformatics units, its management and a small museum displaying memorabilia from the life and work of the institute's founder, Robert Koch. In addition, the mausoleum containing Robert Koch's remains can be visited



General-Pape-Straße contains the Department of Epidemiology and Health Monitoring and the institute's printery



In the 12th century town of Wernigerode, the RKI is housed in modern laboratories and in one of the oldest of its many half-timbered buildings. The main areas of activities are bacterial infections and antibiotic resistance

The Public Health Institute

What is public health?

There are various definitions of public health. The one most commonly used is Acheson's definition which was adopted by the WHO: "Public health is the science and art of preventing disease, prolonging life and promoting health through the organized efforts of society." (Acheson 1988, WHO 2011). Central elements are the twin characteristics of public health as a science and practical discipline, as well as the goal of achieving population health.

Other definitions incorporate additional perspectives. Gerlinger et al. (2012), for example, supplement Acheson's definition by adding the efficient use and fair distribution of resources. Franzkowiak (2015) emphasises the variety of fields of action and of stakeholders. The Institute of Medicine (1988) describes the mission of public health as "the fulfillment of society's interest in assuring the conditions in which people can be healthy"; it thereby identifies a key motivation for promoting public health, whereas Beaglehole et al. (2004) include the aspect of sustainability.

From these definitions, three fundamental characteristics of public health can be derived:

- ▶ **Practical application:** Public health is theory and practice. Scientific knowledge and its application are always interlinked. This means that questions regarding the appropriateness of measures and their consequences for society also play an important role.
- ▶ **Relation to the population:** Unlike individual medicine, public health relates to the health of the population. It thus encompasses connections at a system, political and organisational level. Public health is a joint endeavour and a societal responsibility.
- ▶ **Multi- and interdisciplinary:** In line with this comprehensive approach, public health relies on a large number of disciplines and applies a wide variety of methods. Important disciplines for public health include epidemiology, health policy, medicine, natural sciences, health system and health services research, health economics, health psychology, health communication, health and medical sociology, social medicine, prevention and health promotion, as well as public health ethics (Gerlinger 2012, Egger and Razum 2015, Leopoldina 2015).



Robert Koch Institute, main entrance. Completed in 1900, this building with its wealth of history stands at Nordufer in Berlin-Wedding

Objectives, tasks and fields of action for public health

According to the WHO definition, the objectives of public health are to prevent diseases, prolong life and promote health (WHO 2011). With the Essential Public Health Operations (EPHO), the WHO Regional Committee for Europe formulated central tasks in the field of public health (EPHO 1–5) as well as overarching topics (EPHO 6–10) which enable the implementation of these tasks (WHO 2012, WHO 2015):

1. Surveillance of population health and well-being
2. Monitoring and response to health hazards and emergencies
3. Health protection, including environmental, occupational and food safety and others
4. Health promotion, including action to address social determinants and health inequity
5. Disease prevention, including early detection of illness
6. Assuring governance for health
7. Assuring a competent public health workforce
8. Assuring organizational structures and financing
9. Information, communication and social mobilization for health
10. Advancing public health research to inform policy and practice.

The Essential Public Health Operations are part of the European Action Plan for Strengthening Public Health Capacities and Services.

Historical development and new challenges

Early forms of public health services existed in the towns and cities of northern Italy as early as the late 13th/early 14th centuries and, from there, spread to German trading cities. Another important step in the development of public health was the "medizinische Polizey" (medical police) in the emerging territorial states: health assurance by means of public surveillance and health administration. The first modern health sciences began to evolve in the 19th century. Worthy of note for Germany in this context are the subject areas of "social medicine" (Salomon Neumann and Rudolf Virchow), experimental hygiene (Max von Pettenkofer) and ultimately bacteriology, a field through which Robert Koch led a paradigm shift in medicine. From around the year 1900 onwards, social hygiene developed, looking at disease occurrence in specific societal groups and living conditions.

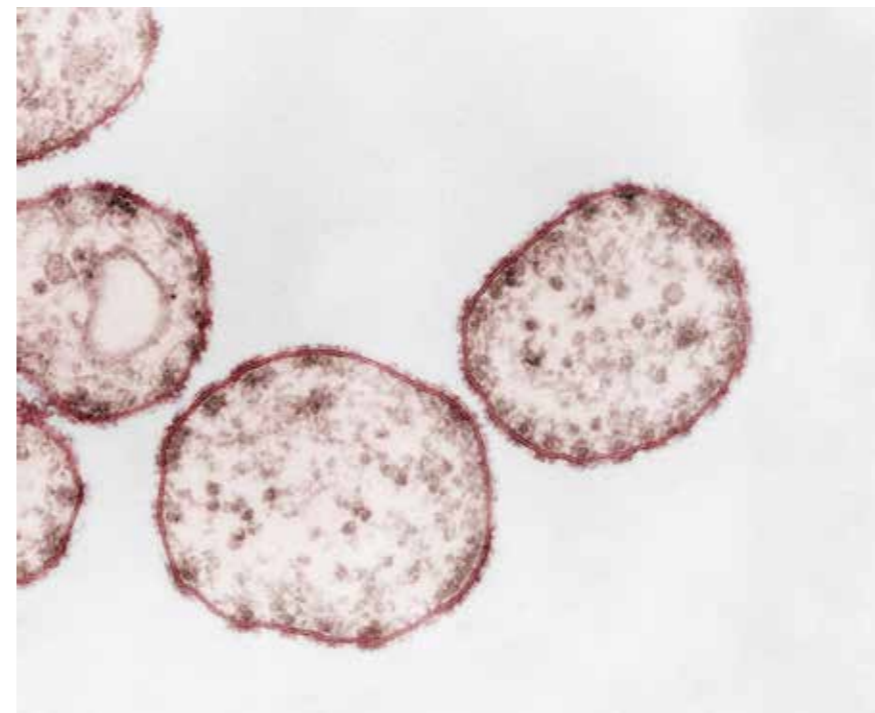
During the period of National Socialism, efforts towards "public health" were perverted and measures, including forced sterilisation and euthanasia, were used to implement notions of racial hygiene. It was impossible, after this, to reconnect with the tradition of social medicine and social hygiene (Hirschberg und Strech 2010). Public health in Germany was not revived until the 1980s, when the country began to close the gap that had opened up between it and other countries throughout the world (Gerlinger et al. 2012).

Hence, public health developed along the conditions for health and disease (e.g. urban living, the risk of epidemics, industrial labour) and the prevailing social and political concepts (Labisch and Woelk 2006, Schwartz 2006). Currently, globalisation and climate change, social inequality, demographic developments and shifts in the disease spectrum set the backdrop for public health action. This is demonstrated by challenges such as emerging (MERS and Ebola) as well as re-emerging infectious diseases (e.g. HIV, malaria and tuberculosis) and increasing developments of resistance. Among the non-communicable diseases, cardiovascular disorders, cancer, diabetes and mental disorders are of particular importance. Special attention must also be paid to certain population groups, such as the elderly, people with a migrant background and refugees.

In the same way that basic conditions for health and disease change, so too must methods and strategies be assessed, adapted and reconceived. Equally, technical possibilities are expanding, leading to new challenges, as demonstrated by the example of "Big Data". In order to master these tasks going forward, public health stakeholders and institutions will have to network and cooperate, even across national borders.



Measles viruses photographed with an electron microscope and coloured. The elimination of measles is an important public health target set by the WHO for Europe and already attained in the Americas



Tasks of the Robert Koch Institute as national Public Health Institute

The responsibilities of the Robert Koch Institute (RKI) as national Public Health Institute derive from the Essential Public Health Operations defined by the WHO and from “old” and “new” public health fields of action. They are reflected in the mission statement “Recognition – Evaluation – Action”.

This process starts with the early recognition of developments and problems affecting public health through the collection of data. This gives the RKI insight into the occurrence of infectious and non-communicable diseases, helps to identify crisis situations, allows monitoring of the state of population health, and contributes to the detection of environmental health risks and tracking of sociodemographic developments.

Independent evaluation of developments and trends allows the identification of health hazards and priority health problems as well as the development of suitable prevention strategies. Prognoses and estimations of the burden of disease in the population are also relevant in this regard, as is the assessment of the effectiveness of implemented measures and prevention strategies.

Action follows on the basis of these findings and evaluations. This includes the development of recommendations for action at federal and state levels, both for prevention and intervention measures, as well as for action and alarm plans for crisis management. In addition to this, the results are used for health reporting and to inform and advise policy-makers and the public.

The programme RKI 2010

In 2008, the programme RKI 2010, aiming to develop the Robert Koch Institute into an efficient, modern public health institute, defined these distinct, new tasks of the RKI:

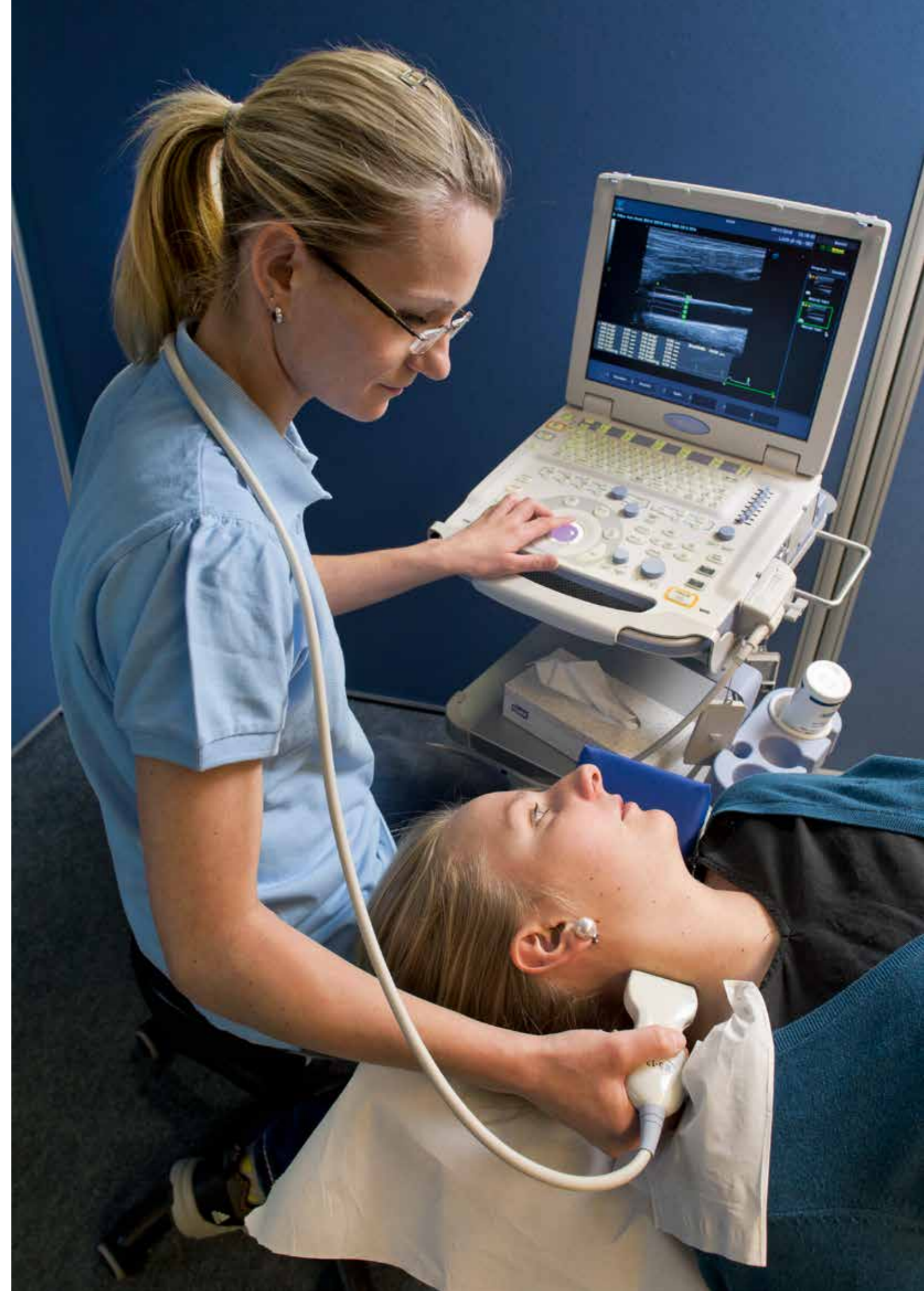
- ▶ Combating infectious diseases: seasonal influenza, zoonotic diseases, HIV and other sexually transmitted diseases, neglected pathogens; antibiotic resistance; vaccinations.
- ▶ Coping with new biological threats: SARS, influenza pandemics, bio-terrorism, crisis management; establishment of high-security laboratories.
- ▶ Combating non-communicable diseases: cancer, cardiovascular disease, diabetes; health monitoring; increasing life expectancy, environment and health, genetics and public health.
- ▶ Networking of the fields of activity: strengthening research activities, qualification of specialized personnel, national and international cooperation, advising, information and risk communication.
- ▶ Research, monitoring, the provision of information, advising, coordination, training, and making recommendations thus make up a comprehensive spectrum of activities.

Outlook

Being an applied discipline that serves society, public health must continue to keep abreast of current developments, identify relevant topics and develop appropriate concepts and strategies. Throughout its 125-year history, the Robert Koch Institute, as national Public Health Institute, has continuously assumed new responsibilities, making essential contributions to maintaining the health of the population. This will continue into the future. To illustrate, the Robert Koch Institute will increasingly address the health of refugees, set up a diabetes surveillance system and further expand the molecular surveillance of infectious diseases. In addition to the tasks outlined above, internationalisation, One Health and Big Data are topics on its agenda. The Robert Koch Institute will thus continue to be an independent, reliable and efficient stakeholder, serving the cause of improving public health in Germany and internationally.

Franziska Prütz, Thomas Ziese

The well-established system of RKI monitoring studies covers a broad spectrum of questions on health status, health behaviour, risk factors, prevention and care





**Equal Opportunity
Commissioner**
J. Masopust

Data Protection Officer
Dr. J. Lekschas

Occupational Safety
K. Mätzke

Social Counselling
A. Weber / Y. Janczak

Quality Management
K. Holschbach-Bussian

Advisory Board
external

Staff Council
M. Seibold

Research Council
internal

**Youth and Trainee
Representative Council**
L. Pfefferkorn

**Severely handicapped
employee representative**
C. Bug

President
President Prof. Dr. L. H. Wieler
Vice President PD Dr. L. Schaade

Fo
Research Coordination/
International Affairs
Dr. H. Maidhof

ZES
Central Ethics Committee for
Stem Cell Research
N.N.

GEKO
Commission on Genetic Testing
Administrative Office
PD Dr. H. Tönnies

GBS
Strengthening Global Health
and Biosecurity
Dr. W. Biederbick

Press
Press, Public Relations, Library
S. Glasmacher

AK Blut
National Advisory Committee
Blood
Dr. R. Offergeld

L
Management Staff
C. Lerch

L 1
Fundamental and Legal Issues
C. Lerch

L 2
Genetic Engineering
Dr. S. Jung

L 3
Regulatory Authority for the
Import and Use of Human
Embryonic Stem Cells
Dr. P. Löser

Department 1
Infectious Diseases
Prof. Dr. M. Mielke

FG 11
Enteropathogenic Bacteria and
Legionella
Prof. Dr. A. Flieger

FG 12
Measles, Mumps, Rubella, and
Viruses Affecting
Immunocompromised Patients
Prof. Dr. A. Mankertz

FG 13
Nosocomial Pathogens and
Antibiotic Resistances
PD Dr. G. Werner

FG 14
Hospital Hygiene, Infection
Prevention and Control
Prof. Dr. M. Arvand

FG 15
Gastroenteritis and Hepatitis
Viruses, Enteroviruses
Prof. Dr. C.-Th. Bock

FG 16
Mycotic and Parasitic Agents and
Mycobacteria
Dr. A. Aebischer

FG 17
Influenza and Other Respiratory
Viruses
PD Dr. T. Wolff

FG 18
HIV and Other Retroviruses
Prof. Dr. N. Bannert

Department 2
Epidemiology and Health
Monitoring
Dr. B. Kurth

ZKRD
German Centre for Cancer
Registry Data
Dr. K. Kraywinkel

FG 21
Epidemiological Data Center/
Research Data Centre
R. Dölle

FG 22
Epidemiology Laboratory
PD Dr. M. Schlaud

FG 23
Health Monitoring Studies and
Survey Methods
P. Kamtsiuris

FG 24
Health Reporting
Dr. T. Ziese

FG 25
Physical Health
Dr. C. Scheidt-Nave

FG 26
Mental Health
H. Hölling

FG 27
Health Behaviour
Dr. C. Lange

FG 28
Social Determinants of Health
PD Dr. T. Lampert

Department 3
Infectious Disease Epidemiology
Dr. O. Hamouda

FG 31
Data Management
Dr. H. Claus

FG 32
Surveillance
Dr. A. Gilsdorf

FG 33
Immunisation
PD Dr. O. Wichmann

FG 34
HIV/AIDS, STI and
Blood-borne Infections
Dr. V. Bremer

FG 35
Gastrointestinal Infections, Zoonoses
and Tropical Infections
Prof. Dr. K. Stark

FG 36
Respiratory Infections
Prof. Dr. W. Haas

FG 37
Healthcare-associated Infections,
Surveillance of Antibiotic Resistance
and Consumption
Dr. T. Eckmanns

ZBS
Centre for Biological Threats and
Special Pathogens
PD Dr. L. Schaade

IBBS
Federal Information Centre for Biological
Threats and Special Pathogens
Dr. C. Herzog

ZBS 1
Highly Pathogenic Viruses
PD Dr. A. Nitsche

ZBS 2
Highly Pathogenic Microorganisms
Prof. Dr. R. Grunow

ZBS 3
Biological Toxins
Dr. B. Dörner

ZBS 4
Advanced Light and Electron
Microscopy
Dr. M. Laue

ZBS 5
Biosafety Level-4 Laboratory
Dr. Andreas Kurth
(ad interim)

ZBS 6
Proteomics and Spectroscopy
Dr. P. Lasch

Project Groups
Speaker:
Prof. Dr. D. Brockmann

P 1
Immune Defense Mechanisms
Prof. Dr. R. Kroczek

P 2
Acinetobacter baumannii -
Biology of a Nosocomial
Pathogen
PD Dr. G. Wilharm

P 3
Epidemiology of Highly
Pathogenic Microorganisms
Dr. F. Leendertz

P 4
Epidemiological Modelling of
Infectious Diseases
Prof. Dr. D. Brockmann

P 5
Virulence Factors in
Salmonella and Campylobacter
Dr. R. Gerlach

Junior Research Groups
Speaker:
T. Semmler

NG 1
Microbial Genomics
T. Semmler

NG 2
N.N.

NG 3
N.N.

NG 4
Bioinformatics
PD Dr. B. Renard

NG 5
Sexually Transmitted Bacterial
Pathogens
Dr. D. Heuer

Administration
Dr. A. Engelbert

ZV 1
Personnel Department
S. Schuckert

ZV 2
Budget/Procurement
M. Pioch

ZV 3
Construction and Technical Services
D. Reichenbacher

ZV 4
Information Technology
Organisation/Controlling
Dr. M. Goltz

ZV 5
Internal Organisation
I. Abramowitsch

Head of the Institute

The Robert Koch Institute is headed by its president, Professor Dr. Lothar H. Wieler. Vice president is Privatdozent Dr. Lars Schaade. They are supported by a team of four secretaries.

The heads of the four departments (Infectious Diseases, Epidemiology and Health Monitoring, Infectious Disease Epidemiology, Centre for Biological Threats and Special Pathogens), the Central Administration as well as the Project Groups and the Junior Research Groups report directly to the President. Directly assigned to the President is the Management Staff (with three departments: Fundamental and Legal Issues, Genetic Engineering and the Centre for Stem Cell Research Authorization), the three staff positions Research Coordination, Press and Public Relations as well as Strengthening Global Health and Biosecurity. The offices of the Central Ethics Committee for Stem Cell Research, Commission on Genetic Testing and the National Advisory Committee Blood are also organizationally attached to the head of the institute.

Our science-based mission is the improvement of public health. In the years between 1996 and 2008 the Robert Koch Institute was evaluated and completely restructured by Professor Dr. Reinhard Kurth as President, and further advanced by his successors Professor Dr. Jörg Hacker and Professor Dr. Reinhard Burger. The agenda RKI 2010 was an important milestone by which the Robert Koch Institute has been redesigned as the central German Public Health Institute. Another big step was the inauguration of the new laboratory and office building located at Seestraße on February 3, 2015, in the presence of chancellor Dr. Angela Merkel and federal ministers Hermann Gröhe and Dr. Barbara Hendricks. The new structure also includes a laboratory of the highest biosafety level BSL-4.

“Our science-based mission is the improvement of public health.”

Prof. Dr. Lothar H. Wieler

Raising the research profile and infectious diseases preparedness of the institute is an important concern of the head of the institute. The tasks of the Robert Koch Institute in health protection and in advising politics can only be provided by scientific distinction. The establishment of an internal committee to ensure the scientific quality was achieved by implementing the Research Council in the late nineties. The Scientific Advisory Board is an external advisory committee that ultimately promotes scientific excellence; it usually makes statements regarding the Robert Koch Institute's professional and scientific performance, it advises the institute and gives scientific evaluations. Research on selected topics is performed in so-called Project Groups. The institute has further

intensified these activities by establishing Junior Research Groups. Here young scientists are offered the possibility to work independently over several years on scientific subjects which fit in with the tasks of the Robert Koch Institute.

The institute's mission is fulfilled by the employees with verve: protect and promote population health and reduce the burden of disease in Germany. This is accomplished by disease surveillance and monitoring as well as recommending and evaluating intervention. The Robert Koch Institute manages to fulfill its various tasks because of the wide range of competency among its staff: physicians, biologists, mathematicians, statisticians, psychologists, sociologists, veterinarians, biochemists, chemists, physicists, information scientists, teachers, lawyers etc. They are supported by technical and administrative staff, maintenance personnel etc. The health challenges have not lessened and new ones will emerge in the future. Examples are the possible effects of international networking and mobility on the transmission dynamics of infections, antibiotic resistance or the future effects of climate change regarding the risk of zoonoses or allergies in our climes or the prevention of chronic diseases due to demography.

The increasing importance and tasks of the Robert Koch Institute over the years is also reflected in the number of its employees: In 2010 some 750 employees worked here, while there are more than 1,100 employees in 2016. Still, staff is tight in regard to the tasks to be fulfilled. The created opportunities need to be channeled onto a precise and successful path of tasks of the Robert Koch Institute. Not only do the world and the challenges regarding health protection of the population change continuously, but changes also occurred in science, technology, health policy as well as legislation in recent years. To recognize and undertake new tasks in a timely manner as

well as learn and apply new possibilities to accomplish the work even better, the Robert Koch Institute constantly develops its research agenda, focusing on central questions such as:

- ▶ What must be tackled to ensure and increase the institute's outstanding role on a national and international level in the future?
- ▶ How can we further develop the research, particularly with regard to risk assessment, surveillance, monitoring and prevention of disease threats?
- ▶ How do we succeed in recognizing at an early stage future practical steps to be taken by politics, society and stakeholders in health sciences or in crisis management and in taking them up optimally in our fields of research?

In order to answer these questions, strategic processes are taking place during which we ask ourselves whether the Robert Koch Institute does “the right thing” and whether it “does it right”. When we emphasize the appropriate features of our tasks we will approach matters using the proper tools,

technologies, processes or partners. Furthermore, we will be continuously watching which progress we have made to reach our fullest potential.

The Robert Koch Institute and its exceptional employees also possess valuable resources on an international level. Our health safety efforts clearly transcend the national framework. International collaboration, cooperation and division of labour in research, analysis, monitoring or also crisis management are becoming increasingly important. The Robert Koch Institute therefore adopts responsibility as an integral part in well-functioning international networks.

In the end we must be measured by the extent to which our recommendations are heard, understood and successfully put into practice in the world beyond the Robert Koch Institute. Only then will our impact on society be manifested comprehensively when our knowledge and expertise will be applied. Success in addressing challenging health priorities guarantees the Robert Koch Institute to offer the most exciting jobs in the health sciences, a cornerstone to live up to the institute's public health mission. www.rki.de/wieler-en



HEAD OF INSTITUTE – Prof. Dr. Lothar H. Wieler (President) – PD Dr. Lars Schaade (Vice President)

SECRETARY – Sabine Tesfayohannes – Annegret Eisele – Jennifer Schmitt – Jennifer Hunziger (from left to right)

Department 1: Infectious Diseases

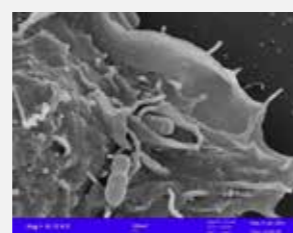
Infections are the result of exposition and disposition of the host and the pathogenicity of the infective agent. In continuation of the classical approach of Koch and Gaffky, most impressively exemplified in the context of their cholera expedition in 1883, the work in Department 1 "Infectious Diseases" is laboratory based and public health oriented.

Our mission is

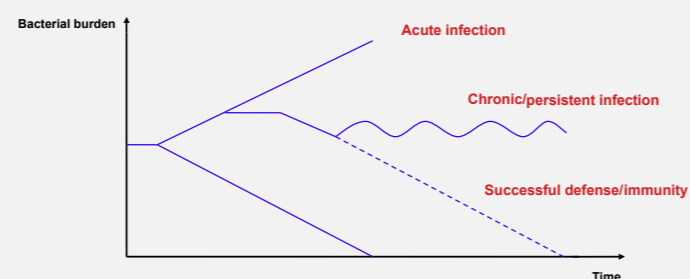
- ▶ to offer best practice, i.e. sensitive and specific identification of endemic pathogens,
- ▶ to follow the emergence and spread of pathogens by means of highly discriminatory molecular epidemiological methods, e.g. in the context of molecular surveillance or outbreak management
- ▶ to investigate changes in key features of pathogens like virulence factors and mechanisms of resistance or stress tolerance and
- ▶ to offer laboratory expertise necessary to certify the eradication of measles and poliovirus or to contribute to population based studies in collaboration with the departments for epidemiology.

In 8 divisions bacteria, viruses, fungi and parasites of endemic public health and paradigmatic importance are investigated. Using state-of-the-art microbiological as well as genomic and molecular biological methods enables us to host 5 National Reference Centres (for Staphylococci and Enterococci, Salmonella and other enteric bacterial pathogens, MMR, Poliomyelitis and Enteroviruses, and Influenza) and 5 Consultant Laboratories (Norovirus, Rotavirus, Listeria, RSV, hMPV, PIV, Cryptococcus/invasive fungi) with extensive and long-standing collections of medically important strains.

Questions addressed include the phylogenetic relationship of circulating as well as clustered microorganisms and the factors that determine their pathogenicity and virulence. A special focus is the description and in-depth analysis of changes in the characteristics of infective agents and mechanisms that render bacteria, viruses and parasites resistant to therapeutic agents. In close interaction with the departments for epidemiology within the Robert Koch Institute and laboratories all over Germany the reference laboratories are able to detect trends in the population dynamics and the development of antimicrobial resistances very early. Currently, whole genome sequencing is established to adapt and develop methods for subtyping routines and for the prediction of virulence and antibiotic resistance in bacteria.



The macrophage has a most decisive role in the defense against invading microorganisms. Interaction of macrophages with facultative intracellular bacteria and paradigmatic courses of infections



Staff in Wernigerode

In addition, the inactivation of infective agents by chemical and physical methods is investigated and certified in the unit for Hospital Hygiene, Infection Prevention and Control which also hosts the Commission for Hospital Hygiene and Infection Prevention. The respective recommendations describe the national best practice standards for the prevention of nosocomial infections.

Publications

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“The most basic approach to reduce antimicrobial resistance is to understand microbial evolution and to prevent infections.”

Prof. Dr. Martin Mielke

The transfer of the newly obtained and available knowledge into public health actions is performed by promptly and regular reports, original publications and evidence based national and international guidelines, education and training, as well as by the participation in national and international expert groups (WHO and ECDC) and the support of the national regional networks established for the implementation of measures to defend the distribution of antimicrobial resistant bacteria.

www.rki.de/abt1-en



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Unit 11: Enteropathogenic Bacteria and Legionella

The unit for Enteropathogenic Bacteria and Legionella studies important food- and waterborne human pathogenic bacteria, such as *Salmonella enterica*, *Escherichia coli*, *Campylobacter* spp., *Yersinia enterocolitica*, *Shigella* spp., *Listeria monocytogenes* and the lung pathogen *Legionella pneumophila*. Expertise in diagnostics, taxonomy and epidemiology of *Enterobacteriaceae* is flanked by research into the epidemiology, pathogenicity, and persistence of *Salmonella*, intestinal pathogenic *E. coli*, *L. monocytogenes* and *L. pneumophila*. It is particularly noteworthy that the German National Reference Centre for *Salmonella* and other Bacterial Enteric Pathogens is integrated in the unit. The reference centre focuses on the laboratory based epidemiology including outbreak detection and investigation of food borne bacterial pathogens such as *Salmonella*, *Shigella*, Shiga toxin producing/enterohaemorrhagic *E. coli*, *Y. enterocolitica*, *C. jejuni* and *C. coli*. Moreover, within the scope of the German-Austrian Binational Consiliary Laboratory for *Listeria*, the unit as the German partner together with the Austrian Agency for Health and Food Safety also contributes to a laboratory-based analysis of *L. monocytogenes* epidemiology.

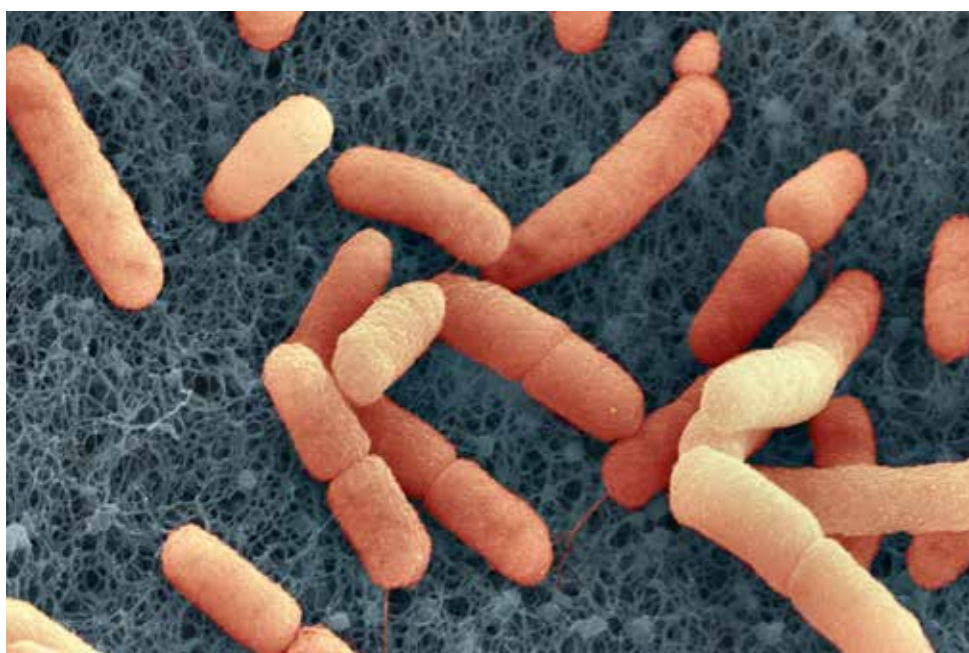
Given the large number of infections (e.g. gastroenteritis) and the possible severe outcome of infections (e.g. HUS) caused by the pathogens under investigation, the applied research and reference work done at the unit are of great public health importance. Immediate value for pathogen surveillance and outbreak investigation appears from the cooperation with the epidemiologists at the unit "Gastrointestinal Infections, Zoonoses and Tropical Infections" at the Robert Koch Institute, public health authorities of the federal states, and with the respective foodstuff control and veterinary authorities in case of outbreak investigations.

Methodologically, the basic approach in laboratory-based epidemiology is strain typing. At the unit "Enteropathogenic Bacteria and Legionella" phenotypically oriented conventional subtyping methods such as serotyping, phage typing or antibiotic susceptibility testing as well as modern molecular DNA-based techniques such as PCR, macrorestriction/PFGE, MLST or MLVA are applied in order to discriminate taxonomically and epidemiologically unrelated bacterial strains or to identify clonal relationships between independent isolates. Currently, whole genome sequencing is established in the unit to adapt and develop methods for subtyping routines and for the prediction of virulence and antibiotic resistance. A detailed characterization of pathogen isolates based on their genome sequences allows the identification of clonal relationships

"Synergy between reference centre work and analysis of pathogen life-style promotes control of infectious diseases."

Prof. Dr. Antje Flieger

ships between independent isolates more precisely. Reliable information about the epidemiological relatedness of pathogen isolates will improve outbreak investigations aiming at the detection and elimination of sources and routes of infections. Moreover, comprehensive genomic characterization of a pathogen isolate will allow improved predictions of virulence and the risk potential for particular clones among the pathogen species investigated. Beyond this main business of the unit "Enteropathogenic Bacteria and Legionella" that is related to



EHEC bacteria can cause serious intestinal infections



epidemiology and surveillance of pathogens for public health purposes there are various additional applied research activities. Investigations into the bacterial persistence and survival in various environments include analysis of cultivation conditions for improved detection of pathogens in clinical microbiology. When experiencing stress, bacteria may enter into a viable but non-culturable stage and thereby bypass detection. Our work therefore focuses on the discovery of molecular key characteristics of enteric pathogens and *L. pneumophila* facilitating persistence in growth arrested- or slow growth states by means of proteomic, transcriptomic and microbiological approaches. Intervening establishment of persistent phenotypes will contribute to improved pathogen control.

Another pathogen, *L. monocytogenes*, is used as a genetically tractable model organism to understand how fundamental life processes such as cell wall biosynthesis, cell division and protein secretion contribute to invasion and intracellular growth of bacteria in eukaryotic cells. A particular emphasis is laid on the study of such proteins that are highly conserved, fold into unique structures and are indispensable for *in vitro* virulence. These proteins may be suitable target candidates for future therapeutic drug development.

Studies of *L. pneumophila* focus on secreted virulence factors, primarily phospholipases. The molecular characterization of these enzymes targets the understanding of virulence-associated processes such as modulation and destruction of lung cells during legionellosis and aims at establishing new therapeutic strategies for inhibition of cell destruction.

www.rki.de/fg11-en

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Unit 12: Measles, Mumps, Rubella, and Viruses affecting Immunocompromised Patients

Highly transmissible viral pathogens such as measles, mumps, rubella, varicella zoster and cytomegalovirus are investigated in unit 12. These viruses predominantly infect children and young adults. Since infection can lead to severe complications and cause large outbreaks, it is fortunate that safe and effective vaccines are available against measles, mumps, rubella and chickenpox. The main focus of our work is (I) to detect these viruses and determine their prevalence within the German population, and (II) to analyze their transmission, molecular evolution, basis of pathogenicity and interaction with the immune system. Besides collaborating with the German Public Health System, we also conduct research and teach university students.

Measles and rubella may be finally eradicated by global vaccination programmes. To monitor the elimination process in Germany, laboratory surveillance is performed in the National Reference Centre Measles, Mumps, Rubella in close cooperation with the WHO. We advise colleagues from laboratories, hospitals and public health organizations on how to diagnose cases in outbreak settings and are involved in the development of ring trials as an external quality assessment. Molecular surveillance includes genotyping of measles viruses from outbreaks to uncover the origin of the virus, track its spread and determine the length of virus transmission chains (Figure). We provide evidence that the vaccines still protect against contemporary viruses by monitoring antigenic variation and suspected vaccination failures. We participate in seroprevalence studies conducted by our colleagues in Department 2 assessing the German population's immunity against measles, mumps, rubella, chickenpox and cytomegalovirus. These results contribute to Germany's progress towards the elimination of measles and rubella scheduled for 2020. Since rubella virus infection during early pregnancy can result in heart, eye and ear malformation or even death of the unborn child, we carry out basic research that analyzes gene expression

in rubella virus-infected cells. A second project we address is the interaction of the mumps virus with the innate immune system. Varicella vaccination of children in Germany was first recommended in 2004. In a joint effort with unit 33, sentinel surveillance of varicella involving approximately 1,000 German physicians was established in 2005. Molecular methods were developed to differentiate between wild-type varicella virus and vaccine-type varicella. Based on clinical reports and laboratory investigations, the impact of vaccination frequency is continuously analyzed. In addition, molecular characterization of varicella vaccines and varicella-zoster virus from vaccine-related skin lesions is carried out. This surveillance study has revealed that after a decade of varicella vaccination, varicella incidence has declined, and varicella disease in vaccinated individuals is a rare event.

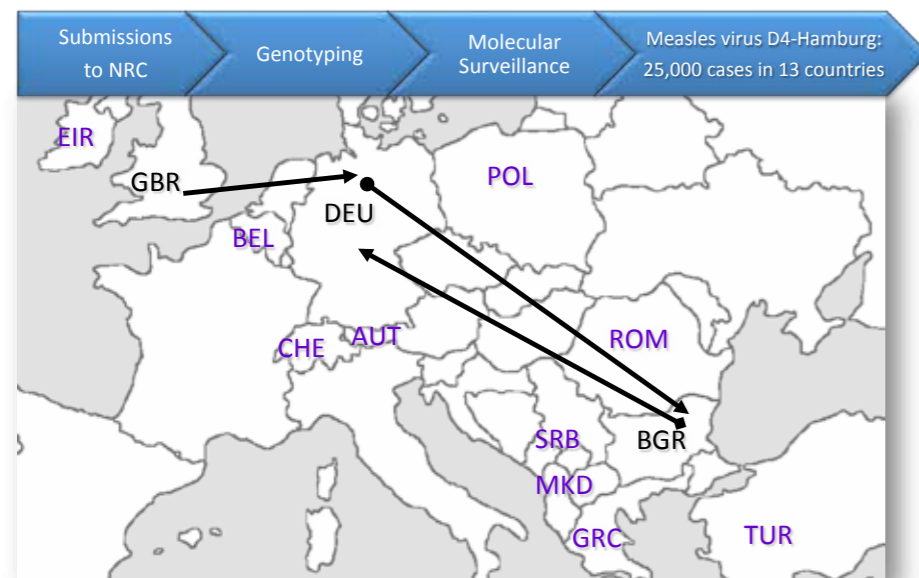
To search for new animal viruses that could become a health hazard for humans, we study the evolution of adeno-, herpes-, and polyomaviruses in collaboration with RKI unit P3. We focus on viruses detected in apes, rodents, domestic

“Measles virus is highly infectious, but vaccination prevents the infection safely and efficiently.”

Prof. Dr. Annette Mankertz

animals and pet animals, i.e. species with a similar genetic background to humans or with an environmental proximity, in order to assess their potential transmission to humans. A plethora of viruses have been identified and the evaluation of their potential impact on human health using molecular methods is an ongoing task.

Furthermore, we are interested in characterizing adeno- and cytomegalovirus infections frequently affecting immunosuppressed children after hematopoietic stem cell transplantation. Cytomegalovirus also can result in major



Molecular surveillance enables us to follow the transmission of measles virus closely. Here a variant was tracked from Germany to Bulgaria and finally throughout Europe



birth defects including hearing loss. We are interested in mechanisms used by these viruses to circumvent the host immune response, involving molecules that were captured from the host itself during evolution. These viral analogues target different types of immune cells and silence them. By characterizing these interactions, we gain a better understanding of viral pathogenesis and how the immune system fights these infections. In addition, we want to identify strategies that lead to better virus control in case of viremia in immunosuppressed individuals. Since the strong side effects of antiviral therapy frequently lead to treatment discontinuation, other treatment options like adoptive transfer of virus-specific T lymphocytes are needed.

The unit for Animal Experiments is also affiliated with unit 12 and serves RKI scientists conducting animal experiments that study infection and immunisation. These are mainly trials with a variety of different viruses, bacteria, and parasites, and are carried out by qualified animal keepers and handlers. Mice, rats, hamsters, guinea pigs and rabbits are kept under conditions that meet the requirements of animal protection law and the relevant regulations. The unit's animal keepers are trained every year. www.rki.de/fg12-en

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UNIT FOR ANIMAL EXPERIMENTS ~ APPRENTICE ~ Juliette Schuster

Unit 13: Nosocomial Pathogens and Antibiotic Resistances

Unit 13 addresses nosocomial bacterial pathogens with a high clinical and public health impact. Microbial characteristics important for diagnostics, infectivity, epidemicity as well as for infection prevention and control are determined. The focus is on key hospital pathogens such as Methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant enterococci (VRE) and ESBL- and carbapenemase-producing Enterobacteriaceae (CPE). The group hosts the National Reference Centre (NRC) for Staphylococci since its introduction in 1995; in 2012 the NRC was expanded by the enterococci.

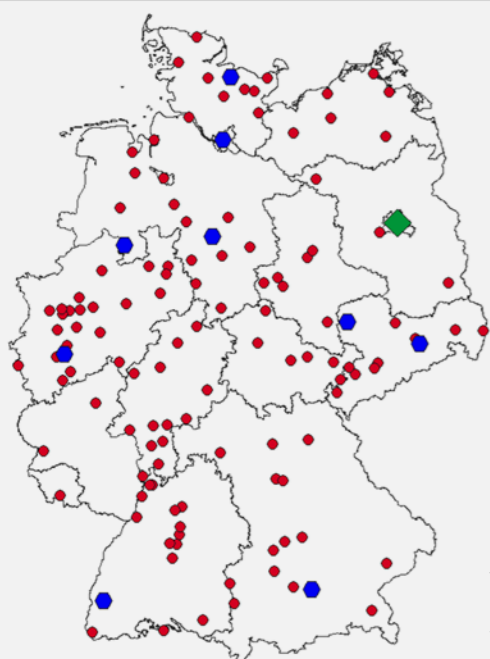
Molecular typing and analysis of the population structure of the above-mentioned nosocomial pathogens as well as detection and molecular analysis of virulence and resistance genes are in the centre of the work in unit 13 and the NRC for Staphylococci and Enterococci. Furthermore, our work comprises validation and comparison of molecular methods to improve diagnostics and typing of bacterial pathogens. Key aspects cover the following topics: (a) Determining the occurrence and spread of *Staphylococcus* spp., *Enterococcus* spp. and Enterobacteriaceae strains with specific clinical and epidemiological importance in terms of pathogenicity, epidemic strengths and antibiotic resistances; (b) molecular analysis and typing of nosocomial *Staphylococcus*, *Enterococcus* and enterobacterial isolates (ESBL-, AmpC- and/or Carbapenemase-producing isolates); (c) analysing ways of emergence and spread of genetic determinants of antibiotic resistance and pathogenicity hereby particularly focusing on plasmid biology and horizontal gene transfer via ICE (integrative and conjugative elements) such as pathogenicity and genomic islands; (d) planning and executing prospective studies (with external partners) to study pathogen reservoirs and spread of pathogens with specific characteristics.

As an inherent and important part of our work we support public health officials, diagnostic laboratories and hospital hygiene specialists with state-of-the-art molecular analysis and strain characterizations in order to elucidate possible outbreak scenarios. In this regard, we regularly cooperate with colleagues from the Department of Infectious Disease Epidemiology, unit 37.

“Against every antibiotic men introduced to treat bacterial pathogens, they have developed and will develop resistances and we are fascinated by learning how they manage it and how they spread these capabilities.”

PD Dr. Guido Werner

The NRC Staphylococci and Enterococci promotes an intense exchange with European reference laboratories and with European and international agencies (ECDC, WHO). Within Germany, we build our work on the basis of a productive and successful network of diagnostic and reference laboratories sending in strains for further characterisation. We have established strong collaborations with the NRC for Gram-negative Nosocomial Pathogens (Ruhr-University Bochum, Prof. Gatermann) as well as with the NRC for the Surveillance of Nosocomial Pathogens (Charité, Berlin, Prof. Gastmeier); both as part of our regular work and as part of externally funded research projects (see below). Our group hosts the network of reference laboratories on antimicrobial resistance.



Left: Network of collaborating laboratories sending MRSA/staphylococci for analysis to the National Reference Centre

Right: Co-resistances in MRSA from German hospital patients 2008–2015 (data of the NRC)

| Antibiotic | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---------------|------|------|------|------|------|------|----------------|----------------|
| Oxacillin | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Ciprofloxacin | 91 | 90 | 86 | 93 | 87 | 82 | 80 | 80 |
| Moxifloxacin | 90 | 87 | 86 | 91 | 86 | 81 | 80 | 80 |
| Erythromycin | 81 | 67 | 65 | 64 | 66 | 59 | 58 | 56 |
| Clindamycin | 73 | 60 | 59 | 60 | 59 | 51 | 50 | 48 |
| Mupirocin | 5,3 | 4,0 | 4,6 | 6,9 | 6,7 | 6,2 | I:5,8 R:1,2 | I:4,1 R:1,2 |
| Gentamicin | 10,5 | 9,5 | 5,3 | 4,4 | 5,7 | 5,0 | 6,6 | 5,4 |
| Tetracycline | 7,3 | 8 | 6 | 4,6 | 7,4 | 7,2 | 8,6 | 10,9 |
| Rifampicin | 0,4 | 1,6 | 0,8 | 1,7 | 1,4 | 0,8 | 1,5 | 0,79 |
| Cotrimoxazole | 10,8 | 5,3 | 0,8 | 0,7 | 0,5 | 0,4 | 0,8 | 0,95 |
| Fusidic acid | 2,0 | 5,2 | 4 | 2,7 | 3,5 | 4,0 | 4,7 | 4,6 |
| Fosfomycin | 1,1 | 0,15 | 0,6 | 0,4 | 0,4 | 0,2 | 0,5 | 0,45 |
| Linezolid | 0,1 | 0,1 | 0,08 | 0 | 0 | 0,1 | 0,03 | 0,11 |
| Tigecycline | 0 | 0 | 0,12 | 0 | 0,13 | 0,04 | 0,23 | 0,23 |
| Daptomycin | 0,58 | 1,25 | 1,6 | 2,1 | 1,0 | 2,7 | 2,9 | 3,2 |
| Vancomycin | 0 | 0 | 0 | 0 | 0,2 | 0,04 | 0,03 | 0,04 |
| Teicoplanin | 0 | 0 | 0 | 0,1 | 0,3 | 0,3 | 0,13 | 0,04 |

● 1-3 laboratories ● 4-10 laboratories ● >10 laboratories



Together with professionals from the institute we support the work of internal and external expert groups, committees and commissions who establish guidelines for infection prevention and control and for treatment of the above mentioned important nosocomial pathogens MRSA, VRE and ESBL bacteria or CPE. Scientists from our division serve as experts in national and international societies and their corresponding boards and study groups (ESCMID, DGHM, Paul Ehrlich Society), as editors and reviewers for many scientific journals, as referees of funding agencies (European Commission, BMBF) and as representatives for European and international working groups, for instance at the European Centre for Disease Prevention and Control (ECDC).

Part of our work is dedicated to national and international research activities. At present, scientists from our unit are involved in research projects (a) addressing various aspects of the influence of targeted infection prevention and intervention studies (in cooperation with the Charité hospital); (b) quantifying the zoonotic potential and One-health aspects of antibiotic resistant bacteria in animals, food and humans (BMBF-funded; in cooperation with groups/laboratories from the BfR, FLI, several German universities); (c) elucidating novel mechanisms of antibiotic resistance and analysing aspects of bacterial fitness, and (d) assessing the benefit and suitability of novel next generation sequencing technologies for molecular surveillance and outbreak analysis (BMBF-, BMG- and EU-funded).

www.rki.de/fg13-en

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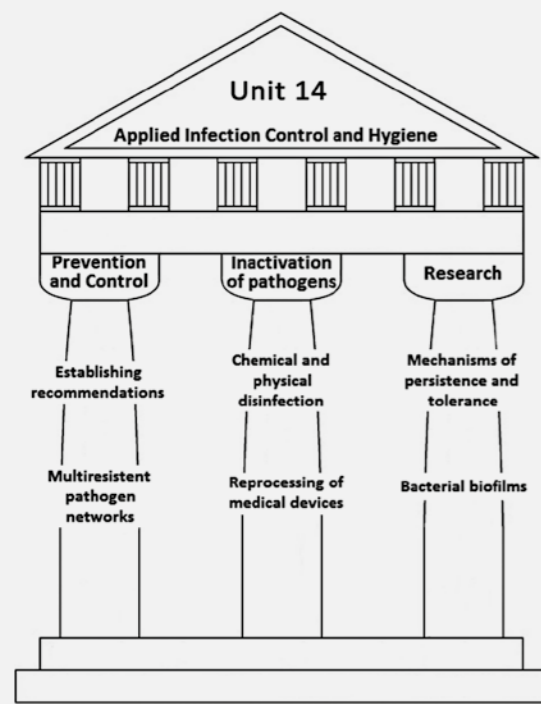
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Unit 14: Hospital Hygiene, Infection Prevention and Control

The unit for Hospital Hygiene, Infection Prevention and Control in Department 1 is most directly engaged in the transfer of knowledge in the field of prevention and control of infectious diseases, the development and validation of methods to inactivate medically important pathogens, and research into the mechanisms by which pathogens tolerate stress. These areas of expertise are supported by three columns:



Prevention and control of healthcare-associated infections

More than 18 million hospitalisations are reported in Germany each year and during treatment, an estimated 380,000 to 430,000 HAI are acquired. Indeed, on a given day, about 5% of all admitted patients suffer from such a complication. One of our major questions is how this number can be reduced.

Supported by external experts in the field, we provide independent evidence-based recommendations for the prevention of HAI and infections by multidrug-resistant organisms (MDRO). The Commission for Hospital Hygiene and Infection Prevention (KRINKO) was therefore established at the Robert Koch Institute in accordance with the Protection against Infection Act. Our unit provides scientific and administrative assistance to this commission, publishes the resulting national best practice recommendations, and investigates and supports their implementation. Further information concerning KRINKO can be found on page 115.

An important instrument for the implementation of infection control measures outside of hospitals is nationwide regional networks to combat the spread of MDRO, which we support through dissemination of information and meetings. This structure is invaluable for gaining deeper insights into the prevalence and risks of HAI in long-term care facilities.

For example, in this context, the prevalence, clinical impact and prevention of colonisation or infection with MDRO and *Clostridium difficile* have been targeted.

As a public health service, we continuously provide advice and answers to questions from healthcare professionals, the media, and governmental institutions concerning the interpretation and implementation of the recommendations. Furthermore, we are involved in many reviews aimed at evaluating and improving the safety of patients and healthcare workers.

Inactivation of Pathogenic Microorganisms

It was Robert Koch himself who, more than 100 years ago, established methods to assess the efficacy of disinfection and sterilisation procedures in the laboratory. His fundamental work continues to influence the assays to this day. We have further developed and extended these methods by assessing the efficacy of chemical and physical approaches to inactivate a broad range of microorganisms, including highly resistant bacterial spores, fungi, viruses, and pathogenic protein aggregates. This evaluation and approval of disinfectants is a legal task of the unit. In addition, strategies to assess the inactivation of relevant pathogens such as *C. difficile* or norovirus, and novel disinfection procedures such as fumigation with hydrogen peroxide, are being evaluated.

Even today, contaminated medical instruments (e.g. endoscopes) can act as a source of infection and a thorough and professional reprocessing of medical devices is therefore crucial. Recommendations for this are provided by our unit in cooperation with the Federal Institute for Drugs and Medical Devices (BfArM).



Research

Biofilms are a major medical problem because the associated pathogens are often refractory to antimicrobial agents and chemical disinfection. Recognised guidelines for testing the efficacy of disinfectants against bacterial biofilms are presently lacking. *In vitro* models help us understand the underlying mechanisms of biofilm formation and the development of tolerance and resistance. For example, a “bead assay for biofilms” was developed in cooperation with the Centre for Biological Threats and Special Pathogens (ZBS) at the Robert Koch Institute that can be used to evaluate the effectiveness of chemical disinfectants in a standardized manner. This low cost, rapid assay combines simple handling with high reproducibility and throughput.



“The art of healing can alleviate much suffering, but better is the art of preventing a disease before it appears.”

Max von Pettenkofer (1818–1901)

A second area of research is stimulated by the similarity of substances used for disinfection with those involved in the inactivation of certain pathogens (e.g. intracellular pathogens) under physiological conditions. Here, we analyse the tolerance to stress of bacteria that have the ability to persist even in activated macrophages, focusing on Gram-negative bacteria and using the vaccine strain *Brucella abortus* S19 as a model for a chronically persistent, difficult-to-treat bacterial pathogen lacking classical virulence factors. Our findings suggest that under antimicrobial selection pressure the bacteria are able to modify sugar and iron metabolism. These modifications result in changes in growth kinetics (small colony variants), tolerance to oxidative stress (H₂O₂), and persistence in activated macrophages.

In summary, unit 14 is a unit that takes a multi-faceted approach to achieving one goal: minimizing the risk of HAI in hospitals and other healthcare facilities. www.rki.de/fg14-en

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Unit 15: Gastroenteritis and Hepatitis Viruses, Enteroviruses

The unit for Viral Gastroenteritis and Hepatitis Viruses, Enteroviruses in the Department is engaged in primarily fecal-orally transmitted human pathogens of viral gastroenteritis (calici- and rotaviruses), hepatitis viruses (particularly HEV, and HAV to HDV) and enteroviruses. The focus is on the analysis of changes in the characteristics (phenotype) and variability (genotype) of the pathogens for monitoring of virus circulation using modern molecular epidemiological methods. A recent report by Balabanova et al. (*PLOS ONE* 2011) listed these viruses as high and highest prioritized pathogens in accordance with their importance for national surveillance and epidemiological research. The unit hosts the National Reference Centre for Poliomyelitis and Enteroviruses (NRC PE) which is also a Regional Reference Laboratory of WHO/Europe for Poliomyelitis, and since 2010 the Office of the National Certification Committee for Polio Eradication in Germany (NCC). Furthermore, the Consultant Laboratory for Noroviruses (CL Norovirus) and the Consultant Laboratory for Rotaviruses (CL Rotavirus) are affiliated in the unit.

The main tasks of the NRC PE and the CLs include the surveillance of circulating viruses and population dynamics, special diagnostics (e.g. fine-typing), quality assurance (e.g. preparation of external quality assessments), maintaining of virus strain collections, as well as analyses of outbreaks

(in cooperation with the Department for Infectious Disease Epidemiology at the RKI). Our laboratories carry out consulting and scientific studies within the framework of their remit.

The special task of the NRC PE is the monitoring of the polio-free status of Germany. Therefore, the enterovirus surveillance based on investigation of patients with aseptic meningitis/encephalitis and acute flaccid paralysis was established. Molecular-epidemiological analysis of selected enterovirus serotypes (e.g. EV-A71), intratypic differentiation of polioviruses and studies on population immunity to poliomyelitis as well as organization of proficiency tests for quality assurance are also performed.

The CL Norovirus is engaged with investigation of recombination of viral RNA and the pathogenesis of noroviruses, while the CL Rotavirus is focused on the circulation of rotavirus A using G/P typing, intragenotypic characterization, and diagnostic differentiation of rotaviruses (e.g. wild type and vaccine strains).

The hepatitis virus group focuses on carrying out special diagnostics including mutational and antiviral resistance analysis. The goal, especially for HEV, is to characterize the risk potential emerging from wild type viruses and virus variants.

The investigations are performed in close cooperation with national and international networks, e.g. NoroNet, Euro-RotaNet, LaNED (network for enterovirus diagnostics), and WHO Polio Laboratory Network. The NRC PE and the CLs for noroviruses and rotaviruses are accredited to DIN EN ISO 15189 and DIN EN ISO/IEC 17025.



In order to gain new insights into the pathogenesis and virus-host interaction the unit is concerned with biomedical research. An example is the use of a murine norovirus (MNV) model system showing that MNV can persist due to the evasion of the host immune system which is controlled by inflammatory signal transduction. The understanding of how the innate

Publications

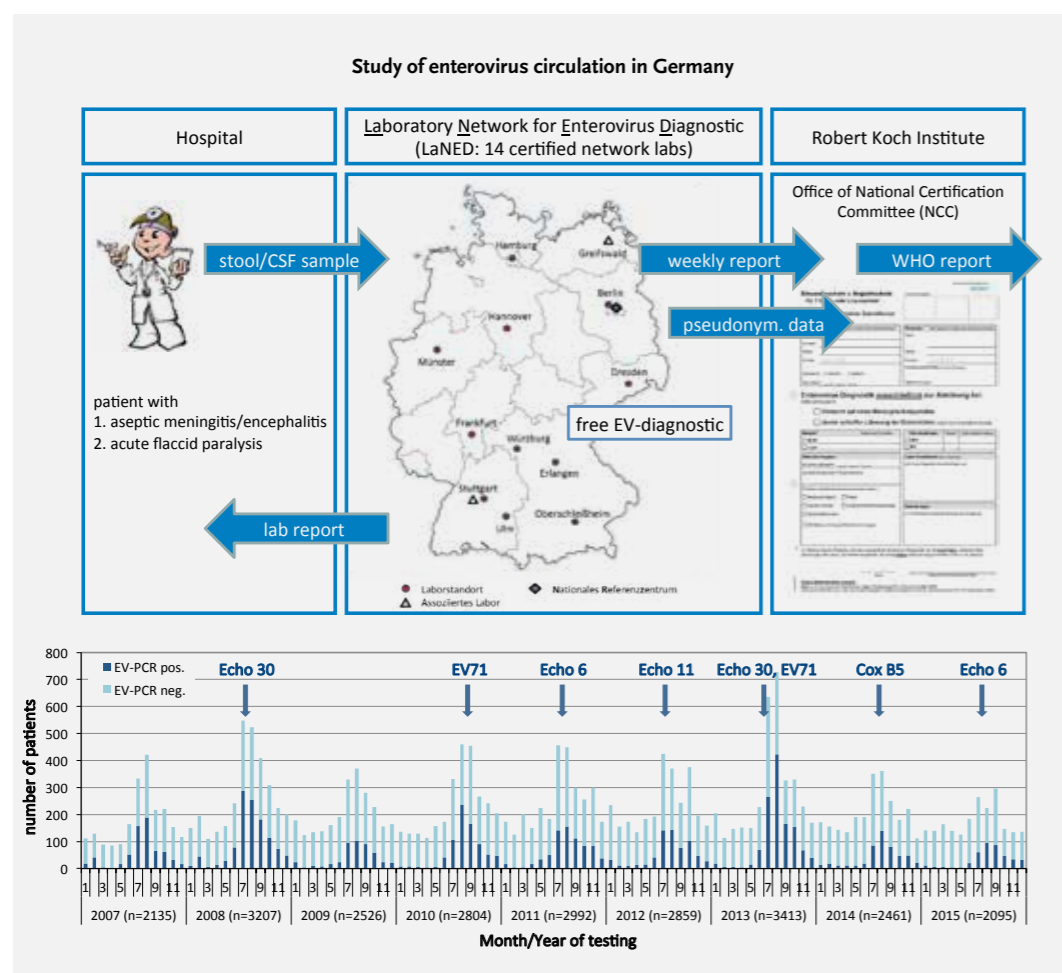
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“To identify the smallest is the challenge of the big picture.”

Prof. Dr. C.-Thomas Bock

immune system efficiently clears norovirus infections will be important to identify pathogenic mechanisms for the control of persistent norovirus infections in humans. Another example of our research is the characterization of the pathogenesis of HEV infection. HEV can cause acute and chronic hepatitis which can lead to hepatic failure. We studied HEV infection in HBV-positive patients to understand the consequences of HEV superinfection. The findings of this study indicate that HEV superinfection can influence progression of HBV-related liver disease by aggravation of the clinical outcome.

The findings of the research projects are translated into the molecular diagnostics in terms of new diagnostic approaches which will help to react on public health burden by, e.g. adjusting diagnostic methods to emerging viral variants (mutants and genotypes). www.rki.de/fg15-en



Top: Scheme of the enterovirus surveillance

Bottom: Seasonal distribution of EV-positive/EV-negative samples and predominant enterovirus serotypes

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Unit 16: Mycotic and Parasitic Agents and Mycobacteria

The unit is concerned with consultancy on, training in and research into infections by eukaryotic pathogens and mycobacteria (mainly non-tuberculous mycobacteria) in the context of Public Health. Our research addresses these aspects by focusing on relevant endemic parasitoses, on systemic mycoses and on infections with mycobacteria, i.e. NTM. The microorganisms studied are widespread in the environment, some considered zoonotic and they can cause difficult to treat infections in vulnerable groups, including children and immunocompromised hosts. Neglect at various levels is a common denominator that characterizes the societal response to the health threat inflicted by these pathogens especially in developed countries. However, with an ageing population and significant changes in globalization and climate we are well advised to remain alert. Our activities aim at: 1.) advancing pathogen identification and diagnostic methods; 2.) contributing to a better molecular understanding of virulence, pathogenicity and drug resistance mechanisms of these pathogens; 3.) exploiting the knowledge gained to expand the tool box of molecular epidemiology; and, 4.) improving rational risk assessment and informing policy in said areas (Figure 1).

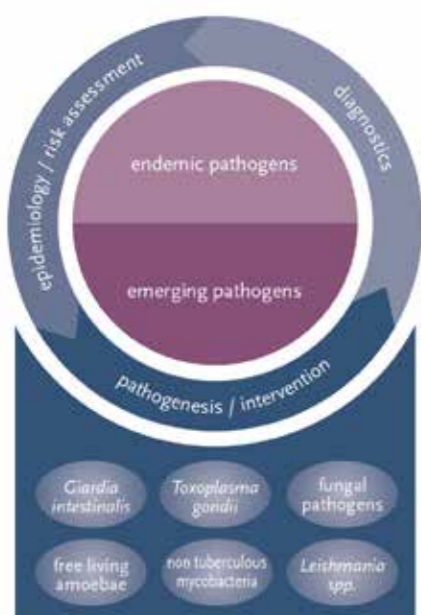


Fig. 1: Main objectives and focal pathogens of unit 16
Main objectives are: i) Improving identification and diagnostic methods; ii) better molecular understanding of virulence, pathogenicity and drug resistance; iii) expand the tool box of molecular epidemiology and improving rational risk analysis. The work relies on specific expert teams concerned with the indicated pathogens

With respect to diagnostics and pathogen identification, often available tests are either not commercially available or only exist in formats that are not suitable e.g. for epidemiological surveys. The unit hosts an accredited laboratory for the identification of fungi pathogenic to humans. By the development and implementation of sequence-, chip-, MS and FISH-based identification methods, and by improvement of serological assays the spectrum of tools available to this laboratory suited both for single case analysis and for molecular epidemiological surveillance is continuously expanded. In many infections due to ubiquitous environmental organisms, such as NTM, distinguishing disease from mere colonization is a challenge.

“We do care about neglected infections!”

Dr. Anton Aebischer

Monitoring specific cell mediated immune responses holds some promise to tell these conditions apart, is the basic concept behind the Quantiferon (Mtb-infection indicating) IFN- γ release assays, and the idea behind our efforts to adapt these tests e.g. for NTM infections.

Nowadays, genome information is often instrumental to forge novel diagnostic strategies to detect rare, non-model pathogens. We adopted this approach to improve diagnostics for rare amoebiasis. These can cause severe encephalitis with no proven therapeutic options and a near 100% fatality rate. We are currently mining genome information for targets of existing drugs and for antigens to develop a specific sero-diagnostic test.

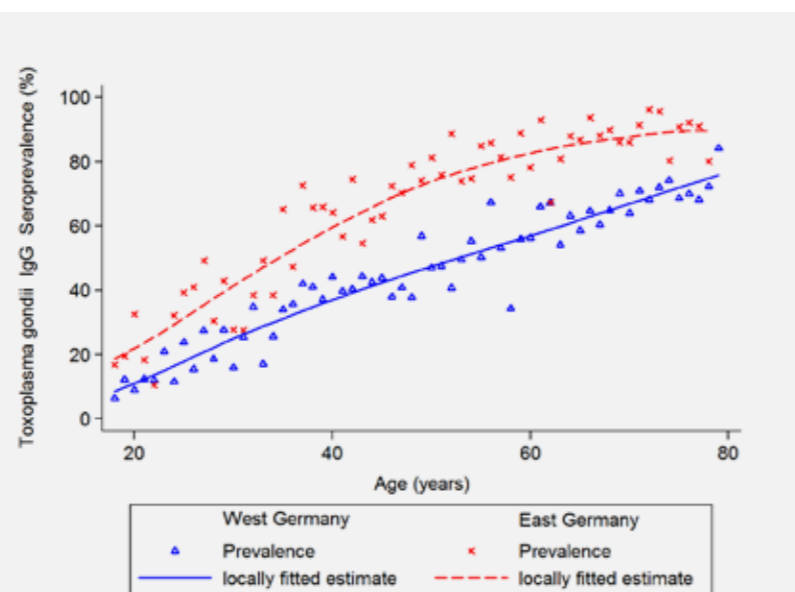


Fig. 2: Prevalence of Toxoplasma gondii based on a representative cross section of the population in Germany



Giardiasis, the most prevalent of the reportable parasitic infections in Germany, is our study case for gastrointestinal infections. Genotyping algorithms are continuously improved to serve both molecular surveillance and tracking of etiologic agents during outbreak situations.

With respect to virulence, pathogenicity and drug resistance, a key objective is understanding these aspects at the molecular level. To this end, we initiated biobanking projects with the goal to probe parasite, fungal or mycobacterial pathogen populations genomically and functionally. *G. duodenalis*, for instance, the protozoan parasite causing the abovementioned giardiasis constitutes a formidable example in that context. Treatment-resistant infections are relatively common but underlying mechanisms of drug resistance are unknown. The population structure is highly complex and, to date, only a minute fraction of this genetic diversity has been characterized functionally, e.g. in drug-sensitivity testing. The biobank significantly expands the possibilities of functional pathogen characterization for the clinically relevant discrimination of these agents. For *Cryptococcus* spp. and NTM we pursue similar goals. In cooperation with clinical institutions, we focus on fungal and NTM isolates of patients with cystic fibrosis. These patients are a relevant proxy for the large group of vulnerable patients suffering from chronic obstructive pulmonary diseases (COPD). The unit is also investing into numerous readout systems to evaluate pathogenicity. This activity ranges from establishing human intestinal organoids for analysis of human-specific gastrointestinal pathogens to wax moths as a cost-efficient fast in vivo model to compare virulence of e.g. Cryptococci or, generally, microbial pathogens with a broad host range.

In the context of epidemiology and risk assessment and in cooperation with the institute's departments of epidemiology and of health reporting, we investigate prevalence of parasitic infections in a nationally representative population cohort. For the prevalence of *Toxoplasma gondii* infection, arguably the most prevalent endemic parasitic infection, only few countries have collected representative data. Our data establish the baseline for Germany (Figure 2). Analysis of associated risk factors suggests that eating behavior contributes significantly. A finding that will be used to improve respective health literacy.

www.rki.de/fg16-en

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Unit 17: Influenza Viruses and Other Respiratory Viruses

Two of Robert Koch's most talented colleagues, Richard Pfeiffer and Shibasaburo Kitasato, worked frantically in 1891 at the "Institut für Infektionskrankheiten" on the isolation of a pathogen causing worldwide waves of influenza since the winter of 1889/90. Thus, influenza and its causative agents have been in the focus of RKI's research from the beginning. Today, influenza viruses are intensively investigated and monitored by unit 17 of RKI. These infectious disease agents are microscopic quick-change artists due to their error-prone polymerase, the segmented nature of their genome and the separation into three virus types and multiple influenza A subtypes, by which they can trick the human immune system and cause periodic epidemics and occasional pandemic outbreaks.

WHO coordinates a worldwide surveillance network in more than hundred states that closely monitors circulating influenza viruses and allows adjustment and formulation of effective responses. The unit contributes to this global network as it houses the German National Influenza Centre (NIC) (Head: Dr. Brunhilde Schweiger) and is also an active partner of the European Influenza Surveillance Network. A major task is to conduct virological surveillance at the national level by cooperating with sentinel physicians all over Germany and investigating respiratory tract samples from patients with influenza-like illness in the context of the nationwide sentinel surveillance system for influenza (Arbeitsgemeinschaft Influenza, AGI). Molecular methods are used for detection, typing and subtyping of influenza viruses along with virus isolation. Comprehensive characterizations of circulating strains include molecular and phylogenetic features, monitoring of antiviral resistance patterns, as well as analyses of the antigenic

profile to monitor the similarity of these viruses with current vaccine strains and the occurrence of new variants. Isolated viruses as well as characterization data are timely shared with the Influenza WHO Collaborating Centre in London. Surveillance findings are reported continuously during the influenza season at global, European and national level.

In an effort to determine the roles of other pathogens in causing influenza-like illness we also investigate other circulating respiratory tract viruses including respiratory syncytial viruses (RSV), adenoviruses, human metapneumoviruses (HMPV), rhinoviruses, coronaviruses and parainfluenza viruses (PIV). In fact, the status of a consultant laboratory dedicated to respiratory syncytial virus, human metapneumovirus and parainfluenza virus, headed by Dr. Janine Reiche, has been assigned to the unit in 2015. Further research fields include the development of laboratory diagnostics, genetic variability and evolution of influenza viruses, inter- and intrasubtype reassortment, antiviral resistance as well as serological studies to investigate the efficacy of influenza vaccination in specific risk groups.

Tracking of influenza A viruses is complicated by their circulation in a number of feral and domestic animal species such as ducks, geese and pigs. Animal virus strains usually do not transmit easily to humans. However, there is an increasing

"Expect the unexpected working with influenza viruses."

PD Dr. Thorsten Wolff

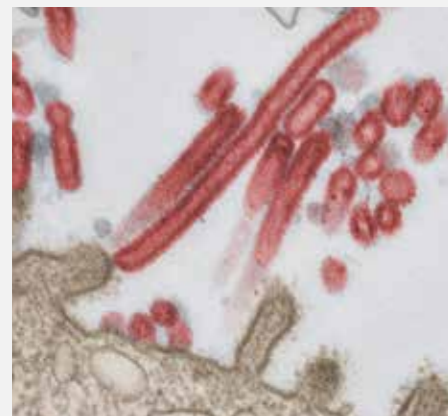
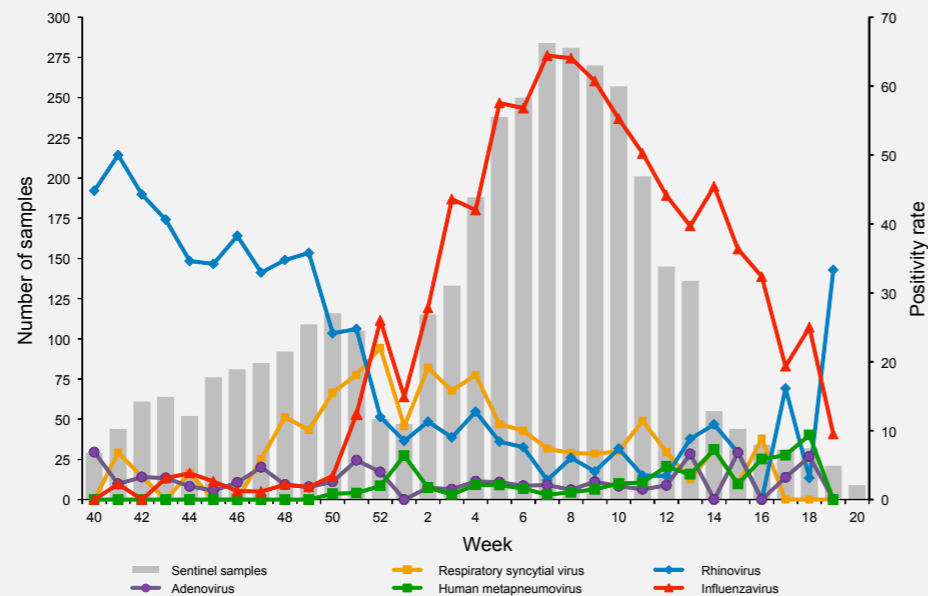


Figure 1 (top): Transmission electron microscopy shows budding of human influenza A virus (H₃N₂) from a type II pneumocyte in human alveolar lung tissue infected *ex vivo*. Released virus particles were colored in red distinguishing them from microvilli on the surface of the infected cell

Figure 2 (right): Detection and positivity rate of indicated respiratory viruses within the AGI sentinel in season 2014/2015



number of documented zoonotic trans-species infections, some of which are accompanied by an unusually high case-fatality of patients such as seen for H7N9 or H5N1 subtype viruses. Although these transmissions have not resulted in sustained spread among humans and did not occur in Europe, it is part of the NIC routine to develop and have dedicated diagnostic tests for the detection of zoonotic influenza viruses in patients ready to use.

Apart from the activities immediately contributing to protect people from circulating influenza viruses the unit pursues additional research to gain a better understanding of the factors determining viral pathogenicity and virulence on a molecular level. Classical virological methods are combined with reverse genetic-, biochemical-, cell biological and immunological tools within state-of-the-art BSL-2 and BSL-3 laboratory environments. Results of this work are not only important for the assessment of novel virus strains, but will hopefully also enable the derivation of novel principles for the control of these notorious pathogens.

Respiratory tract viruses remain a formidable challenge for public health as some of them lay considerable socio-economic burden on societies by causing regular epidemics affecting millions each year, whereas others emerge from animal reservoirs and induce severe disease with high case fatality. Unit 17 aims to provide physicians, epidemiologists, the vaccine sector and the general public not only with topical information on the circulation of respiratory viruses and the properties of epidemic strains, but also to help with an assessment of the pathobiology of novel virus strains.

www.rki.de/fg17-en

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Unit 18: HIV and Other Retroviruses

Unit 18 for HIV and Other Retroviruses in the Department of Infectious Diseases is mainly engaged in HIV surveillance projects and carries out research into several aspects of retroviral infections.

HIV is the most prominent member of the family of retroviruses. These viruses are able to integrate their genome into the DNA of the infected cell and establish a lifelong chronic infection. The high incidence rate of HIV, the lack of a vaccine and the need for infected people to always maintain antiretroviral therapy to avoid progression to AIDS are among the reasons why this pathogen remains of utmost relevance to public health.

To allow the HIV-variants currently circulating in Germany to be analysed, we recently established a monitoring scheme based on new HIV diagnoses that are reported to the Robert Koch Institute as a statutory duty for anonymous notification. Approximately 60% of the notifications are accompanied with dried serum spot (DSS) samples that are examined serologically to discriminate between recent and long-standing infections. Using these and other results, the Department of Infectious Disease Epidemiology is then able to estimate the incidence rates for HIV infection. The DSS also

provide a source of viral RNA that is used to determine the HIV subtype and identify transmitted drug resistance (TDR). TDR is of particular clinical relevance as it is associated with increasing rates of antiretroviral therapy failure. Knowledge of the different HIV subtypes currently circulating within a country and the dynamics of their spread is also of great

“It is time to change the course of HIV epidemic in Germany and effectively reduce the number of new cases and transmitted resistances. A reinforced monitoring and molecular analysis of circulating HIV genotypes supports these efforts.”

Prof. Dr. Norbert Bannert

epidemiological and clinical relevance, as these influence the safety and accuracy of HIV diagnostics and disease progression, and is also important for various aspects of HIV prevention and vaccine development. In addition, the sequence data collected is used to identify and explore HIV transmission networks, helping to better develop suitable prevention strategies.

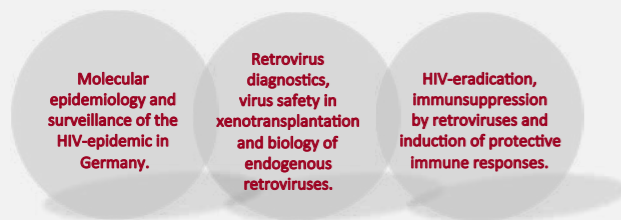
Various clinical implications of HIV infection are investigated in the HIV-1 seroconverter study. These include the impact of TDR and its persistence on treatment success and the roles played by co-infections and host genetic factors on disease progression and virus evolution. This longitudinal study was initiated in 1997 in collaboration with unit 34 and currently involves a cohort of about 3,400 patients with known dates of infection. Results and HIV sequences from this study form the basis for collaborations and cooperations in national and international networks including HIV-GRADE, HIV-Resistenzverbund, DZIF, HIV-ERA and the EU-funded EUROCOORD-CASCADE and SPREAD/ESAR.

Within unit 18, HIV diagnostics are conducted in a DIN EN ISO 15189 and DIN ISO/IEC 17025 accredited laboratory using modern molecular technologies such as next generation sequencing. Tests for HTLV and for a panel of non-human retroviruses are also routinely performed within the framework of cross-sectional epidemiological studies and confirmatory diagnostics that are regularly requested by external laboratories. In addition, our unit manages a BSL3 facility, contributes to the EUPHEM training program of the ECDC by providing a Scientific Coordinator and is involved in WHO-supported projects and collaborations aimed at capacity building for HIV resistance testing.

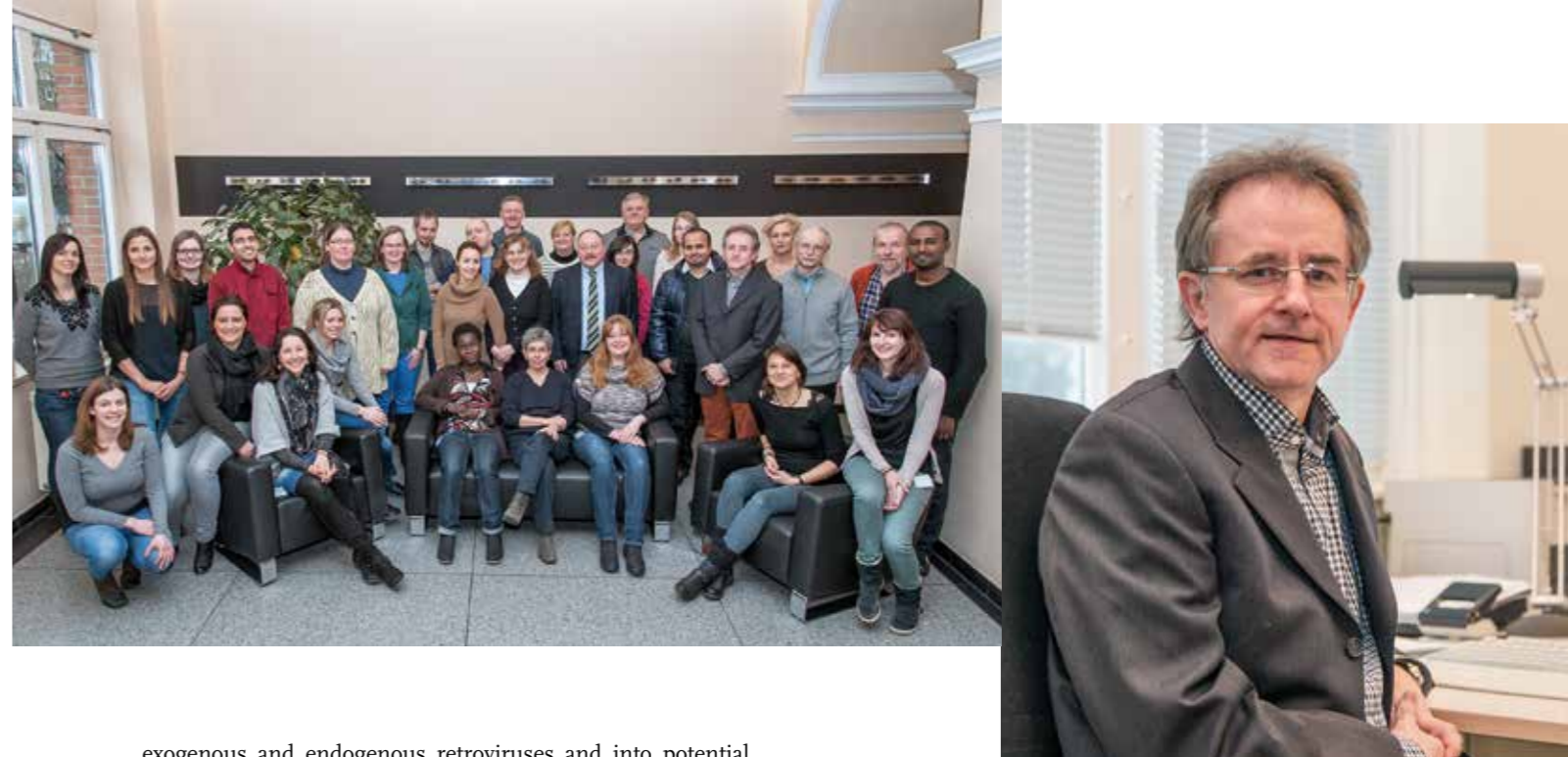
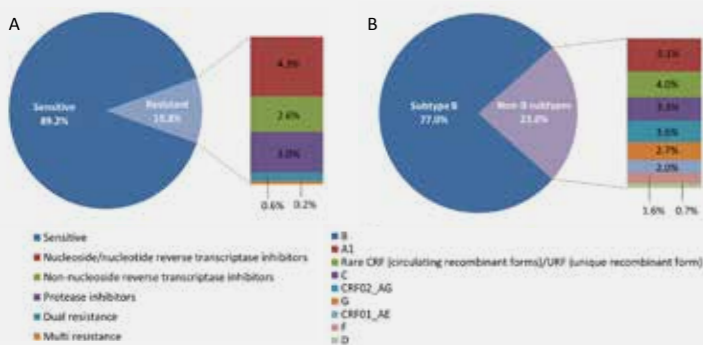
The unit is also engaged in several projects designed to optimise the sensitivity and specificity of tests for detecting and quantifying retroviruses. For example, refined diagnostic methods are being applied in a DFG-funded SFB project aimed at safeguarding xenotransplantation and exploring the risks imposed by endogenous retroviruses and other possible pathogens from the donor species.

Novel insights into retrovirus/host interactions are being gained within the framework of additional biomedical research projects. These projects include investigations at the molecular level into the cell tropism and cell entry of human

Major fields of surveillance and research in unit 18



Molecular surveillance of recently acquired HIV-1 infections 2013–2014.
(A) Transmitted drug resistance. (B) HIV-1 subtype distribution



exogenous and endogenous retroviruses and into potential options for therapeutic intervention. We are also studying host cell mechanisms that prevent the excessive expression and proliferation of endogenous retroviruses. In addition, the unit is investigating strategies for the induction of effective antiretroviral immune responses and mechanisms of immunosuppression associated with the transmembrane protein of retroviruses. More recently, projects were initiated to explore options for HIV eradication in patients undergoing effective long term therapy. In this context, subpopulations of memory CD4 T cells are being examined and highly sensitive diagnostic methods for the quantification of proviruses in these cells developed.

We are confident that the molecular surveillance and research in unit 18 will continue to make valuable contributions to our understanding of retroviruses and to national efforts aimed at changing the course of HIV epidemic in Germany.

www.rki.de/jg18-en

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TECHNICIANS – Katrin Arndt – Ewelina Caspers – Martina Keller – Sabrina Neumann – Nicole Norley – Hanno von Spreckelsen – Nadine Weser

Department 2: Epidemiology and Health Monitoring

The main topics handled in this department are the significant health challenges and burdens placed on the population in general and the healthcare system in particular. These challenges are characterised by rapidly changing working and living conditions, demographic change, the increase in life expectancy and associated ageing of the population, and the shift in the spectrum of diseases towards chronic-degenerative and mental illnesses.

The focus is placed on diseases relevant to public health and their risk factors, in accordance with the “WHO global action plan for the prevention and control of noncommunicable diseases 2013 – 2020”:

- ▶ Physical health
- ▶ Mental health
- ▶ Health-related behaviour
- ▶ Social determinants and health

The department carries out nationwide health monitoring for this purpose. The data collected in the regularly recurring representative health surveys are included in the health reporting of the federal government. The department bears responsibility for the content of these data. At the same time, the data form the basis of analytical, epidemiological evaluations by scientists within the department. The results of these evaluations are used for policy advice, developing preventative

approaches, providing information to the public, and teaching and research. The overriding objective is to improve the health of the population.

The department works in a close network of cooperative partnerships with national and international scientific institutions (see below) and is a member of diverse research associations. It is involved in the German Centre for Cardiovascular Disease and the German Centre for Diabetes Research. All units work according to the life course approach and take the specifics of the various stages of life into account. In its activities, the department is well-connected on a global level, and particularly within Europe. Within the remit of the European Commission, the department is involved, for example, in the implementation of European health indicators (ECHIM, DG Santé) and in conducting the European Health Interview Survey (EHIS). At the OECD, the department is represented in working groups in the areas of healthcare quality, patient orientation, cancer treatment and mental health.

“Make Public Health work.”

Dr. Bärbel-Maria Kurth

Department 2: working group “German National Cohort”



Department 2: administrative staff

Child and youth health

In view of the particular significance of the childhood and adolescence stage, a Child and Youth Health steering committee is part of the department’s management. In this committee, proposals are developed for the strategic objectives of the department in the area of children’s and adolescents’ health and support is provided in the implementation of these proposals. The steering committee supports the extension of networks with national and international stakeholders in this field and serves as a first point of contact for the subject of children’s and adolescents’ health within the department. The steering committee is made up of one scientist from each unit as a representative of the respective unit.

External quality assurance project

Due to its experience in conducting epidemiological prospective studies, the department was awarded the contract for an external quality assurance project within the prospective “German National Cohort” study. In this context, a working group refines the submitted quality assurance concept continuously. Amongst others they conduct routinely on-site monitoring in all 18 study centres, develop quantitative and qualitative methods such as statistical procedures for data quality or analyses of study documents.

The enhancements of the quality assurance concept expands into the needs of own data gathering activities in the Department of Epidemiology and Health Monitoring. The overall aim is to create a comprehensive quality management concept as a prerequisite for consistently high study and data quality in epidemiological studies.

The staff of the central department administration

The staff of the central department administration conduct day-to-day administrative and secretarial tasks, such as electronic filing and processing, handling correspondence, planning business trips, ordering, coordinating appointments, telephoning and providing assistance, for example in the preparation of presentation slides. In addition to these general tasks, the central department administration supports the department’s scientists, (for example in the preparation of publications by conducting literature searches, preparing figures, formatting text and reviewing) and helps plan, organize and execute national and international meetings, conferences and workshops.

www.rki.de/abt2-en

HEAD OF DEPARTMENT ~ Dr. Bärbel-Maria Kurth

ADMINISTRATIVE STAFF ~ Katharina Behrendt ~ Edelgard Bittner ~ Ursula Fischer ~ Susanne Klettke ~ Diana Kühnel ~ Sabrina Winselmann

HEADS OF UNITS ~ Dr. Klaus Kraywinkel ~ Dr. Rüdiger Doelle ~ PD Dr. Martin Schlaud ~ Panagiotis Kamtsiuris ~ Dr. Thomas Ziese (Deputy of the Head of Department) ~ Dr. Christa Scheidt-Nave ~ Heike Hölling ~ Dr. Cornelia Lange ~ PD Dr. Thomas Lampert

German Centre for Cancer Registry Data

Cancer is a disease that places a high burden on individuals and society. It is responsible for one out of four deaths in developed countries, where surveys have found that it is the most feared among life-threatening diseases, also called the “emperor of all maladies”. However, cancer has become, in many cases, a treatable or even curable condition. Recent data suggest that more than half of all cancer patients either can be cured or die *with* rather than *from* their cancer. Not only our biological and clinical, but also our epidemiological knowledge about cancer is constantly growing. This has spurred the development of effective primary and secondary cancer prevention measures.

The roots of cancer registration in Germany can be traced to a nationwide physicians’ survey on the occurrence of cancer in the year 1900, where Robert Koch himself was a honorary member of the steering committee. Beginning in the second half of the 20th century, population-based cancer registration was gradually established, as it was in many other developed countries, finally reaching nationwide coverage in 2009. The network of cancer registries in Germany is nowadays not only an important measure of cancer control, but also a fruitful basis for various cancer research projects. The main objectives of cancer registration are:

- ▶ Quantifying the cancer risk in the population, focusing on surveillance of temporal trends and regional variations
- ▶ Studying the effects of screening programmes, such as mammography screening, on population health
- ▶ Evaluating the effects of primary prevention measures, such as HPV vaccination programmes

- ▶ Monitoring progress in cancer treatment using mortality and survival data
- ▶ Identifying the need for future research in cancer epidemiology
- ▶ Supporting scientific research on cancer, e.g. providing baseline data, enabling data alignment with cohort studies or patient recruitment for case-control studies

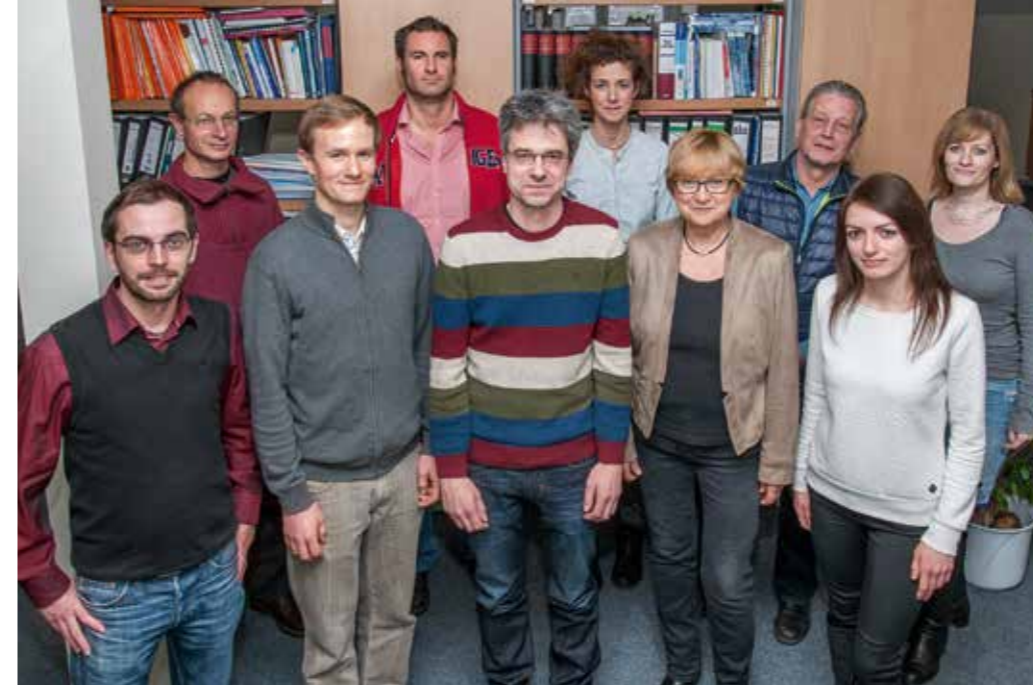
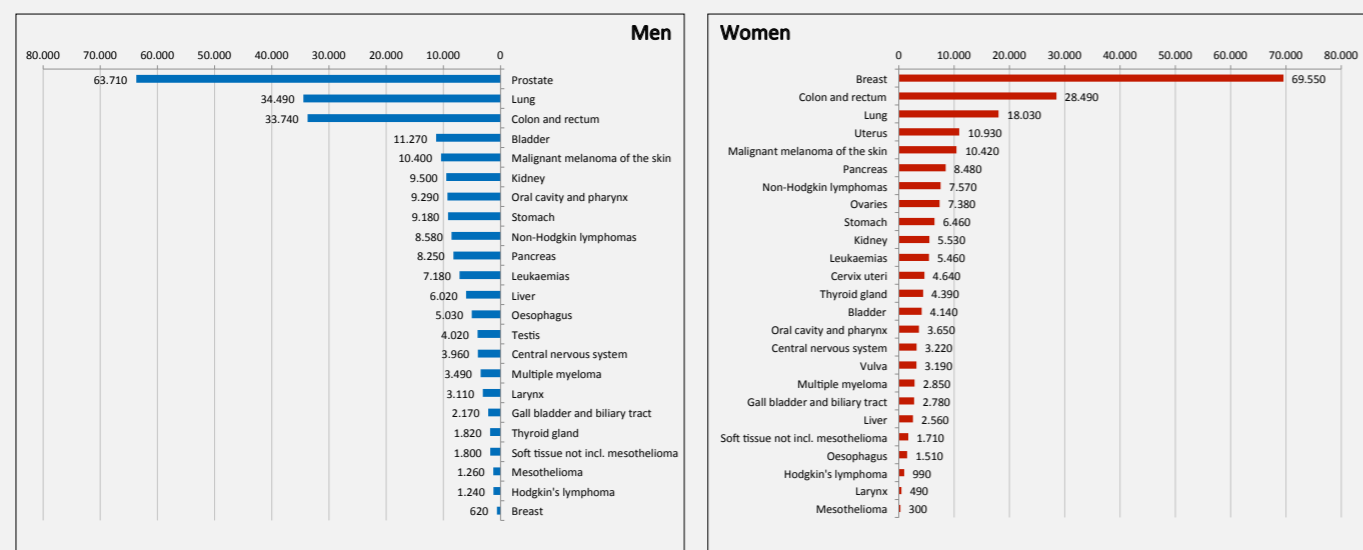
“Our mission is to provide information on cancer risks in the population, for scientists and decision makers as well as for the general public.”

Dr. Klaus Kraywinkel

As cancer registries in Germany are run by the individual federal states, the Centre for Cancer Registry Data acts as a national cancer surveillance unit, responsible for analysis of the pooled data and for monitoring cancer risks and providing cancer statistics at the national level.

The German Centre for Cancer Registry Data (Zentrum für Krebsregisterdaten, ZfKD) collaborates continuously with the state registries to improve and standardize methods of registration, coding, data processing and analysis. It regularly estimates the completeness of case ascertainment for each registry, and performs plausibility checks and additional tests, for example to identify duplicate cases in multiple states.

The most frequent cancer sites in Germany by sex, 2012 (estimates)



The main mission of the ZfKD is to provide national incidence, prevalence, survival, and mortality statistics for malignant diseases. Other indicators, such as the distribution of tumor stages, are also regularly calculated and reported. Based on these data, we highlight increasing trends or large regional or international variations, suggesting the need for more scientific research. Our own scientific efforts focus on cancer sites where public health interventions like screening programs or primary prevention measures might have a substantial impact on incidence, mortality or quality of life.

An important publication is “Cancer in Germany”, which the ZfKD and the Association of Population-based Cancer Registries in Germany release jointly every two years. It not only covers the basic statistics for 27 different cancer sites and childhood cancer, but also includes specific and evidence-based information on risk factors. Every five years, a more comprehensive report is published, including additional aspects like cancer care, early detection and health policy developments.

The ZfKD has an active presence on the internet. On www.krebsdaten.de, we publish short articles on current topics in cancer, give an overview of population-level statistics for common cancer types, and provide information on our analysis methods. Furthermore, we maintain an online database that allows interactive analysis of the latest national cancer statistics.

In addition to the web-based analysis tool, the pooled dataset of the German population-based cancer registries can be made available to external scientists on application. As cancer registration in Germany covers a population of approximately 80 million and contains close to 700,000 incident cases a year (including non-melanoma skin cancer and some pre-malignant conditions), this dataset is especially valuable for analysis of rare cancers and clinically relevant cancer subtypes.

The team of the ZfKD is committed to providing accurate, understandable information on cancer epidemiology. We answer a growing number of enquiries from politicians, health administrations, scientists, healthcare professionals, media, and also from the general public.

The ZfKD is involved in national and international committees for cancer registration, cancer screening and cancer epidemiology and actively contributes to Germany's National Cancer Plan. www.rki.de/zfkd-en

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Unit 21: Epidemiological Data Centre/ Research Data Centre

This unit is made up of two functional sub-units, the Epidemiological Data Centre (EDC) and the Research Data Centre (RDC). In this unit, the epidemiological data acquired through the health monitoring is compiled into databases and prepared for scientific evaluation.

“Excellent data
for high
level research.”

Rüdiger Dölle

The EDC is responsible for merging, preparing and assuring the quality of the survey data.

To this end, parallel to data acquisition, data is continuously checked for possible examiner or equipment effects. In addition, the second recording of a portion of the collected questionnaires serves to check the quality of the acquired data. In the EDC, the survey data is checked for consistency, completeness, uniqueness and plausibility, new variables are generated, and all data preparation steps are documented with notes for the evaluators.

The RDC manages and publishes the checked and adjusted data on the state of health and the health-related behaviour of the population resident in Germany in the form of Public Use Files. In addition, the RDC deals with specific statistical issues. These include primarily the creation of weighting factors for random samples and evaluation instructions for the checked and adjusted survey data.

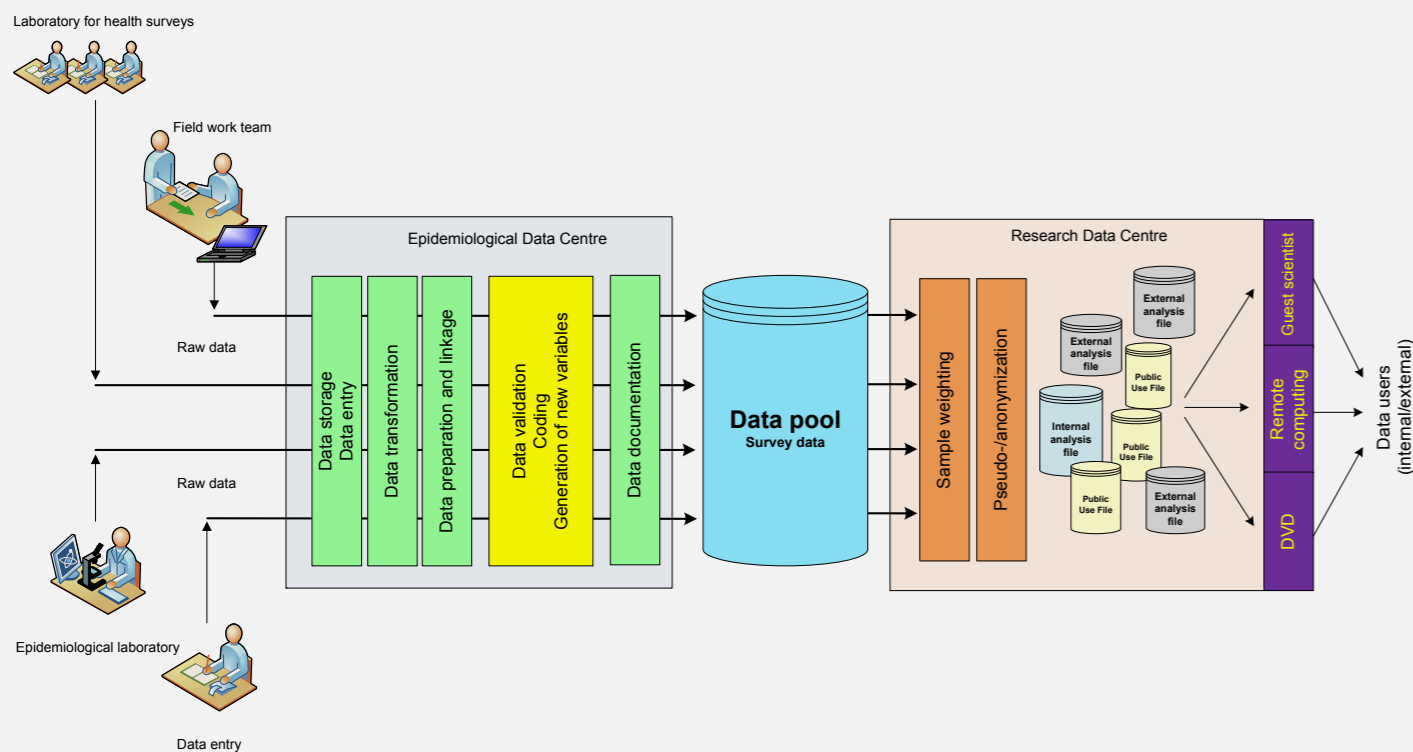
The statistics working group for the entire department is also part of this unit.

www.rki.de/fg21-en

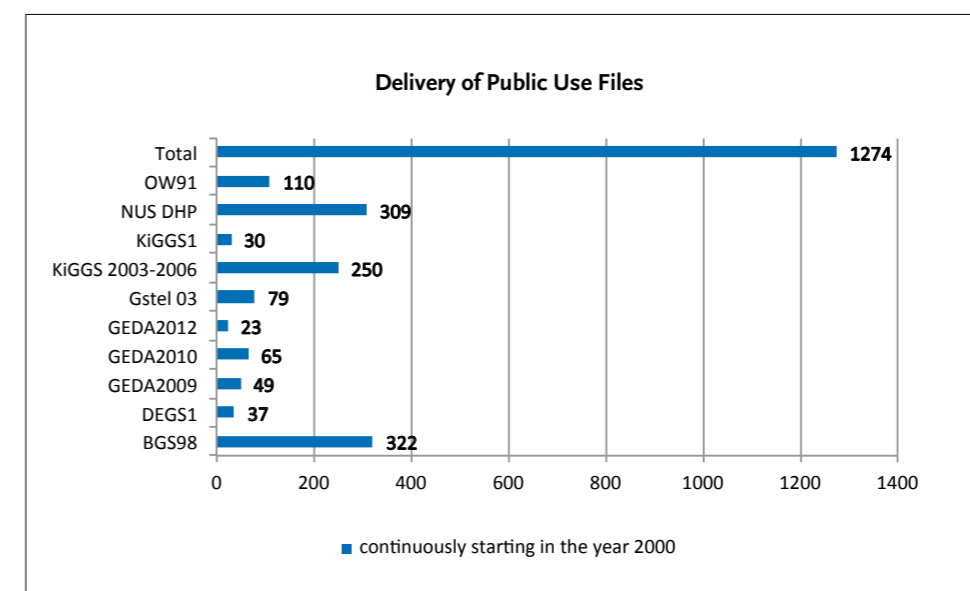


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2. Brettschneider AK, Schaffrath Rosario A, Wiegand S, Kollock M, Ellert U (2015) Development and validation of correction formulas for self-reported height and weight to estimate BMI in adolescents. Results from the KiGGS study. *Obesity Facts* 8, 30–42. doi: 10.1159/000375109.
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5. Stolzenberg H, Dölle R, Kurth BM (2012) National Health Data from the Robert Koch Institute. *Schmollers Jahrbuch*; 132: 123–40.



Main Data Workflow



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DATA MANAGER/IT SUPPORT ~ Andreas Babig ~ Stefan Köbernick

Unit 22: Epidemiological Laboratory

Results from laboratory tests of blood and urine samples can provide valuable information on risk factors or health problems unknown to individuals, and can validate information given by participants in epidemiological studies. This is why data from biospecimens complement data from standardized questionnaires and tests obtained in population-based studies. Combined data can provide a comprehensive picture of health in a population.

The unit “Epidemiological Laboratory” is responsible for the processing of blood and urine samples taken from participants in the nation-wide health examination surveys of the Robert Koch Institute. This task includes contributions to the planning of new studies (what biospecimens should be taken in what way, what biomarkers should be analyzed by what method), the processing and laboratory testing of blood and urine samples, the validation of test results and their epidemiological use. The unit also runs a biorepository where serum and urine samples from participants of all surveys are stored for long-term scientific use.

The unit “Epidemiological Laboratory” is structured into two sub-units: The laboratory sub-unit is responsible for laboratory analyses of biospecimens, e.g. in the fields of clinical chemistry, immunology and infectious disease epidemiology. The laboratory has been accredited since 2012 and continuously takes part in national and international external quality assessment schemes.

The sub-unit for laboratory-based epidemiology is involved both in planning of epidemiological studies, and in statistical analyses and epidemiological interpretation of laboratory test results. The sub-unit also strives to create a scientific network between the unit and other relevant epidemiological studies.

Laboratory

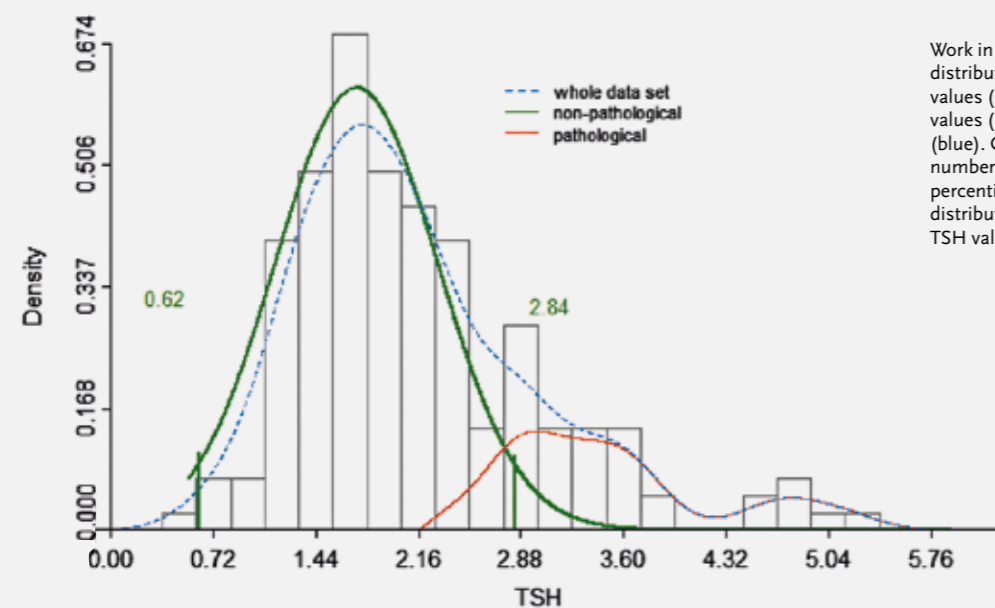
- ▶ Laboratory analyses of biospecimens, i.e. blood and urine samples
- ▶ Participation in international and national standardization programs for laboratory parameters
- ▶ Continuous adaptation to standard requirements (international and national standards and guidelines; e.g., Rili-BÄK – Guidelines of the German Medical Board for Quality Assurance of Quantitative Medical Laboratory Tests)
- ▶ Creation of age-dependent, method-specific reference ranges
- ▶ Identification of current trends in laboratory diagnosis, assessment of value for the Robert Koch Institute, cost-benefit analyses of laboratory tests
- ▶ Operation and further development of the biorepository

“Population-based data from biospecimens for public health.”

PD Dr. Martin Schlaud

Laboratory-based epidemiology

- ▶ Planning and conceptual design of sero-epidemiological parts of population-based studies, including the selection of measured values and determination of their relevance to public health
- ▶ Conducting and coordination of the epidemiological use of laboratory data, in cooperation with the other units
- ▶ Networking of laboratory-assisted epidemiology with national and international working groups www.rki.de/fg22-en



Work in progress: estimated distributions for non-pathological values (green curve), pathological values (red) and whole data (blue). Green lines (and given numbers) indicate 2.5 and 97.5 percentiles of the estimated distribution for non-pathological TSH values (RL) in males



Publications

1. Blümel B, Schweiger B, Dehnert M, Buda S, Reuss A, Czogiel I, Kamtsiuris P, Schlaud M, Poethko-Müller C, Thamm M, Haas W (2015) Age-related prevalence of cross-reactive antibodies against influenza A(H3N2) variant virus, Germany, 2003 to 2010. *Euro Surveill* 20 (32): 1–9.
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5. Wilking H, Fingerle V, Klier C, Thamm M, Stark K (2015) Antibodies against *Borrelia burgdorferi sensu lato* among Adults, Germany, 2008–2011. *Emerging Infectious Diseases* 21 (1): 107–110.



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Unit 23: Health Monitoring Studies and Survey Methods

Unit 23 is responsible for planning, designing and conducting health surveys and cohort studies with questionnaire and examination components. It develops complex tools for study administration and evaluates survey methods and process related data continuously.

Based on the health studies DEGS (German Health Interview and Examination Survey for Adults), GEDA (German Health Update) and KiGGS (German Health Interview and Examination Survey for Children and Adolescents), the unit monitors health status, health behavior, living conditions and healthcare utilization in all age groups on a regular basis. The different projection of the studies enables cross-sectional, trend and longitudinal comparisons. The thus established nationally representative data base is used in public health research and allows the RKI to give evidence based health policy recommendations to promote and protect health and prevent diseases.

Organizationally, unit 23 is subdivided into the subunits “survey metrics/survey methods”, “monitoring office”, “monitoring survey field work”, and the “laboratory for health surveys”. In addition to these key areas, the unit coordinates the setting of content-related priorities with internal and external cooperation partners.

Furthermore, unit 23 is committed in EU projects on establishing and conducting a European health survey system (EHIS: European Health Interview Survey, EHES: European Health Examination Survey).

Survey metrics/Survey methods

- ▶ Study planning, concept creation and design development
- ▶ Random sampling, obtaining participants and incentive concepts
- ▶ Conceptual design and conducting of process checks to identify sources of errors and optimise processes
- ▶ Analyses of response, non-response and representativeness
- ▶ Development and systematic testing of new data collection methods
- ▶ Preparation of publications describing the study and methods
- ▶ Conceptual design and establishment of an RKI health panel




Monitoring office

- ▶ Planning and management of operational business for conducting surveys (e.g. obtaining addresses and telephone numbers, invitation procedures and field inspections, sending of questionnaires and collection of missing documents, supporting participants)
- ▶ Conceptual design and execution of measures to increase the re-participation of cohort-participants
- ▶ Implementation of measures to increase participation of migrants
- ▶ Design and performance of study-related press and public relations
- ▶ Conceptual design of the necessary database applications, documentation and staff training

Monitoring survey field work

- ▶ Conducting examination surveys
- ▶ Selection of survey methods
- ▶ Scientific field management

Overview studies health monitoring

| |  Studie zur Gesundheit von Kindern und Jugendlichen in Deutschland |  Studie zur Gesundheit Erwachsener in Deutschland |  GESUNDHEIT IN DEUTSCHLAND AKTUELL |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Title | German Health Interview and Examination Survey for Children and Adolescents | German Health Interview and Examination Survey for Adults | German Health Update |
| Population | Children, Adolescents and young adults | Adults | Adults |
| Type | Cross- and longitudinal study | Cross- and longitudinal study | Repeated cross-sectional study |
| Method | Questionnaire and examination components | Questionnaire and examination components | Questionnaire |

Overview of studies, period of time, number of participants, age groups

| Study | Period of time | n = | Age |
|--------------------------------------------------------------------------|----------------|--------------|-----------|
| GEDA2014/2015-EHIS | 2014 – 2015 | appr. 25,000 | 15 – 79 + |
| GEDA 2012 | 2012 – 2013 | 19,294 | 18 – 79 + |
| GEDA 2010 | 2009 – 2010 | 22,050 | 18 – 79 + |
| GEDA 2009 | 2008 – 2009 | 21,262 | 18 – 79 + |
| KiGGS Wave 2 | 2014 – 2016 | appr. 23,000 | 0 – 29 |
| KiGGS Wave 1 | 2009 – 2012 | 12,368 | 0 – 24 |
| KiGGS-Baseline | 2003 – 2006 | 17,460 | 0 – 17 |
| DEGS 1 | 2009 – 2011 | 7,987 | 18 – 79 |
| German National Health Interview and Examination Survey 1998 (GNHIES 98) | 1998 – 1999 | 7,124 | 18 – 79 |



“Data for action.”

Panagiotis Kamtsiuris



Publications

1. Kurth BM, Kamtsiuris P, Hölling H, Schlaud M, Döller R, Ellert U et al. (2008) The challenge of comprehensively mapping children's health in a nation-wide health survey: design of the German KiGGS-Study. BMC Public Health 8: 196.
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3. Scheidt-Nave C, Kamtsiuris P, Gößwald A, Hölling H, Lange M, Busch M, et al. (2012) German health interview and examination survey for adults (DEGS)-design, objectives and implementation of the first data collection wave. BMC public health 12: 730.
4. Lange C, Jentsch F, Allen J, Hoebel J, Kratz A, von der Lippe E et al (2015) Data Resource Profile: German Health Update (GEDA) – the health interview survey for adults in Germany. International Journal of Epidemiology 44(2): 442–450.
5. Mindell J, Giampaoli S, Gößwald A, Kamtsiuris P, Mann C, Männistö S et al (2015) Sample selection and recruitment in health examination surveys in Europe – experience from seven national surveys. BMC Medical Research Methodology 15: 78.

- ▶ Organisation of field work, field team training, field logistics
- ▶ Examination and interviewing of participants
- ▶ Systematic quality assurance of data collection process

Laboratory for health surveys (LfG)

- ▶ Conducting interview surveys by means of various survey methods (telephone-, web- and paper-based) and ensuring their technical and logistical reliability
 - ▶ Developing the necessary database applications, as well as programming and operationalisation of data collection tools
 - ▶ Field organisation and staff training
 - ▶ Data recording and quality assurance of the data collection process
 - ▶ Internal RKI platform for online data collection
 - ▶ Support of other units in pandemic/outbreak situations
- www.rki.de/fjg23-en

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Unit 24: Health Reporting

Federal Health Reporting (Gesundheitsberichterstattung des Bundes, GBE) analyses and describes the health of the population in Germany (see Fig 1 and 2), its health-related behaviour, the prevalence of risk factors, the use of healthcare services, as well as costs and resources of the healthcare system.

The many health-related issues are addressed in different publication formats. In regularly published booklets, scientists from the RKI cover current health-related topics in cooperation with external experts from various research institutions. The “GBE kompakt” and “Fact Sheets” published online provide a brief and timely overview of the survey results of RKI health monitoring.

The results obtained are used for policy advice and to provide information for actors in the health system, the scientific community and interested members of the public.

The Federal Health Monitoring follows a pluralistic approach. The issues and needs of the various actors in the German healthcare system are considered and prioritised in the RKI-run GBEMON committee.

All health monitoring results are made available online as well as in parallel in the information system of the federal health monitoring. This information system is managed by the Federal Statistical Office.

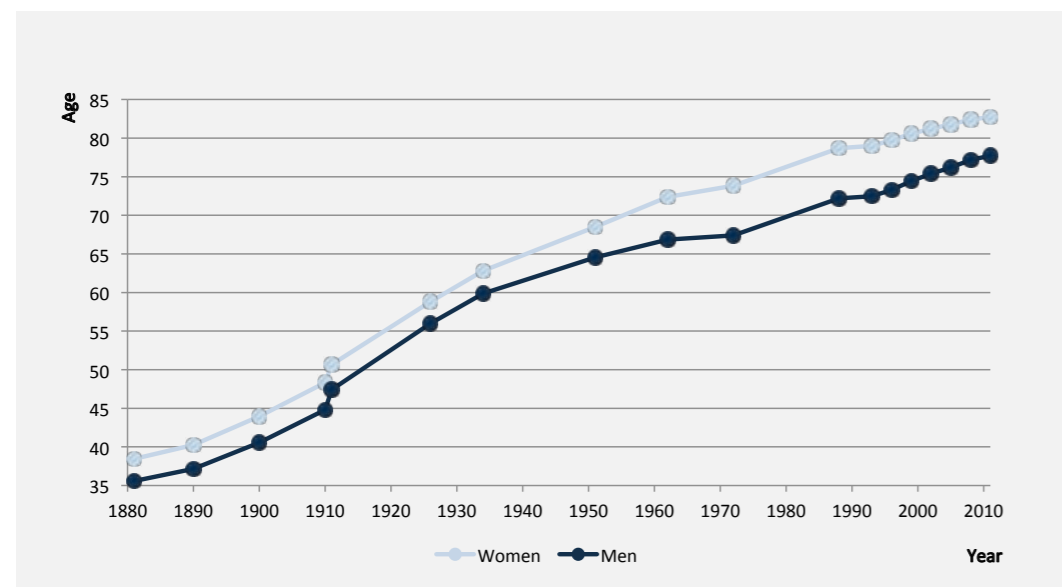


“Better information
for better policy.”

Dr. Thomas Ziese



Around three-quarters of women and men in Germany assess their health condition as good or very good



Life expectancy has continuously increased over the past decades: Girls born today can on average expect 82.7 and boys 77.7 years of age

Tasks

- Concepts, coordination and compiling of health reports (GBE booklets, GBE kompakt, Fact Sheets)
- Scientific support and evaluation of health policy processes such as national health objectives
- Engagement in setting up a European health monitoring system; cooperation in the development of European health indicators
- Providing health-related data sources in cooperation with the Health Data Information and Documentation Centre at the Federal Statistical Office
- Networking of the health monitoring of the federal government with comparable reporting systems at a national and EU level
- Committee for Environmental Medicine, involvement in environment-related panels www.rki.de/fg24-en



Publications

1. Robert Koch-Institut (Hrsg) (2015) Gesundheit in Deutschland. [Health in Germany.] Gesundheitsberichterstattung des Bundes. Gemeinsam getragen von RKI und Destatis. RKI, Berlin.
2. Neuhauser H, Sarganas G (2015) High blood pressure. Publ. Robert Koch Institute, Berlin. GBE kompakt 6 (3). www.rki.de/gbe-kompakt.
3. Robert Koch-Institut (Hrsg) (2013) Gastritis, Magen- und Zwölffingerdarmgeschwüre. [Gastritis and peptic ulcer] Gesundheitsberichterstattung des Bundes. Heft 55. RKI, Berlin.
4. Robert Koch-Institut (Hrsg) (2014) Gesundheitliche Lage der Männer in Deutschland. [Men's health in Germany]. Beiträge zur Gesundheitsberichterstattung des Bundes. RKI, Berlin.

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Unit 25: Physical Health

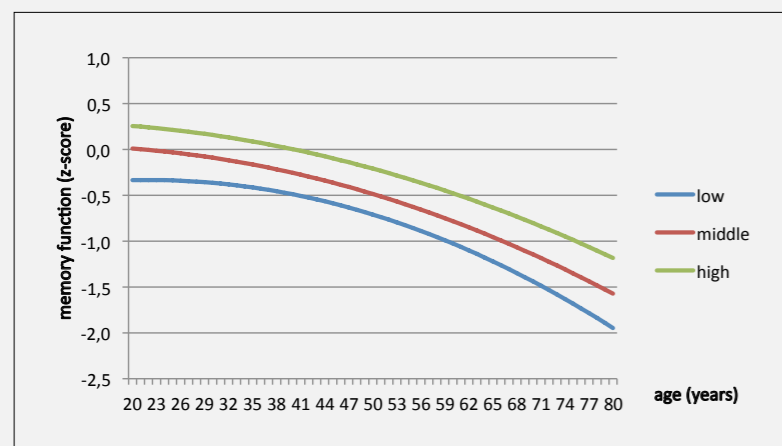
The unit is committed to maintaining and improving physical health and functional resources in the population across all age groups. The unit analyses time trends in the distribution of highly prevalent and disabling non-malignant diseases, preceding risk conditions, physiological risk factors and functional capacities with high relevance for public health. Analyses focus on life-phase specific physical health issues, healthcare needs and opportunities for prevention. Specific health topics include cardiovascular and metabolic diseases (e.g. coronary heart disease, stroke, subclinical cardiovascular disease, high blood pressure, diabetes, prediabetes, dyslipidaemia), chronic respiratory diseases and pulmonary function, and functional aspects of physical health (e.g. chronic pain, balance, grip strength, walking speed and cognitive functioning). Epidemiological and public health analyses conducted in unit 25 contribute to national health reporting, health policy advising and public health research.

Cross-sectional and time-trend analyses are based on data collected as part of the continuous health monitoring system in periodically conducted national health interview and examination surveys for adults (GEDA, DEGS) and for children

“Health is Wealth.”

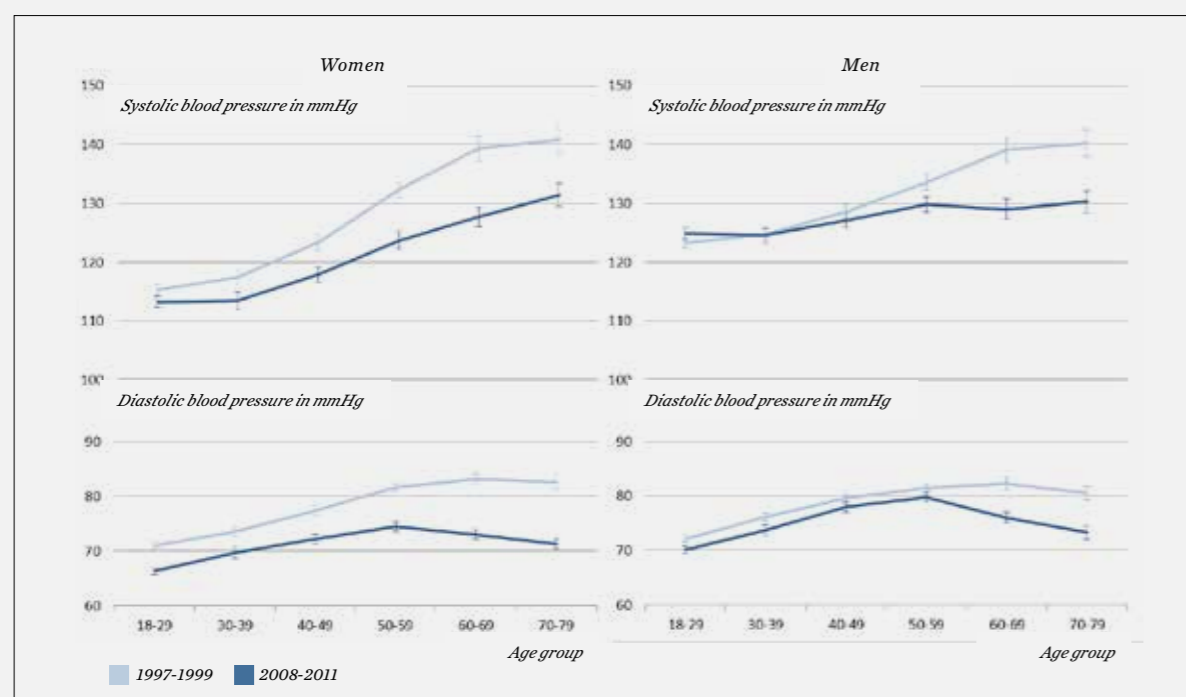
Dr. Christa Scheidt-Nave

and adolescents (KiGGS) in Germany. In addition, data from official health statistics and disease registers are used for indicator-based surveillance activities. Longitudinal analyses are based on the national cohort study for children and adolescents in Germany (KiGGS cohort) and on mortality follow-up of DEGS participants.



Memory function according to age and level of education among adults in Germany. Source: German Health Interview and Examination Survey for Adults 2008–2011 (DEGS1)

Systolic and diastolic blood pressure in Germany 1997–1999 vs. 2008–2011. Source: German National Health Interview and Examination Survey 1997–1999 and German Health Interview and Examination Survey for Adults 2008–2011 (DEGS1)



Objectives

- ▶ To determine age and sex specific prevalence estimates and time trends in the prevalence of morbidity, risk profiles, and functional impairments
- ▶ To determine time trends in the distribution of continuous cardiometabolic risk factors (e.g. blood pressure, serum cholesterol, glycosylated hemoglobin A_{1c}) and functional capacities (e.g. grip strength, cognitive functioning)
- ▶ To provide population-based reference values for continuous risk factors and functional capacities, considering the impact of age, sex, and other confounding factors (e.g. education for cognitive functioning)
- ▶ To analyse health risks with high potential for prevention in specific subgroups of the population defined according to age, sex, life phase (e.g. precursors of cardiovascular disease in childhood or multimorbidity, polypharmacy, falls and frailty in older age)
- ▶ To estimate absolute disease risk based on risk factor prevalence estimates and established prediction algorithms
- ▶ To analyse sex differences in modifiable predictors of mortality
- ▶ To contribute to the development and evaluation of national health goals (currently Healthy Ageing and diabetes mellitus)

Specific tasks

- ▶ Member of the German Centre for Cardiovascular Research (DZHK)
- ▶ Project partner in the German Centre for Diabetes Research (DZD)
- ▶ Scientific lead and network manager of the national diabetes surveillance system

- ▶ Scientific lead of the Robert Koch Institute public health research initiative on Healthy Aging
- ▶ Coordinator of the Robert Koch Institute steering group Health of Children and Adolescents. www.rki.de/jg25-en

Publications

1. Buttery AK, Busch MA, Gaertner B, Scheidt-Nave C, Fuchs J (2015) Prevalence and correlates of frailty among older adults: findings from the German health interview and examination survey. *BMC Geriatr* 15:22. doi: 10.1186/s12877-015-0022-3.
2. Heidemann C, Du Y, Paprott R, Haftenberger M, Rathmann W, Scheidt-Nave C (2015) Temporal changes in the prevalence of diagnosed diabetes, undiagnosed diabetes and prediabetes: findings from the German Health Interview and Examination Surveys in 1997–1999 and 2008–2011. *Diabet Med* doi: 10.1111/dme.13008.
3. Neuhauser HK, Adler C, Rosario AS, Diederichs C, Ellert U (2015) Hypertension prevalence, awareness, treatment and control in Germany 1998 and 2008–11. *J Hum Hypertens* 29: 247–253. doi: 10.1038/jhh.2014.82.
4. Schmitz R, Thamm M, Ellert U, Kalcklösch M, Schlaud M (2014) KiGGS Study Group. Verbreitung häufiger Allergien bei Kindern und Jugendlichen in Deutschland. Ergebnisse der KiGGS-Studie – Erste Folgebefragung (KiGGS Welle 1). *Bundesgesundheitsbl* 57: 771–778.
5. Steppuhn H, Langen U, Mueters S, Dahm S, Knopf H, Keil T, Scheidt-Nave C (2016) Asthma management practices in adults – findings from the German Health Update (GEDA) 2010 and the German National Health Interview and Examination Survey (DEGS1) 2008–2011. *J Asthma* 53: 50–61.

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Unit 26: Mental Health

Unit 26 is responsible for the monitoring of mental health of the general population including children, adolescents, adults of working age and the elderly. The unit primarily focuses on mental disorders with a high burden of disease as well as on health-related quality of life and social participation in the context of psychological distress and mental disorders. Examining the change in prevalence of mental distress and disorders over time (trend analysis) is as important in the unit's work as monitoring changes throughout people's life span (longitudinal analysis). All aspects are considered at the personal, familial, social and societal level.

The main topics cover the following fields:

- ▶ Burden of disease: epidemiology of common mental disorders with high public health relevance, particularly depression, anxiety disorders, sleeping disorders, alcohol abuse and dependency in adults and psychological problems, ADHD and eating disorders in children and adolescents.
- ▶ Psychological determinants: developmental and functional competencies, resilience, self-efficacy and motivation.
- ▶ Quality of life, well-being and life satisfaction in the context of physical and mental health.

- ▶ Contextual factors: parental stress and parental psychopathology, day care for children and adolescents, chronic stress, work stress and burdens and opportunities, late adulthood, societal attitudes towards mental disorders.
- ▶ Psychometrics and the further development of methods for the assessment of mental health problems in large, population-based epidemiological studies.

www.rki.de/jg26-en

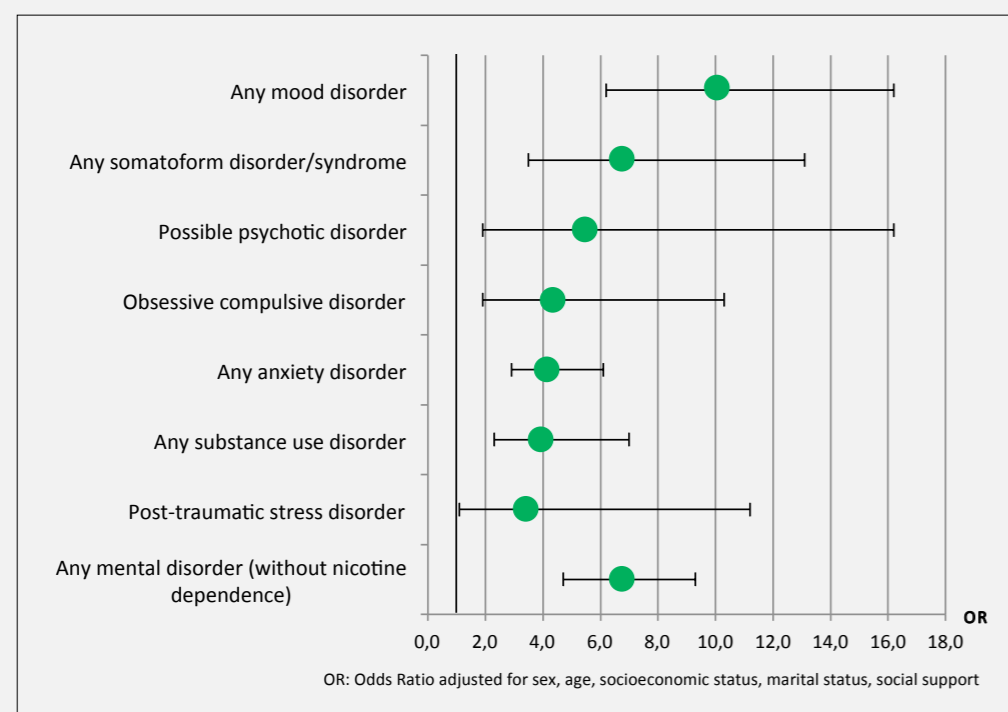
“No health
without mental health.”

Heike Hölling



Publications

- Hapke U, Maske UE, Scheidt-Nave C, Bode L, Schlack R, Busch MA. (2013) Chronischer Stress bei Erwachsenen in Deutschland: Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1). [Chronic stress among adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)] Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz 56(5/6), 749–754.
- Hölling H, Schlack R, Petermann F, Ravens-Sieberer U, Mauz E, KiGGS SG (2014) Psychische Auffälligkeiten und psychosoziale Beeinträchtigungen bei Kindern und Jugendlichen im Alter von 3 bis 17 Jahren in Deutschland – Prävalenz und zeitliche Trends zu 2 Erhebungszeitpunkten (2003–2006 und 2009–2012). Ergebnisse der KiGGS-Studie – Erste Folgebefragung (KiGGS Welle 1). [Psychopathological problems and psychosocial impairment in children and adolescents aged 3–17 years in the German population: prevalence and time trends at two measurement points (2003–2006 and 2009–2012): results of the KiGGS study: first follow-up (KiGGS Wave 1)]. Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz 57, 807–819.
- Maske UE, Riedel-Heller SG, Seiffert I, Jacobi F, Hapke U (2016) Häufigkeit und psychiatrische Komorbiditäten von selbstberichteten diagnostiziertem Burnout-Syndrom: Ergebnisse der bevölkerungsrepräsentativen “Studie zur Gesundheit Erwachsener in Deutschland (DEGS1)” [Prevalence and Comorbidity of Self-Reported Diagnosis of Burnout Syndrome in the General Population: Results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Psychiatrische Praxis, 43, 18–24.
- Schlack R, Mauz E, Hebebrand J, Hölling H, KiGGS SG (2014) Has the prevalence of parent-reported diagnosis of attention deficit hyperactivity disorder (ADHD) in Germany increased between 2003–2006 and 2009–2012? Results of the KiGGS-study: first follow-up (KiGGS Wave 1). Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz 57, 820–829.



12-month mental disorders are more frequent in adults who report high levels of chronic stress than in adults who report below-average to average levels chronic stress (based on DEGS1-MH data)

Unit 27: Health Behaviour

What we eat, how much we move, how much we weigh, and if and how much we smoke and drink alcoholic beverages has a major impact on our health and life expectancy. All these factors contribute essentially to the development of non-communicable diseases. However, all these factors are modifiable and therefore they are in focus of health promotion and disease prevention activities.

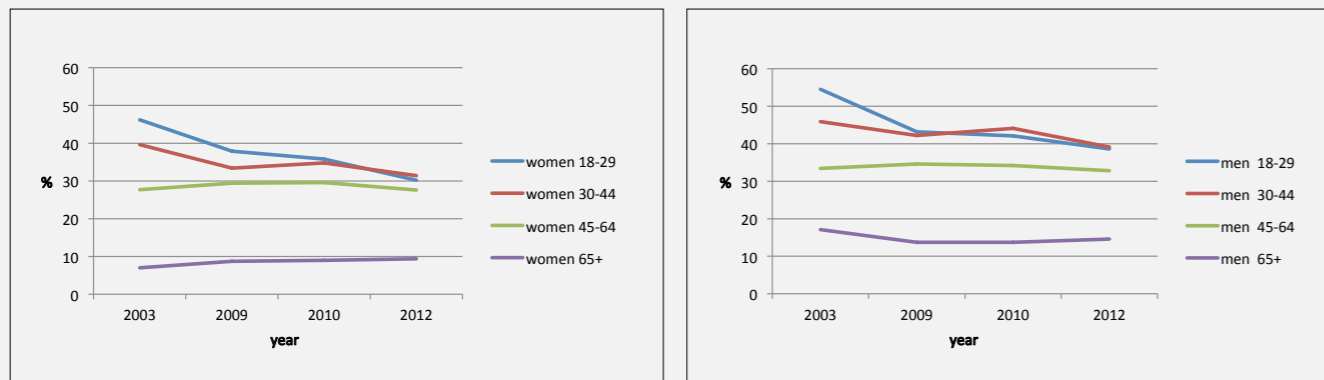
Unit 27 analyses data from the population-wide health and nutrition surveys of the RKI considering the actual situation and the development over time. The focus is particularly on: dietary intake, physical activity, overweight, tobacco and alcohol consumption as well as health promotion and disease prevention activities. In this context, the distribution in the population, the determinants as well as specific and combined associations with health outcomes during all stages of life is taken into account. From the results recommendations for public health activities and their evaluation are drawn.

“Making the healthy choice
the easy choice –
the role of surveillance and
epidemiology.”

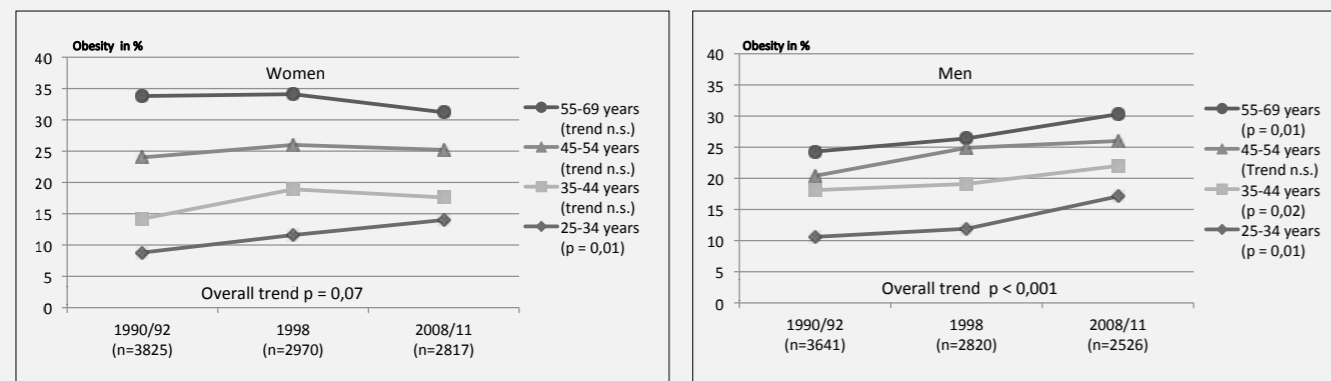
Dr. Cornelia Lange



Proportion of smokers (daily and occasionally) over time. Data source: GEDA studies



Trends in obesity. Data sources: OW91, GNHIES98, DEGS1



Objectives

- Population-wide monitoring of health-related behaviour as well as health promotion and disease prevention; collaboration to develop and evaluate national health objectives
- Determination of reference values for physical fitness and anthropometrics
- Epidemiologic analyses of health conditions, health-related lifestyle and utilisation of health promotion and disease prevention activities
- Epidemiologic analyses of health-related behaviour and risk factors for non-communicable diseases
- Design, conduct and analysis of nutrition surveys
- Development of appropriate assessment tools for health behaviour
- The Prevention and Health Promotion working group based in our unit supports the department to integrate aspects of disease prevention, health promotion and healthcare in its research
- Support of the Health Reporting unit in the preparation of health reports www.rki.de/jg27-en

Publications

1. Finger JD, Tylleskär T, Lampert T, Mensink GBM (2013) Dietary Behaviour and Socioeconomic Position: The Role of Physical Activity Patterns. PLoS ONE 8: e78390.
2. Haftenberger M, Mensink GBM, Herzog B et al. (2015) Changes in body weight and obesity status in German adults – results of seven population-based prospective studies. Eur J Clin Nutr: advance online publication, <http://dx.doi.org/10.1038/ejcn.2015.179>.
3. Jordan S, Von Der Lippe E, Starker A, Hoebel J, Franke A (2015) Einflussfaktoren für die Teilnahme an Bonusprogrammen der gesetzlichen Krankenversicherung. Ergebnisse der Studie “Gesundheit in Deutschland aktuell”. Gesundheitswesen 77(11) S 861–868.
4. Manz K, Schlack R, Poethko-Muller C, Mensink G, Finger J, Lampert T, & KiGGS Study Group (2014) Körperlich-sportliche Aktivität und Nutzung elektronischer Medien im Kindes- und Jugendalter. Ergebnisse der KiGGS-Studie – Erste Folgebefragung (KiGGS Welle 1). Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 57: 840–848.
5. Mensink GBM, Fletcher R, Gurinovic M et al. (2013) Mapping low intake of micronutrients across Europe. Br J Nutr 110: 755–773.

Unit 28: Social Determinants of Health

This unit analyses the social determinants of health and the resulting health inequalities with consideration of relevant social developments. A particular focus is placed on exploring the relationship of social inequality and health, working conditions and health, migration and health, regional differences and health, and demographic change and health.

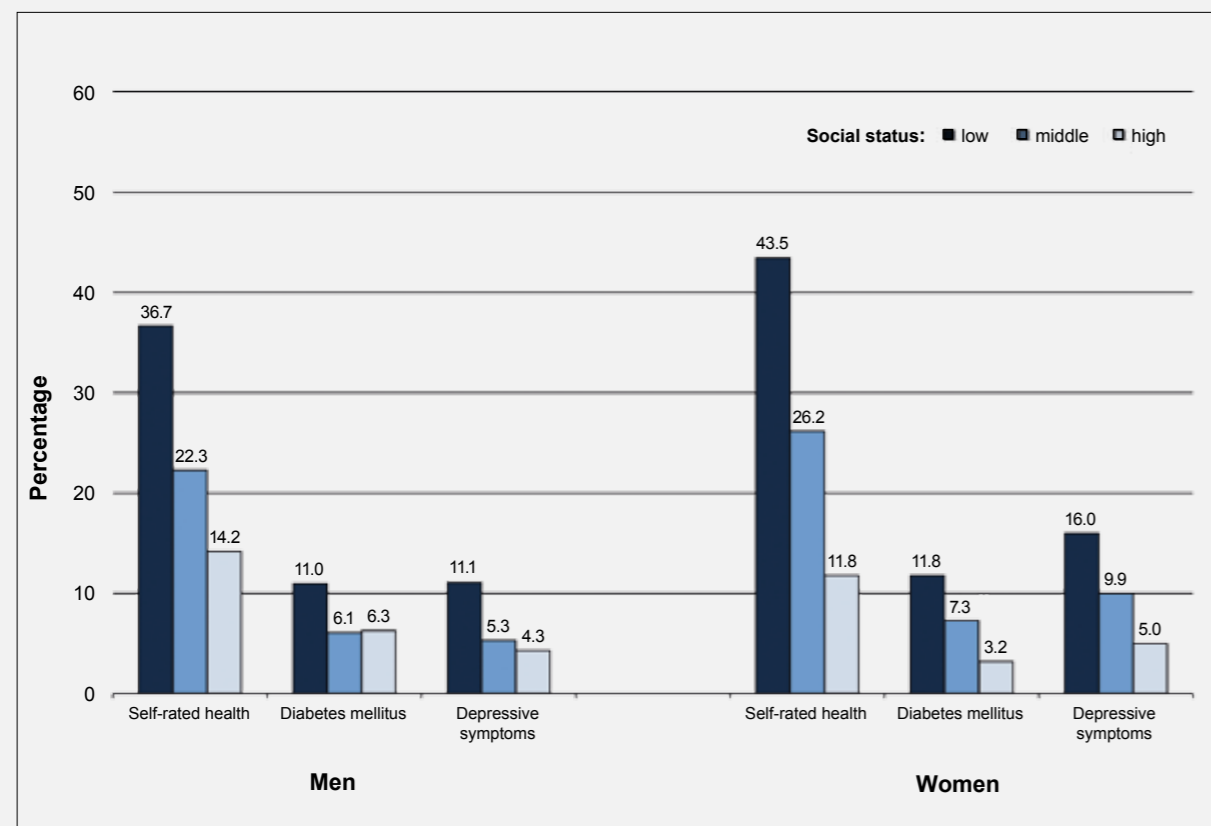
The analyses are based primarily on data from the health monitoring system administered by the Robert Koch Institute and secondarily on other representative population data sources. In addition to conducting epidemiological analyses, the unit also supports the health monitoring studies and health reporting operationally. The results are used for policy advice, particularly identifying and describing population groups and regions for which specific requirements must be assumed with respect to prevention, health promotion and healthcare.

“Understanding the societal causes of health and diseases.”

PD Dr. Thomas Lampert



Social differences in self-rated health (“fair”, “poor” or “very poor”), diabetes mellitus and depressive symptoms



Tasks

- ▶ Analysis of social differences in the prevalence and development of physical and mental health and its associated risk factors
- ▶ Investigation of the effect of education and a family's social status on health development during childhood and adolescence, as well as in later life
- ▶ Description of the health status of children, adolescents and adults with migration background
- ▶ Examination of correlations between professional qualifications, occupation, working conditions and health
- ▶ Analysis of health-related causes and consequences of unemployment or precarious employment
- ▶ Identification of social and regional differences in the use of prevention, health promotion and healthcare services
- ▶ Consideration and analysis of families, day-care centres for children, schools and companies as living environments and settings for disease prevention and health promotion
- ▶ Estimation of regional prevalence rates and prognoses for non-communicable diseases and associated risk factors
- ▶ Analysis of the effects of demographic change on the burden of disease and its regional differences, need for nursing care and healthcare requirements

www.rki.de/fg28-en

Publications

1. Kuntz B, Lampert T (2016) Smoking and passive smoke exposure among adolescents in Germany. Prevalence, trends over time, and differences between social groups. *Deutsches Ärzteblatt International* 113 (3): 23–30.
2. Kroll LE, Müters S, Lampert T (2016) Unemployment and Health. An overview of current research results and data from the 2010 and 2012 German Health Update. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 59(2): 228–237.
3. Lampert T, Richter M, Schneider S, Spallek J, Dragano N (2016) Social inequality and health. Status and prospects of socio-epidemiological research in Germany. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 59(2): 153–165.
4. Lampert T, Kuntz B, Hoebel J, Müters S, Kroll LE (2016) Gesundheitliche Ungleichheit [Health inequality]. In: Statistisches Bundesamt (Destatis), Wissenschaftszentrum Berlin für Sozialforschung (WZB) (Eds.) *Datenreport 2016. Ein Sozialbericht für die Bundesrepublik Deutschland*. Bonn: Bundeszentrale für politische Bildung, S. 259–271.
5. Rattay P, von der Lippe E, Lampert T, KiGGS Study Group (2014) Health of children and adolescents in single-parent, step-, and nuclear families. Results of the KiGGS study: first follow up (KiGGS Wave 1). *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 57(7): 860–868.

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Dr. Margrit Kalcklösch ~ Dr. Benjamin Kuntz ~ Stephan Müters ~ Enno Nowossadeck ~ Petra Rattay ~ Maria Schumann ~ Rahsan Yesil-Jürgens

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Department 3: Infectious Disease Epidemiology

The mission of the Department of Infectious Disease Epidemiology is to prevent, detect and control the spread of infectious diseases in the general population in Germany. Therefore, the department supports the German public health service by maintaining a comprehensive national surveillance system and providing a nationwide accessible 24/7 on call duty system as well as an Epidemiological Situation Centre. In addition, the department offers scientific support for preparedness and response to infectious diseases, deploys epidemiological teams for outbreak investigations and offers special training for the respective target groups.

The department consists of eight units (unit 31–37 plus the training programmes). All are well integrated into the public health services in Germany and ensure the fulfilment of the department's mission with

- ▶ Continuous surveillance and assessment of the epidemic situation
- ▶ Implementation and support of outbreak investigations
- ▶ Development and evaluation of strategies for prevention and intervention
- ▶ Research and method development in the field of infectious disease epidemiology
- ▶ Execution of legal duties in the field of infection protection
- ▶ Support and advice for other partners of the public health services and political decision makers
- ▶ Development of evidence-based recommendations for the public health community
- ▶ Information of health professionals and the scientific community
- ▶ Exchange with other national and international health authorities
- ▶ Qualification and further training in the field of public health with emphasis on infectious disease epidemiology

Surveillance of notifiable infectious diseases, complementary monitoring and surveillance of non-notifiable infectious diseases, international reporting obligations within the Early Warning and Response System (EWRS) of the European Union and the International Health Regulations (IHR) are part of these primary responsibilities of the department. Coordination of response to public health emergencies of infectious origin also lies within its portfolio. Upon request the department provides immediate technical support to local public health services, ranging from scientific advice on the phone, to provision



Our aims for the future are divided into three areas of responsibility:

Data Management and Analysis

- ▶ Surveillance activities
- ▶ Protection against Infection Act – Reporting system
- ▶ Electronic reporting system (DEMIS)
- ▶ Secondary data use

Development of Public Health Actions

- ▶ Applied research
- ▶ Vaccination
- ▶ Antibiotic resistance
- ▶ Health economy
- ▶ Hospital and mortality surveillance

Expansion of (Inter)National Structures

- ▶ Strengthening and networking of public health service and international health authorities
- ▶ Education and training
- ▶ Outbreak investigations
- ▶ Crisis management
- ▶ Political consultancy
- ▶ International health

“Research, surveillance and recommendations on infectious diseases to improve public health.”

Dr. Osamah Hamouda



Head of Department with administrative and scientific staff

of technical tools up to the deployment of epidemiologic investigation teams on-site. Here epidemiologists of the department supported and partially coordinated the investigation of major outbreaks in the last years, e.g. measles outbreak 2015, Norovirus outbreak 2012 or E. coli outbreak 2011. Especially during the Influenza pandemic 2009 and the Ebola outbreak 2014/2015 the department was part of the crisis management for Germany.

Another important task of the department is to provide risk assessment and scientific advice for the government, policy makers and health professionals. Six different national advisory committees are hosted and scientifically supported by respective units of the department. The scientific office of the Advisory Board for Public Health Microbiology is directly situated under the department head. All units of the department contribute to the yearly epidemiological report, regularly publish in peer-reviewed journals as well as in the RKI Epidemiological Bulletin and contribute to the RKI fact sheets for physicians which are also coordinated and edited in the department.

The department's scientific activities have clearly increased in quantity and level of sophistication. Scientists of the department are renowned experts visible through publications, memberships in international advisory groups, and invited presentations. Furthermore, the department is engaged in various training activities in the field of infectious disease epidemiology (for details see the chapter on training and education p 106–107): the two-year fellowship programme “Postgraduate Training for Applied Epidemiology” (PAE) is based at the department and provides training and practical experience using the “learning by service” approach. Since 2009 a Master of Science programme in Applied Epidemiology (MSAE) has been integrated in the training in cooperation with the Charité in Berlin and the Berlin School of Public Health. MSAE is the first Master of Science programme to be run by a federal institute. Moreover, the department has initiated the instalment of the first joint professorship appointment in the remit of the

Federal Ministry of Health, both of it indicate the scientific liaison between academia and the RKI.

The department is also hosting fellows and coordinators for the European Programme for Intervention Epidemiology Training (EPIET) in collaboration with the European Centre for Disease Prevention and Control (ECDC). As an important platform for exchange, the department organizes a training course with two modules (Epikurs@RKI) for the staff working in the German Public Health Service (Öffentlicher Gesundheitsdienst) on local and state level.

For the future, a tight link of epidemiological and laboratory data seems of high importance. The Department of Infectious Disease Epidemiology already collaborates closely with relevant institutes in Germany as well as with other departments of the RKI.

www.rki.de/abt3-en

Publications

1. Beermann S, Allerberger F, Wirtz A, Burger R, Hamouda H: Public health microbiology in Germany: 20 years of national reference centres and consultant laboratories. *Int J Med Microbiol* 2015; 305(7): 595–600.
2. Bernard H. et al: Large multistate outbreak of norovirus gastroenteritis associated with frozen strawberries, Germany, 2012. *Euro Surveill.* 2014 Feb 27;19(8): 20719.
3. Frentz D. et al: Patterns of transmitted HIV drug resistance in Europe vary by risk group. *PLoS One.* 2014 Apr 10;9(4): e94495.
4. Karo B, Krause G, Hollo V, van der Werf MJ, Castell S, Hamouda O, Haas W: The impact of HIV infection on treatment outcome of tuberculosis: analysis of surveillance data from nine European countries, 2010–2012. *AIDS.* 2016 Jan 8.
5. Schmidt D. et al: From pills to patients: an evaluation of data sources to determine the number of people living with HIV who are receiving antiretroviral therapy in Germany. *BMC Public Health.* 2015 Mar 17;15: 252.

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SCIENTIFIC STAFF ~ [Dr. Sandra Beermann](#) ~ [Dr. Andreas Bergholz](#) ~ [Dr. Markus Kirchner](#)

HEADS OF UNITS ~ [Dr. Katharina Alpers](#) ~ [Dr. Viviane Bremer](#) ~ [Dr. Hermann Claus](#) ~ [Dr. Tim Eckmanns](#) ~ [Dr. Andreas Gilsdorf](#) (Deputy of the Head of Department) ~ [Prof. Dr. Walter Haas](#) ~ [Prof. Dr. Klaus Stark](#) ~ [PD Dr. Ole Wichmann](#)

Unit 31: Data Management

The Data Management unit is responsible for the design, development and management of IT projects within the Department of Infectious Disease Epidemiology at the RKI. We provide scientific services and consultancies for other units at the RKI and for external partners as well as the general public.

The central task of the unit is the continuous improvement of the national reporting system for surveillance of notifiable infectious diseases (SurvNet@RKI) according to the German Protection against Infection Act ("Infektionsschutzgesetz" – IfSG). We develop and maintain a number of surveillance applications in the field, such as those for influenza ("Arbeitsgemeinschaft Influenza" – AGI), sexually transmitted diseases (in particular HIV) and antibiotic resistance (ARS). Many of the laboratory information management systems in use at the RKI are built and steadily improved by us.

All these projects include the joint conceptual design with experts and potential users as well as the development of all required IT components (databases, desktop applications, web applications). Furthermore, we conduct the complete management, technical support and allocation of appropriate tools to analyze the data including the provision of official data for publishing. This includes the various kinds of mathematical analysis for users at RKI and external users alike. Our goal is to provide automated solutions for all data processed.

Our unit has recently realized a project on epidemiological modeling of infectious diseases and co-initiated a EU-funded project to use natural language processing and other data

mining methods to make web 2.0 contents usable for public health topics. During the Ebola outbreak 2014 in West Africa, the unit developed a contact tracing tool for mobile devices in cooperation with national and international partners. This tracing tool contains a simulation framework which enables anyone to test such applications systematically with realistic data. Our focus is the management of applications and processes for ongoing projects, the adaption to new software methodologies and new technologies. By using modern technologies (Online Analytical Processing (OLAP)) for data mining and multi-dimensional data processing, we are able to support users of all current projects by providing tools to handle large amounts of data fast and easily even in urgent and complex situations. This requires a smart storage of metadata to ensure the integrity of information and consistency of data across different applications as well as innovative visualization techniques.

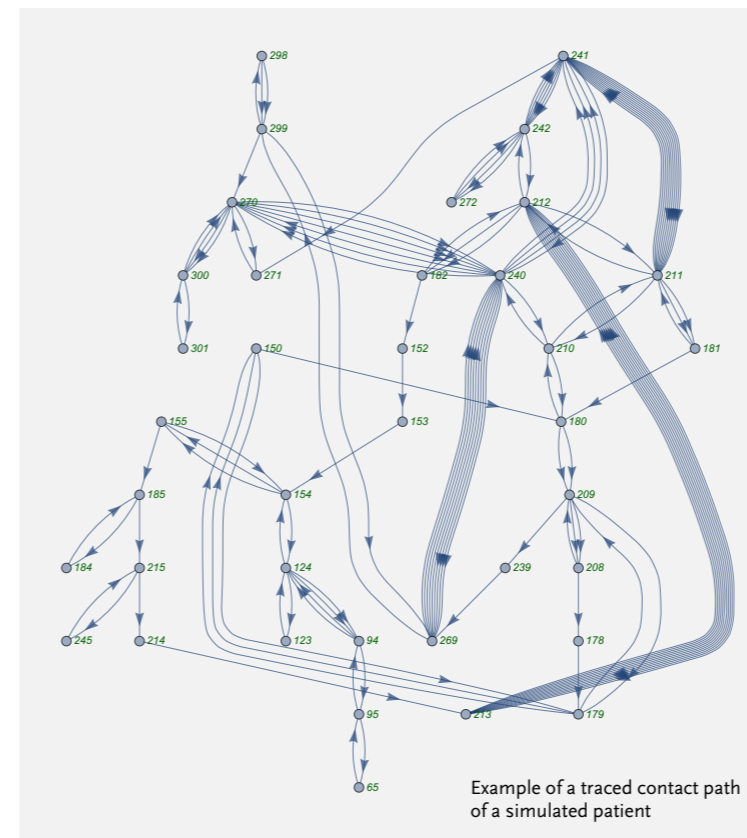
www.rki.de/fg31-en

**"We provide tools
to transform data into knowledge
and insight."**

Dr. Hermann Claus



Schematic system overview of SORMAS (Surveillance and Outbreak Response Management System)



Publications

- SurvNet3@RKI 0.9.19 http://www.rki.de/DE/Content/Infekt/IfSG/Software/software_inhalt.html.
- Velasco E, Agheneza T, Denecke K, Kirchner G, Eckmanns T (2014) Social Media and Internet-Based Data in Global Systems for Public Health Surveillance: A Systematic Review. *Milbank Quarterly* 92(1): 7–33.
- Fähnrich C, Claus H, Kirchner G, et. al. (2016) Ebola Outbreak Containment: Real-Time Task and Resource Coordination with SORMAS, *Journal of Biomedical and Health Informatics*. Submitted.
- Haller S, Eckmanns T, Claus H, et.al. (2014) Results from the First 12 Months of the National Surveillance of Healthcare-associated Outbreaks in Germany, 2011/2012; *PLoS ONE* 9(5).
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Unit 32: Surveillance

Epidemiological surveillance is the ongoing systematic collection, analysis, evaluation and dissemination of health data for the purpose of planning, implementation and evaluation of disease control measures.

The Surveillance Unit is primarily responsible for the implementation of the notification system within the framework of the German Protection against Infection Act (Infektionsschutzgesetz, IfSG). The Surveillance Unit supports disease-specific units with their surveillance activities and international reporting. The cross-cutting nature of the work involves coordination of new and further development of existing surveillance methods and tools, optimization of early warning systems and early detection of outbreaks and the RKI Epidemiological Situation Centre management. The Surveillance Unit acts as the contact point for public health services at municipal and state level in Germany and for the international health authorities of the European Union (EU) and the World Health Organization (WHO).

The main working tasks cover the following areas:

Notification system within the framework of the IfSG

- ▶ Quality management and evaluation of surveillance of notifiable biological threats
- ▶ Continuous epidemiological analysis of surveillance data
- ▶ Early detection and prevention of spread of infectious diseases
- ▶ Development of case definitions and criteria for data transmission and evaluation of notified cases
- ▶ Reporting (e.g. annual epidemiological report on notifiable infectious diseases, Epidemiological Bulletin) and scientific publications
- ▶ Development of new and optimisation of existing surveillance methods and tools
- ▶ Development of recommendations on surveillance of infectious diseases

Crisis management

- ▶ Coordination and management of the RKI Epidemiological Situation Centre
- ▶ Provision of support to the regional and local public health services in disease outbreak investigations

National cooperation

- ▶ Contact point for the public health services at local and state level in Germany
- ▶ Organization of weekly conference with the Federal States epidemiologists in order to continuously assess the epidemiological situation nationwide
- ▶ Coordination of the Federal State working group on surveillance of infectious diseases and the federal and state reporting procedures

International networks and early warning systems

- ▶ Focal point for international public health authorities of the EU and the WHO with emphasis on the early warning systems as part of the International Health Regulations (IHR) (2005) and the European Network "Early Warning and Response System (EWRS)"
- ▶ National coordinator for Germany's cooperation with the European Centre for Disease Prevention and Control (ECDC)
- ▶ International cooperation within the framework of ECDC's European network for the epidemiological surveillance (TESSy)
- ▶ Provision of support to the Federal States in the implementation of the IHR (2005)
- ▶ Provision of support to partner countries in the implementation of the IHR (2005) and in improving surveillance and response capacities

"We collect data for knowledge and for action."

Dr. Andreas Gilsdorf



Our main goals include:

Development and improvement of surveillance standards

Surveillance methods and possibilities including IT solutions are changing in the wake of new scientific discoveries; therefore an efficient surveillance system needs continuous revision. A vitally important modern electronic notification system will be developed in future for all users of the notification system. Enabling the linking between national and international surveillance databases is the next item on the agenda. It is also necessary to establish mechanisms for the use of available data collected for other purposes (e.g. generated by medical insurance companies) for surveillance purposes.

Strengthening of public health services

The public health services are responsible for the control of infectious diseases. The Surveillance unit is the central partner for the regional and local public health services. This cooperation should be extended through closer interaction in order to strengthen the public health service capacities. International cooperation with public health services in partner countries and with international public health organisations contribute to the global health cooperation and needs to be continued and enhanced.

Fostering preparedness planning and crisis management

The Surveillance unit has a long-standing experience with crisis management at the RKI and will use this knowledge to advance crisis planning. Crisis planning is also an important aspect covered by the international projects run by the Surveillance unit.

www.rki.de/fg32-en

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| Generic surveillance, mandatory reporting: data for action | | | |
|------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| | Development and improvement of surveillance standards | Strengthening public health systems | Fostering of preparedness planning and crisis management |
| National | Further development of the reporting system | Cooperation with German Federal States | Crisis management: situation centre |
| | Further development of the Protection against Infection Act | | Development of a RKI Crisis Plan |
| | Use of secondary data | Activities to improve collaboration with clinicians | Coordination of activities in crisis: Federal States, other sectors |
| International | International alerts (EWRS, IHR) | Support of surveillance activities in partner countries | Support of outbreak and crisis management in partner countries |
| | Cooperation with international surveillance systems | Support of IHR implementation Cooperation with international organizations | National and international projects on infectious diseases and transport |

Main areas of work of the Surveillance Unit

The collection of data on infectious disease is important allowing timely identification and assessment of risks of infectious threats in the population. Close collaboration with the regional and local public health services additionally helps to strengthen public health and enables RKI to translate data into action. Strong surveillance and response structures are an extremely important component of an efficient public health system

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Unit 33: Immunisation

The Immunisation unit is responsible for a wide range of activities related to the development and evaluation of evidence-based vaccination recommendations in Germany. According to the German Protection against Infection Act, the unit hosts the executive secretariat of the German Standing Committee on Vaccination (STIKO), responsible for developing national vaccination recommendations. These recommendations serve as a basis for the federal states' vaccination guidance, for the inclusion in the immunisation directives of the Federal Joint Committee (that regulates reimbursement of vaccines), and as a "best-practice" guidance to clinicians. Focus of the unit's activities is therefore the generation of evidence and review of scientific literature, but also the communication of the recommendations as well as monitoring their implementation and impact in the population (Figure).

Evidence assessment

A standard operating procedure (SOP) for the systematic development of vaccination recommendations was endorsed by STIKO in 2011 (www.stiko.de/en) and updated in 2014 and 2016. Systematic reviews and assessments of the quality of evidence belong to the major tasks of the STIKO secretariat to support STIKO decision-making (see example: [1]). Besides data on the efficacy and safety of vaccines (available from published literature) and country-specific disease burden, transmission modelling and health economic evaluations provide important information to guide decisions on to adopt a vaccination into the national immunisation plan or not. In 2014–16 a methodology for the modelling of epidemiological and health economic effects of vaccines in Germany and for the consideration of results from such models in decision-making

was developed following discussions at an international [2] and national workshops organized by the Immunisation unit with funding provided by the Federal Ministry of Health.

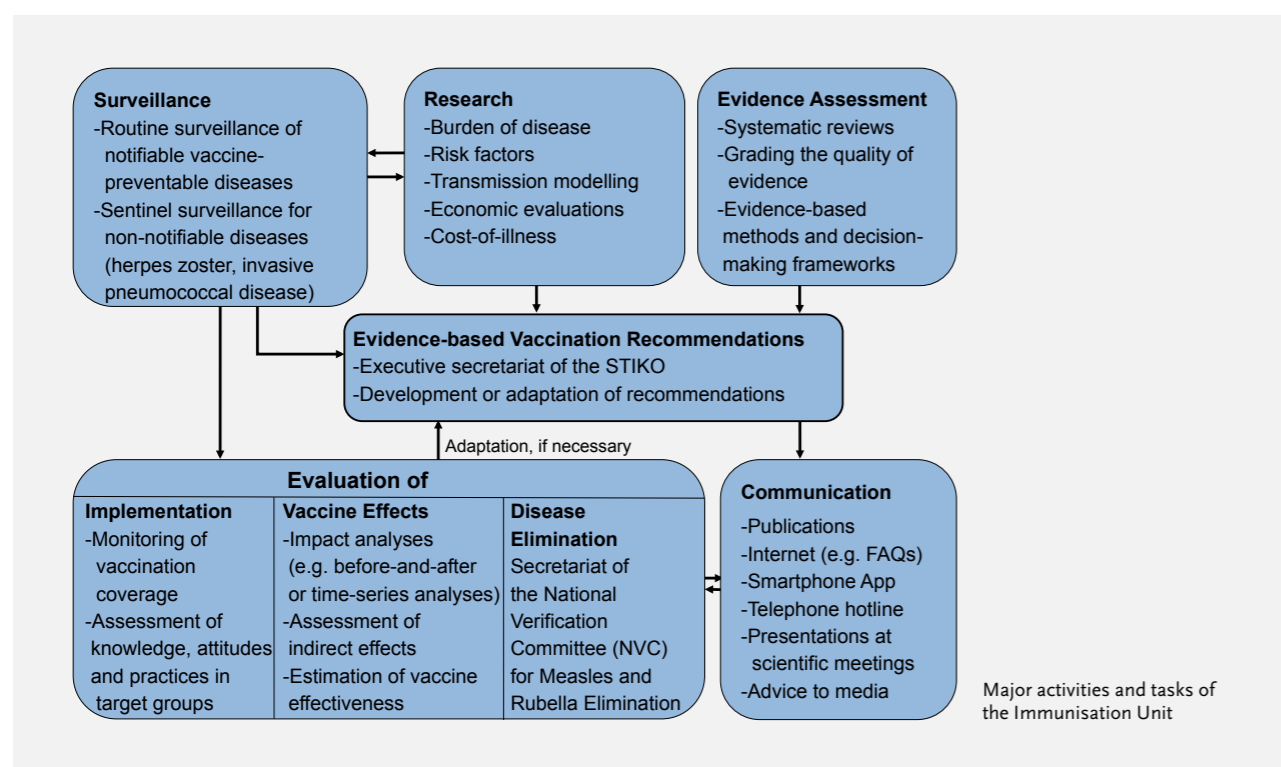
Surveillance, research and evaluation

The unit monitors the burden of vaccine preventable diseases and vaccination impact through epidemiological analysis of notification data in Germany [3]. In addition, it currently operates an enhanced sentinel surveillance system for varicella/herpes zoster and a laboratory-based sentinel system for invasive pneumococcal diseases. The unit also conducts epidemiological research on disease burden using additional data sources [3, 4], the effectiveness of vaccines in the post-licensure phase [4], and the impact of vaccination at population level, as well as projects on disease transmission modelling and health economic evaluations of vaccines.

Target-group specific vaccination coverage data are essential to identify the degree to which vaccination recommendations are

“Vaccines are among the most powerful public health tools. Our aim is to reduce infection-related morbidity and mortality in our population through vaccination based on the best available scientific evidence and in collaboration with national and international partners.”

PD Dr. Ole Wichmann



implemented, to enhance/optimize communication activities and to enable the interpretation of epidemiological data after vaccine introduction. One of the tasks of the Immunisation unit is to collate, analyze and publish vaccination coverage data at a national level that are routinely collected by local health authorities at school entry. In addition, claims data are routinely transmitted to RKI by all 17 Associations of Statutory Health Insurance Physicians in Germany (covering approximately 85% of the total population) for monitoring of vaccination coverage and the effects of vaccination. The unit also conducts research on barriers and factors that facilitate vaccine uptake in specific target groups [5].

Data on vaccination coverage and the disease epidemiology are also essential for the documentation and verification of national elimination efforts (i.e. for poliomyelitis, measles and rubella) and are key indicators to be annually reported to WHO. The executive secretariat of the National Verification Committee (NVC) for Measles and Rubella Elimination in Germany was installed at the RKI Immunisation unit at the end of 2012. In 2014/15 the unit led an interdisciplinary group of stakeholders that developed a National Action Plan for the elimination of measles and rubella in Germany 2015–2020. The action plan was endorsed by the Conference of Federal States' Health Ministers and the German Federal Ministry of Health in 2015.

Communication

Healthcare professionals and local/state health authorities, but also media, are the main target groups of the health-communication activities of the unit, with the aim of improving knowledge and advising on appropriate procedures concerning vaccinations. In recent years the Immunisation Unit has updated and expanded its online information services, including FAQs that provide a broad overview on questions related to immunization and vaccines, also for the general public (www.rki.de/impfen and www.stiko.de). In 2015, there

were more than 4.3 million clicks on these two webpages. In 2015 the unit received also funding from the Federal Ministry of Health to develop a smartphone app that supports physicians in their vaccination activities with up-to-date information and recommendations. A beta version is planned to be released and piloted in mid-2016. www.rki.de/jg33-en

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Unit 34: HIV/AIDS, STI and Blood-borne Infections

The main task of the unit for HIV/AIDS, STI and Blood-borne Infections is to collate comprehensive data on HIV/Aids, sexually transmitted infections, viral hepatitis and Creutzfeldt-Jakob disease in order to understand the epidemiology of these infections (see Figure 1). These data are used to set up, adapt or evaluate prevention strategies and to inform guidelines for diagnosis and disease management.

Our unit is responsible for the collation and analysis of the anonymous notification of HIV/AIDS and syphilis infections, the analysis of laboratory notification of hepatitis B, C and D as well as Creutzfeldt-Jakob disease. In addition, we are in charge of collecting data on blood donations and infections among blood donors. We complement HIV notification data by clinical-microbiological long-term cohort studies (ClinSurv and HIV seroconverter study). This allows us to gain insight into infection dynamics, resistance patterns and clinical management of HIV infections. In addition, we collect data on gonococcal resistance and chlamydia through laboratory sentinel systems.

We use integrated biological and behavioural surveys to gain information on prevalence of infections and sexual and other risk behaviour in key populations. We collaborate with Department 2 to test serological parameters in the general population (KiGGS, DEGS) and perform surveys in key populations such as men who have sex with men (EMIS) and sex workers. We continue to develop our survey methods to improve our access to marginalised populations such as sex workers (Outreach) and drug users (DRUCK). We are also increasingly using secondary data from health insurances and pharmacies to gain insight into prevalence of infections, frequency of diagnostic measures and clinical management. For example, we have

carried out a thorough review of the epidemiological situation of hepatitis B and C in Germany (Hep-Epi).

We use notification and clinical data to model the prevalence and incidence of HIV and AIDS in Germany. This model helps decision makers such as the Federal Ministry of Health and the Federal Centre for Health Education as well as NGOs to evaluate whether the current prevention strategies remain successful or need to be scaled up. Our data on HIV drug resistance has led to the decision of the Federal Joint Committee to reimburse resistance testing for every newly diagnosed HIV patient. The results of the HIV incidence surveillance help us to further understand the dynamics of the HIV epidemic, while the clinical surveillance provides clinicians and stakeholders with an overview on currently used HIV treatment regimens and treatment outcomes.

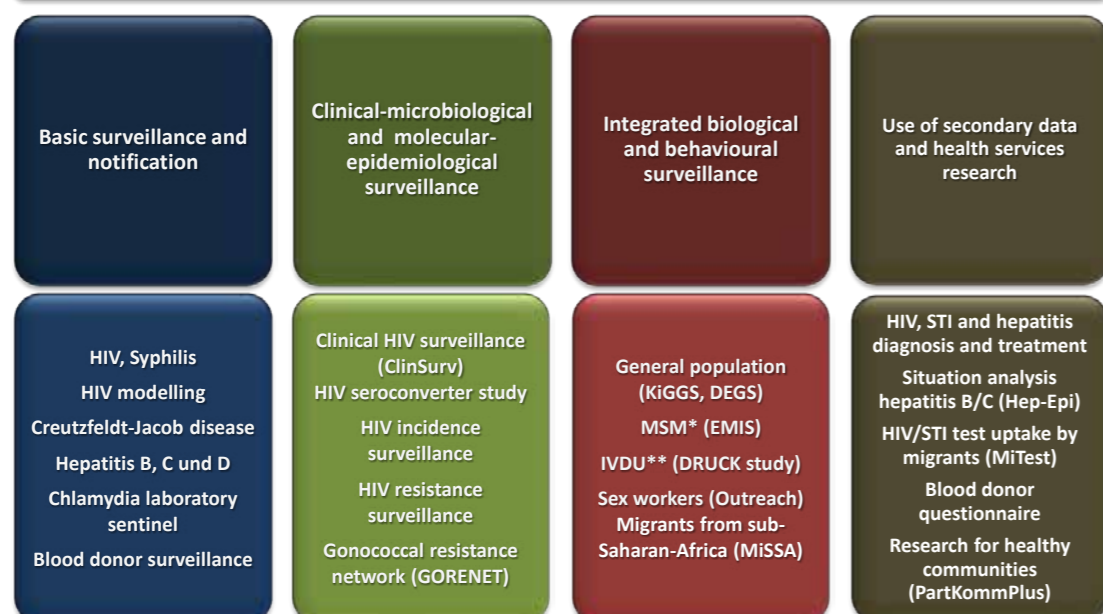
“Our data puts us in a unique position to guide policy makers in developing new strategies.”

Dr. Viviane Bremer

Our sentinel surveillance on gonococcal resistance (GORENET) is used to inform the development of treatment guidance. Data on chlamydia infections were used to evaluate the uptake of the screening of women <25 years. The regular publication of syphilis notification data has led to a higher awareness among key populations. The data from blood donors and donations are used to monitor the safety of blood and blood products. The impact of measures such as the introduction of a test algorithm for hepatitis C on safety can be monitored by this system.

* Men who have sex with men; ** i.v. drug users

Activities of the unit for HIV/AIDS, STI and Blood-borne Infections



Our large nation-wide integrated biological and behavioural survey among i.v. drug users (DRUCK study) has demonstrated the need to upscale prevention measures such as needles exchange and hepatitis B vaccination in this group. Preliminary results of a survey on sexual health among migrants from Sub-Saharan Africa (MISSA) show that knowledge on transmission and test opportunities could be improved in this group. As the studies were done in collaboration with local partners, recommendations can immediately be put into practice.

The analysis of secondary data has enabled us to gain an actual picture of treatment of HIV and hepatitis C in the general population and in specific settings, such as prisons. Our review of the epidemiological situation of hepatitis B and C in Germany has generated a good picture of what data are missing and will guide our future studies. Using pharmacy data, we are able to monitor how the new treatment options for hepatitis C are being increasingly used in Germany. These results will help to estimate the impact of the new treatment on the burden of disease of hepatitis C in Germany. We have also been able to describe the current barriers as well as examples of good practice for HIV and STI tests for migrants, engaging in an open dialogue with communal testing sites. The PartKommPlus project also intends to improve communal health promotion, by using a participatory health research approach.

The results from our surveillance systems and diverse studies put us in a unique position to guide policy makers in the development of new strategies for HIV, STI and viral hepatitis in Germany and health professionals to improve prevention, counselling, diagnosis and treatment.

www.rki.de/fg34-en

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Unit 35: Gastrointestinal Infections, Zoonoses and Tropical Infections

We work on the epidemiology and prevention of a wide range of gastrointestinal and zoonotic pathogens. The spectrum includes classical gastrointestinal and food-borne pathogens such as *Salmonella*, *Campylobacter*, Shiga toxin-producing *E. coli*, *Listeria*, norovirus, hepatitis A virus, other zoonotic pathogens such as hepatitis E virus, hantavirus, *Coxiella*, *Leptospira*, and vector-borne pathogens (e.g., *Borrelia burgdorferi*, *Plasmodium* species, denguevirus). Our unit holds expertise and maintains cooperation links for this broad range of diseases. Together with our partners we have published scientific data on 27 different infectious disease agents in peer reviewed journals over the last seven years.

One major focus is placed on outbreak investigations. We have coordinated various large outbreak investigations and have supported public health authorities in many local and regional outbreaks. We closely collaborate with the federal food safety authorities, the local and state health departments, and the national reference laboratories. In recent outbreaks the usefulness of the new techniques of isolate typing (whole genome sequencing) in combination with epidemiological data could be demonstrated.

In large multistate outbreaks the unit usually coordinates the investigations in order to control the outbreak. Prime examples are the outbreak of STEC O104:H4 caused by sprouted seeds in 2011, the norovirus outbreak with more than 10,000 cases caused by frozen strawberries in 2012, and various *Salmonella* and *Listeria* outbreaks. The evidence from our epidemiological studies contributed to the timely identification of the vehicles of infection, the removal of dangerous foodstuffs from the market and the prevention of further cases of disease.

Additional important work areas are disease surveillance and research, training of German public health service staff, and the formulation of preventive schemes and public health recommendations based on scientific evidence. In addition, we focus on the topics of climate change and infectious diseases, emerging pathogens and molecular epidemiology.

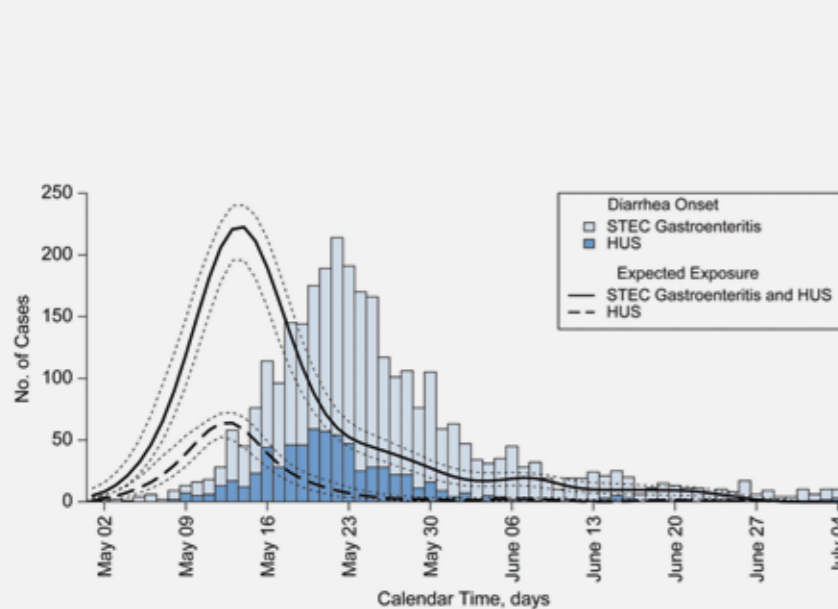
We regularly analyse surveillance data in order to detect changing trends or disease clusters. This forms one basis for outbreak detection and for analyses of spatio-temporal trends. Data on imported mosquito-borne diseases (malaria, dengue fever, chikungunya fever) are constantly monitored and analysed. This enables us to issue pertinent information for travel medicine experts and the public.

Additional research focuses on burden of disease studies, seroepidemiology and risk factor studies. We analysed the burden of disease of haemolytic uraemic syndrome (HUS) and other gastrointestinal infections. Time series analyses reveal

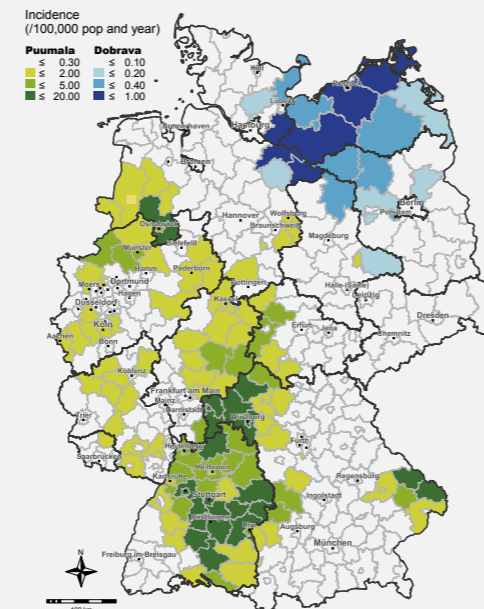
“Diversity, complexity, and dynamics of zoonotic diseases require preparedness, broad expertise and flexible response.”

Prof. Dr. Klaus Stark

temporal trends, geographic and demographic distribution of infectious diseases. We have published such analyses for campylobacteriosis, yersiniosis, norovirus enteritis, brucellosis and leptospirosis providing important clues for prevention and public health. Serosurveys on markers of infection in



Outbreak of HUS and STEC gastroenteritis caused by STEC O104:H4 in Germany, 2011 – Epidemiologic curve and back projection of the exposure phase



Notified hantavirus cases by county of infection and probable virus type, Germany, 2006–2015



representative population samples (Lyme borreliosis, hepatitis E, toxoplasmosis) and in special risk populations (*Coxiella burnetii* in veterinarians) were also conducted.

We performed a large case-control study on risk factors for sporadic yersiniosis in collaboration with the public health service, yielding the surprising finding that even in young children consumption of raw ground pork is the main risk factor for infection. In a recent case-control study on campylobacteriosis important risk factors were the consumption of chicken, consumption of pork, eating out, and use of proton-pump-inhibitors. Recently, we also determined risk factors for sporadic listeriosis and for hepatitis E virus infections with large case-control studies.

Molecular epidemiology at the cross roads between classic infectious disease epidemiology and microbiology/virology becomes increasingly important. Linkage of epidemiological and molecular data allows dynamic monitoring of specific pathogens in various populations, as well as better quantification of the importance of various sources of infection. For example, we conducted studies on campylobacteriosis (collaboration with Hannover Medical School), and hepatitis A and E (collaboration with the consultant laboratories).

For pathogens newly emerging in Germany, it is important to determine possible threats for human health. A good example is Schmallenberg virus (SBV), discovered in November 2011 by the Friedrich-Loeffler-Institut in sick dairy cows. In conjunction with our RKI laboratory experts, we were able to demonstrate in a rapidly performed epidemiological study among shepherds that the human health risk of SBV is negligible. The unit has the appropriate expertise and cooperation links to replicate such rapid risk assessments in similar situations in the future.

Overall, by investigating current trends and events our unit's work is able to directly prevent cases of disease. In our scientific studies we obtain evidence for effective and targeted public health measures.

www.rki.de/fjg35-en

Publications

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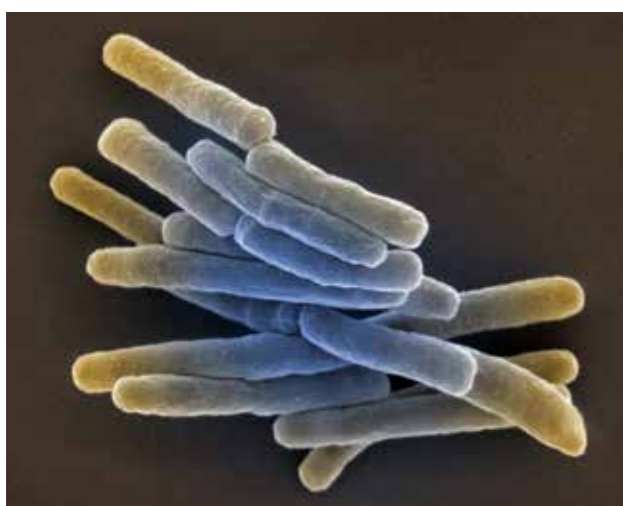
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Unit 36: Respiratory Infections

Robert Koch, the founding director of our institute, is best known for his work on tuberculosis. The unit for Respiratory Infections within the Department of Infectious Disease Epidemiology, founded 10 years ago in 2006, carries on this tradition with its work on the epidemiology of infectious diseases spread by the respiratory route. Today, lower respiratory infections are still among the leading causes of death in Germany and pneumonia contributes about half a million new cases and 200,000 hospitalisations each year. Within the wide spectrum of pathogens we focus on three diseases – influenza, legionellosis, and tuberculosis – that lead to a significant burden of disease in the population and can serve as epidemiological models of respiratory infections. Also new emerging infections, such as SARS, MERS coronavirus or avian influenza, are within the scope of our unit.



Mycobacterium tuberculosis. Scanning electron microscopy

Influenza and other respiratory viruses

Our unit has established and maintains several surveillance systems to assess the epidemiology of influenza and other acute respiratory infections in the German population, which allow us to perform systematic timely analyses of data covering different levels of disease severity. These include a population-based online surveillance system (GrippeWeb) the National Influenza Sentinel Surveillance System of outpatients (Arbeitsgemeinschaft Influenza), and a hospital sentinel of severe acute respiratory cases (SARI-Surveillance) based on ICD-10-Codes. The latter system is a scientific cooperation between the RKI and a large private German hospital network (ICOSARI).

Within the National Influenza Sentinel we assess the influenza vaccine effectiveness against laboratory confirmed influenza in outpatients by conducting a test-negative case-control study each influenza season, because the match between circulating influenza strains and antigens in the influenza vaccine varies considerably between seasons. It is of high importance for the population that influenza vaccine effectiveness estimates are provided, in order to target complementary health measures in groups for which the vaccine is less effective, compare the effectiveness of various influenza (sub-)types

and support the development of better influenza vaccines in the future. We are partner in two European projects, Horizon 2020 (EU Commission) and a tender from the European Centre for Disease Prevention and Control (ECDC) that monitor influenza vaccine effectiveness in Europe (I-MOVE).

In addition, we conduct specific studies to address gaps in knowledge regarding the burden of influenza (and other acute respiratory diseases) and the identification of risk factors for severe disease and complications of influenza and community-acquired pneumonia in Germany.

We collaborate closely with the World Health Organization in the development of a tool to provide a robust and standardised method for making a timely assessment of the severity of a pandemic (PISA) to implement risk management and communications plan accordingly.

Legionellosis

Legionella spp. are important causative agents of sporadic community acquired pneumonia (community acquired Legionnaires' disease; CALD). LD is exclusively transmissible by environmental sources. Because of insufficient diagnostic testing the majority of LD cases are not reported leading to (a) underappreciation of the burden of disease and (b) the consequence that a large number of environmental sources remain unidentified. Since 2015 the Federal Ministry of Health funds a project where RKI, the Federal Environment Agency (Umweltbundesamt (UBA)) and the LD reference laboratory join forces for a research project focusing on three goals: (1) to estimate the proportion of CALD among all cases of community acquired pneumonia, (2) to attribute the proportion of cases of CALD that is due to different sources, in particular piped drinking water, and (3) to identify risk factors for the acquisition of LD

“Working on prevention and control of respiratory infections we take on the challenge of monitoring and tracing airborne transmission of pathogens that can cause large outbreaks and rapidly spread within the population.”

Prof. Dr. Walter Haas

through piped drinking water, such as structural deficiencies in the piping system. Findings may have important implications for regulatory action and/or public health practice. ECDC coordinates the Europe-wide collection, analysis and follow-up of travel (e.g. hotel-) associated cases of Legionnaires' Disease (TALD; ELDSNet) which has become a powerful mechanism for the early detection of LD clusters/outbreaks with international implications. European guidelines ensure proper source management and thus prevention of further cases. For Germany, the RKI reports since 2012 German TALD cases to ELDSNet and informs German health departments



on sources in their jurisdiction, such as hotels, who may have caused international cases or clusters of TALD. Since 2015 an RKI representative is member of the ELDSNet Coordination Committee giving ECDC advice on strategic approaches.

Tuberculosis

With respect to tuberculosis (TB), our unit serves as National TB Contact Point for Germany and is key partner of ECDC and WHO. Our primary tasks include TB surveillance and public health advice on TB for the professional public. Our TB research aims to improve TB surveillance as well as to create and compile scientific evidence for public health action.

Our current activities include:

- ▶ Molecular TB surveillance, i.e. to move towards a routine integration of molecular typing and genome sequencing results of the pathogens. This is to detect clusters of TB cases, to increase our understanding on recent TB transmission, and to target TB prevention and control activities at best. As a part of this large-scale project, we develop new data visualisation and analysis tools to facilitate the monitoring of TB cluster growth.
- ▶ Inventory studies to scientifically ascertain the quality and completeness of TB surveillance data, e.g. drawing on independent secondary data sources. This is important to maintain TB surveillance at a high standard. This is particularly topical in view of a current increase in the TB trend combined with growing challenges in case reporting and follow-up in patient groups with high mobility and a migration context.
- ▶ Research on missed opportunities in TB prevention in children. This is to identify needs and gaps in case management in children exposed to or latently infected with TB.

www.rki.de/fj36-en

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Unit 37: Healthcare-associated Infections, Surveillance of Antimicrobial Resistance and Consumption

Healthcare-associated infections and antimicrobial-resistant pathogens (HAI/AMR) contribute significantly to the overall burden of disease and are likely to increase due to contemporary changes in demographics as well as ongoing medical developments. At the international level, trends for HAI/AMR act more like non-communicable diseases: even with a decrease of infectious diseases in general, HAI/AMR can be expected to increase.

Our unit has been appointed the “Centre for the Prevention and Control of Antibiotic Resistance” and hosts the Commission on Anti-Infectives, Resistance and Therapy (ART); as such, it coordinates and evaluates activities, to initiate projects and assess recommendations on HAI/AMR, both in Germany and worldwide. The German Protection against Infection Act (Infektionsschutzgesetz, IfSG) as well as the German Antimicrobial Resistance Strategy (DART) developed by the Federal Ministry of Health, Ministry of Food and Agriculture, and Ministry of Education and Research (BMBF) provide us with the right framework to outline our priorities, responsibilities and work tasks. Our unit conducts the surveillance for MRSA in blood culture and cerebrospinal fluid as well as for severe cases of *Clostridium difficile* infections, and for healthcare-associated outbreaks. These three infections are mandatorily reported [1]. For most other HAI/AMR entities, data collection is voluntary, and direct responsibility for local surveillance and related activities is with the respective healthcare facilities.

Surveillance and Outbreak Support

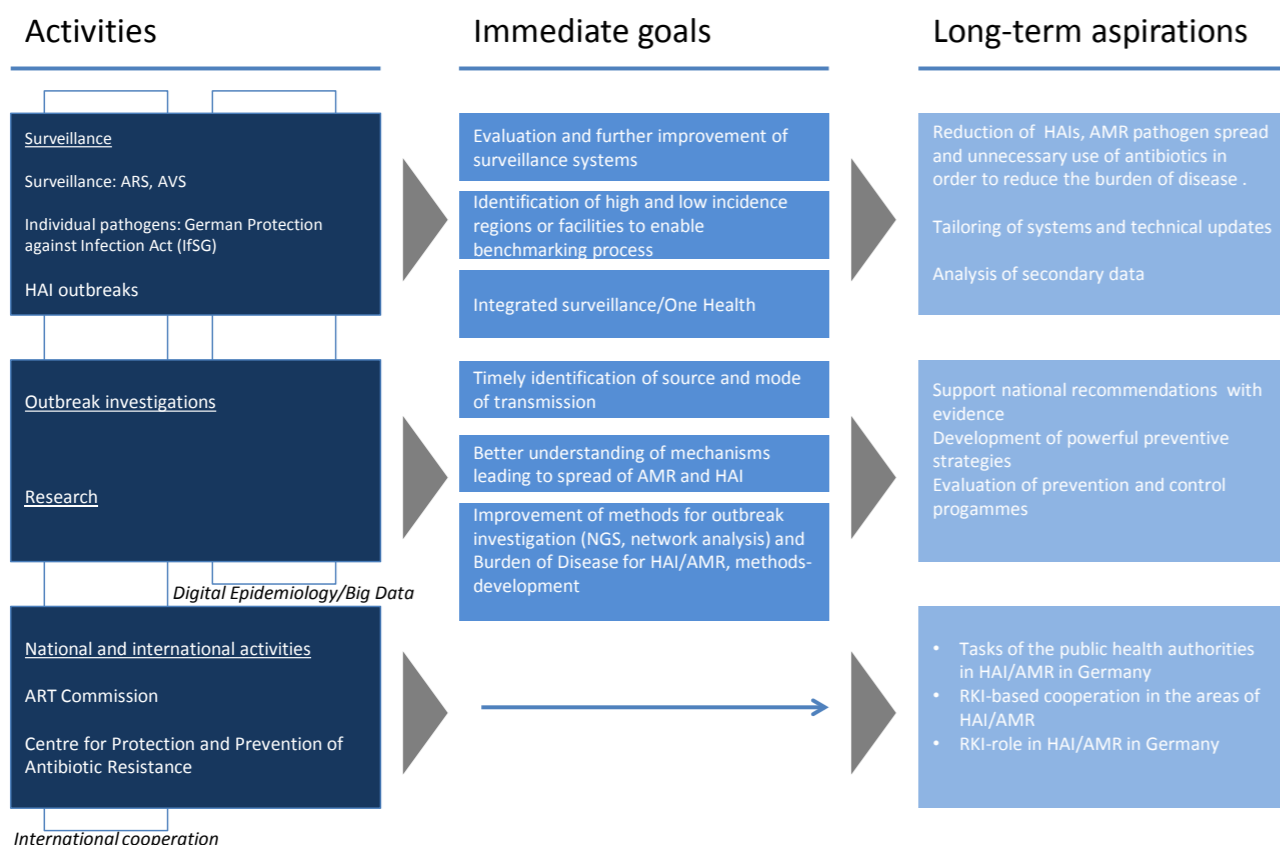
The RKI hosts two dedicated surveillance systems based within our unit. ARS (“Antimicrobial Resistance Surveillance”) is a laboratory-based surveillance system of antimicrobial resistance (ars.rki.de) [1], and AVS (“Antimicrobial Consumption Surveillance”/project collaboration between RKI and Charité) is the surveillance system of antibiotic consumption (avs.rki.de) [2]. Both are voluntary surveillance systems, and the overall objectives of both are to get representative data of the antimicrobial resistance situation in both hospital and outpatient care settings, and data about antibiotic consumption in hospitals for development and implementation of public health actions in Germany.

The data collected in ARS and AVS are processed in a timely manner, and are made available as direct feedback for participating facilities. In addition, reference statistics are available for public and professionals by an interactive database on the RKI website. ARS and AVS support hospitals to meet the requirements given by the German Protection against Infection Act.

Germany is one of a few countries worldwide that has implemented a mandatory timely surveillance for outbreaks of HAI since 2011 [1]. The development of integrated surveillance of antibiotic resistance, antibiotic consumption, HAI and HAI outbreaks is a central objective of our unit.

Cooperation with federal health authorities and joint surveillance have resulted in multiple requests to support local health authorities during outbreak investigations for HAI (e.g. [3]).

Findings from these outbreak investigations directly influence national recommendations, exemplified in the 2012 “Recommendation for the prevention of nosocomial infections for neonatal intensive care newborns with a birth weight



“We work for Global Health with Justice.”

Friedman and Gostin (2015)

less than 1,500 g”. Improvement of methods for outbreak investigation is another objective of the unit. We therefore incorporate next generation sequencing and network analysis into epidemiological outbreak analyses to enable better understanding of outbreak development and pathogen spread.

Further national and international research activities

Our unit strives to integrate internationally recognized scientific methods for measuring HAI/AMR. In cooperation with the European Centre for Disease Prevention and Control (ECDC), we developed an approach to estimate the burden of HAI, taking into account quality of life and the years of life lost (Disability-Adjusted Life Years (DALY)) due to HAI [4].

As HAI/AMR unfolds against a background of developing surveillance technology and increasing digitization, the unit actively seeks to stay abreast of contemporary methods and has examined actionable applications of digital epidemiology into routine surveillance [5] and application of secondary data. It also seeks to integrate the ethical, legal and social implications for conducting research with new methods (DELSI).

The unit is involved in national and international research cooperations focusing on the One Health aspect of antimicrobial resistance (i.e. COMPARE (www.compare-europe.eu), Med-Vet-Staph (medvetstaph.net)).

HAI/AMR is a global health challenge, and we are committed in international projects to actively share our experience and knowledge by supporting local and national public health

institutes which are in a process of establishing antimicrobial resistance and antibiotic consumption surveillance structures themselves, and by strengthening public health and healthcare (i.e. in Africa, e.g. African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA), Research networks for health innovation in Sub-Saharan Africa (BMBF)). Our unit cooperates with the ECDC, the World Health Organization (WHO) and other international partners. All activities within the unit are intended to contribute to evidence based public health [4].

www.rki.de/jg37-en

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ZBS: Centre for Biological Threats and Special Pathogens

The Centre for Biological Threats and Special Pathogens (Zentrum für Biologische Gefahren und Spezielle Pathogene, ZBS) works on a wide range of highly pathogenic bacteria, viruses and proteotoxins that might be used with bioterrorist intent. ZBS provides diagnostics, assesses threats and risks to public health, advises on biorisk management and supports the management of biological incidents. This also includes informing decision-makers and experts on such incidents and to advise them on adequate countermeasures.

In summary, in managing biological incidents, the centre's tasks include

- ▶ identification,
- ▶ preparedness,
- ▶ information
- ▶ and response.

The centre's work is not limited exclusively to the identification, assessment and management of possible bioterrorist attacks. Its expertise and skills are used also to investigate natural outbreaks or incidents caused accidentally by the application of specific highly pathogenic agents including toxins. Recent outbreaks and incidents demonstrate the importance of these activities (e.g. anthrax and wound botulism in heroin addicts; cowpox virus infections in pet owners; release of ricin-containing fertilizer; cases of suicide [attempted/successful] using ricin in Germany; rising incidence of tularaemia in Germany or the Ebola outbreak in West Africa in 2014/2015).

As a reference institution for specific highly pathogenic biological agents, ZBS harbours BSL-3 and BSL-4 high contain-

ment laboratories and conducts research activities necessary for the related tasks, e.g. research in diagnostics, epidemiology and pathogenesis. Some examples for the particular research interests of the centre are the host range of poxviruses, genetics and epidemiology of a newly discovered *Bacillus cereus* biovar *anthracis*, variability and functionality of selected biological toxins, the transmissibility of proteinaceous infectious agents (prions) and rapid and generic diagnostics of pathogens and toxins (e.g. electron microscopy, next generation sequencing, spectroscopy, mass spectrometry and array-based detection technologies). In addition, instruction and training are offered regarding the secure handling of specific highly pathogenic biological agents and the managing of unusual biological events.

Furthermore, in the case of an incident with unusual and high-threat agents it is indispensable to bring together the best available knowledge and to transform it into information and guidance for health professionals that is quickly available and easy to understand. In order to fulfill this task, ZBS works closely together with infectious disease specialists all over Germany and has its own communications abilities. In order to ensure a quick exchange of information and interagency coordination, it serves as a coordinating hub of the Permanent Working Group of Competence and Treatment Centres in Germany (STAKOB) and is interconnected with national (Federal Criminal Police Office [BKA]), Federal Office of Civil Protection and Disaster Assistance [BBK], Federal Centre for Health Education [BZgA], state health authorities) and international institutions and networks (WHO, EU and the Global Health Security Initiative [GHSI]). www.rki.de/zbs-en

“Preparedness for unusual events caused by highly pathogenic agents and the response to them are essential public health functions. The Centre for Biological Threats and Special Pathogens at RKI provides unique capabilities to support the crises management related to highly pathogenic biologicals and to avert health consequences from the population.”

PD Dr. Lars Schaade



Publications

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HEAD OF UNITS ~ Dr. Christian Herzog ~ PD Dr. Andreas Nitsche ~ Prof. Dr. Roland Grunow (*Deputy of the Head of Department*)
Dr. Brigitte Dorner ~ Dr. Michael Laue ~ Dr. Andreas Kurth ~ Dr. Peter Lasch



Biological sample collection during an exercise between operative response teams of law enforcement and public health.

The team was established in response to the anthrax letters that claimed several lives in the US in 2001. It can support and aid federal and local institutions as well as decision-makers in situations where release, spill or leakage of dangerous biological agents is suspected or confirmed. The team is capable of conducting environmental sampling in hot zones (areas where presence of dangerous biological agents is confirmed or most likely). Further, the team analyzes samples taken or supports and advises in safe packaging and transportation measures of samples to competent laboratories for in-depth analysis. Moreover, this team supports federal police during state visits with expert advice and aid in preventive measures

IBBS: Federal Information Centre for Biological Threats and Special Pathogens

The Federal Information Centre for Biological Threats and Special Pathogens (Informationsstelle des Bundes für Biologische Gefahren und Spezielle Pathogene – IBBS) advises on how best to protect public health and reduce health consequences following unusual biological incidents and outbreaks involving highly pathogenic agents. It also supports crisis management during such incidents.



Following the US “Amerithrax” incident, the German Government set up a federal information centre based at the Robert Koch Institute with the aim of providing relevant information for the professional public on bioterrorism relevant agents. Since then, IBBS has played a significant role in strengthening German public health preparedness and response capabilities to unusual biological incidents and outbreaks involving highly pathogenic agents.

Over the last years, IBBS provided expert advice and support to state and local public health authorities and emergency services on different occasions, including suspected bioterrorism incidents, deliberate releases of highly pathogenic agents, white powder incidents, clinical cases of rare, highly contagious and life-threatening diseases, and outbreaks caused by highly pathogenic agents. Most challenging was the coordination of the Ebola preparedness and response activities at RKI during the 2014/2015 outbreak in West Africa.

If an unusual biological incident occurs, IBBS provides relevant authorities with appropriate information on the highly pathogenic agent involved as well as on preparedness and response measures. IBBS gives expert advice on the incident-specific risk assessment and informs on matters related to medical management and infection prevention/control measures. In addition, IBBS informs decision makers at all levels to facilitate evidence-based decision-making. For this purpose, IBBS cooperates closely with experts from RKI on infectious disease epidemiology, hygiene and laboratory analysis among others.

In case of an accidental or deliberate release of a highly pathogenic agent into the environment, initial sampling of visible contaminations will primarily be undertaken by fire services in the immediate incident response. However, strategic sampling to determine the extent of contamination requires expert knowledge. A highly qualified biological incident response team at IBBS is trained and prepared to undertake strategic environmental sampling in situations beyond the capabilities of local and state authorities. It also collaborates closely with police enforcement bodies to ensure adequate sampling at crime scenes.

The management of patients infected by a highly pathogenic agent is very challenging. The Permanent Working Group of Competence and Treatment Centres for Highly Contagious, Life-threatening Diseases in Germany (Ständiger Arbeitskreis der Kompetenz- und Behandlungszentren für hochkontagiöse und lebensbedrohliche Erkrankungen –



**“Prepare. Respond. Recover.
We support and advise
crisis management in all phases
of unusual biological
incidents and outbreaks.”**

Dr. Christian Herzog



STAKOB) brings together experts on public health preparedness and response, as well as on the clinical management of patients with highly contagious and life-threatening diseases. IBBS operates the STAKOB office, supports the coordination of the working group and ensures around-the-clock availability of STAKOB experts for consultation on the clinical management of these patients.

To ensure optimal preparedness for unusual biological incidents and outbreaks involving highly pathogenic agents, IBBS identifies high-priority biological agents and develops preparedness and response frameworks as reference guides. These frameworks provide relevant information and practical, evidence-based recommendations for preparedness and response measures. They also support decision-makers’ strategic decisions taking. The process to develop and revise these frameworks supports preparedness activities at all levels. All relevant stakeholders are engaged in this process and practical solutions for specific problems are discussed and developed together. To increase operational preparedness and capabilities, IBBS organizes regular courses on Advanced Management of Biological Threats (AMBIT), which include table-top exercises and practical training sessions. Information on highly pathogenic agents and unusual biological incidents are provided regularly to the professional public using modern communication tools such as webinars, podcasts and short video sequences.

IBBS is also engaged internationally in supporting countries in their efforts to be well prepared for unusual biological incidents. Together with STAKOB and in close coop-

eration with local partners, IBBS strengthens the capacity of countries to manage safely patients with highly contagious and life-threatening diseases in healthcare facilities.

Overall, IBBS supports state and local authorities in Germany in their preparedness and response activities to biological incidents of low probability but high consequence for public health.
www.rki.de/ibbs-en

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ZBS 1: Highly Pathogenic Viruses

The unit ZBS 1 addresses questions regarding rare and emerging viral diseases which are often caused by viruses of high pathogenicity. This includes viruses that can be imported to Germany from foreign countries and viruses that are suspected to be abused in bioterrorist attacks including viruses purposely genetically modified.

For these rarely occurring viruses, ZBS 1 provides rapid and reliable diagnostics. Since only a limited number of diagnostic laboratories focus on these rare diseases worldwide, there is little interest in the development of commercial test systems. In order to provide rapid and reliable diagnostics, ZBS 1 has developed particular skills in the rapid design, establishment and adjustment of such molecular diagnostic test systems. More than 70 real-time PCR systems are available to exclude or confirm known viral diseases, detecting minute numbers of viral genomes in clinical or environmental specimens in a few hours only. Furthermore we widened the diagnostic view by using generic PCR systems and by application of massive parallel sequencing techniques. Here, we develop detailed lab protocols and bioinformatics approaches for the identification of known as well as unknown pathogens. This spectrum of molecular cutting-edge methods in principle enables ZBS 1 to identify any virus in appropriate specimens.

Hence, ZBS 1 supports national and international outbreak investigations, but also helps to elucidate individual cases suspected to suffer from rare viral diseases.

ZBS 1 has another strong focus on serological diagnostic approaches which are not only used for primary diagnostics, but also for sero-epidemiological studies of rare diseases. Immunofluorescence tests, ELISAs, neutralization tests and modern multiplex techniques are established and are being steadily improved. To characterize viruses, they can be propagated in cell culture up to level BSL-3.

Because one of the major threats of bioterrorism is the deliberate release of Variola virus, the causative agent of the eradicated disease smallpox, ZBS 1 has developed a complete set of diagnostic tools for the identification and differentiation of poxviruses. As the German Consultant Laboratory for Poxviruses, accredited according to ISO 15189 and ISO 17025, we routinely investigate clinical specimens suspected to contain any poxvirus. We give advice and support to clinicians regarding differential diagnoses and suggest options for therapy and are the appointed German representative to the WHO committee discussing the future of Variola viruses.

ZBS 1 is coordinating the German Laboratory Network for the Diagnostics of Bioterrorism Agents (NaLaDiBa) aiming at the improvement of the molecular pathogen detection particularly in environmental samples. The strong focus on diagnostics makes ZBS 1 a reliable partner also in various international projects, aiming at strengthening pathogen iden-

“With our work we intend to contribute to a better understanding and control of highly pathogenic viruses.”

PD Dr. Andreas Nitsche

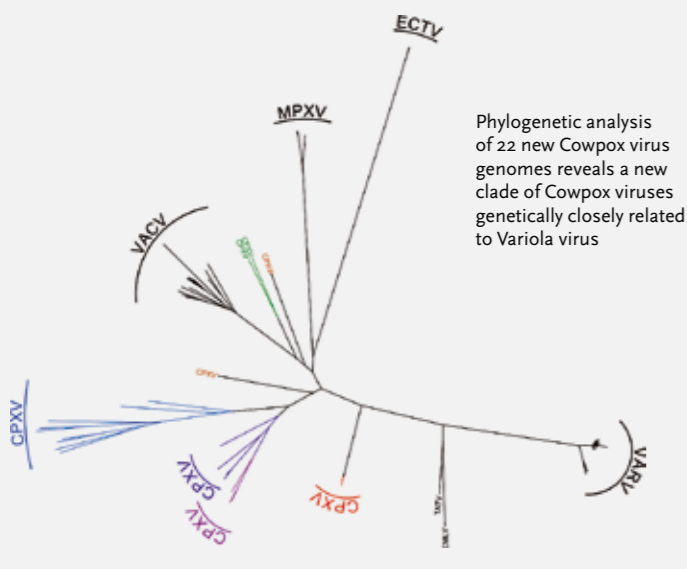
tification to be jointly better prepared to react to public health emergencies of international concern. We are also using and improving the diagnostic skills for capacity building, like the establishment of diagnostic laboratories in various African partner countries. For example, in 2015 we set up a diagnostic laboratory to help control the Ebola outbreak.

The second main pillar of our work is basic research on mechanisms that determine the pathogenicity of highly pathogenic viruses, like poxviruses, flaviviruses and bunyaviruses. One major field we are working in is the host range of poxviruses. So far, it is not understood why Variola virus is strongly restricted to humans while genetically closely related poxviruses are either restricted to certain animal species, like Camel pox virus, or can infect nearly any vertebrate species known, like Cowpox viruses. Full genome sequencing of a huge number of clinically occurring Cowpox viruses showed that a group of Cowpox viruses circulating in Germany is genetically very closely related to Variola virus. To further elucidate this host range phenomenon, we are investigating candidate proteins with classical molecular and virological techniques as well as with modern proteomics, genomics and transcriptomics. The techniques allow us to investigate the biology of the entire infected cell on various levels. Our research projects are complemented using organoids to better simulate the situation in infected tissues, and, where necessary, animal models. In further projects we are investigating the immune response to infection with various viruses or vaccine candidates and are participating in studies identifying new antiviral substances.

Finally, we are pursuing several projects in the field of virus discovery using mainly molecular techniques, including NGS, which closes the circle to the diagnostic applications of molecular diagnostics in ZBS 1.



Human Cowpox infections transmitted by domestic animals.
A: typical lesion,
B: atypical lesion



Phylogenetic analysis of 22 new Cowpox virus genomes reveals a new clade of Cowpox viruses genetically closely related to Variola virus



Service units run by ZBS 1

PCR facility

ZBS 1 is responsible for one of the accredited PCR facilities at the RKI, where diagnostic PCR tests can be performed. We provide qualified personnel for instructions and maintenance of the facility, support colleagues in all questions of PCR diagnostics and assist in designing and validating PCR assays for research and diagnostic applications.

BSL-3 laboratory

The RKI runs different BSL-3 laboratories. ZBS 1 ministers the virological BSL-3 laboratory. Qualified personnel are providing lab introductions according to the regulations regarding good laboratory practice, biosafety and biosecurity.

Sequencing laboratory

The central sequencing laboratory of the RKI offers various variants of DNA sequencing, such as Sanger sequencing (accredited according to ISO 17025) for diagnostic and research purposes, pyrosequencing and next generation sequencing (NGS). The present focus of our work here is the evaluation of NGS instruments and applications for their usefulness in the completion of RKI duties as well as in research projects. We support full genome sequencing, metagenomics, RNAseq, ultradeep sequencing and further approaches on request. We offer advice on questions of sequencing technologies in internal and external collaborations. www.rki.de/zbs1-en

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ZBS 2: Highly Pathogenic Microorganisms

ZBS 2 focuses mainly on bacterial pathogens of risk group 3 such as the causative agents for anthrax, tularemia, plague, melioidosis, glanders, brucellosis, and Q-fever. For these pathogens, ZBS 2 provides flexible accredited laboratory diagnostics according to DIN EN ISO 15189: 2014 and 17025: 2005 and is running a BSL-3 laboratory in addition to BSL-2 laboratories. Depending on the pathogen, various diagnostic approaches are available, including isolation by cultivation using appropriate nutrient media, antimicrobial susceptibility testing, molecular detection, and serology. In addition, ZBS 2 provides typing of *Vibrio cholerae* isolates (serotypes O: 1 and O: 139, Ogawa and Inaba; biotypes classical and El Tor) as well as detection and quantification of the cholera toxin (CTX).

The diagnostics also include the laboratory analyses of suspected bioterrorism samples for bacterial threats and other agents in collaboration with other units of ZBS. The spectrum of diagnostic methods including a number of in-house tests will be continuously developed further and adapted to best international practices and standards. Therefore, a main focus is the quality assurance of the diagnostic approaches, for which the unit is coordinating international activities, currently the EU Joint Action on "Efficient response to highly dangerous and emerging pathogens at EU level – EMERGE" with 38 partners from 25 countries. A bacterial strain collection is maintained for the production of reference materials used in international and national proficiency tests. ZBS 2 comprises the German Consultant Laboratories for anthrax, caused by *Bacillus anthracis*, and tularemia, caused by *Francisella tularensis*.

The research activities of ZBS 2 on questions of epidemiology and ecology, pathogenesis, and decontamination are consequently mainly focused on the two above-mentioned zoonotic bacterial pathogens. Besides classical *B. anthracis*, a cooperative research focuses on the investigation of patho-mechanisms and epidemiology of a new pathogen, named by us as *Bacillus cereus* biovar *anthracis*. This bacterium has been causing a number of deadly anthrax-like infections in non-human primates in West Africa. Currently it appears that

this pathogen is distributed in Africa much wider than thought initially, and the impact on the human population is studied together with partners at RKI, in Africa and other international institutes. The pathogen is unusual because it contains the two virulence plasmids pXO1 and pXO2 of *B. anthracis* in a chromosomal background of *B. cereus*. The consequences of this genetic composition for the pathological mechanisms are studied in ZBS 2 together with other international partners. In addition, classical *B. anthracis* causes outbreaks not only in many other countries but also sometimes in Germany

"The natural prevalence of highly pathogenic bacteria might be relatively low in Germany, but these pathogens have always the potential for causing severe diseases and even large outbreaks. Therefore, we need quality-assured diagnostics and research for better understanding the epidemiology, ecology, and pathogenicity of these bacteria in order to contribute to the health of our society."

Prof. Dr. Roland Grunow

like in cows in 2012 and in 2014. In 2009/2010 and in 2012, anthrax cases were reported in heroin users in several European countries and Germany. ZBS 2 was involved in the diagnostics, phylogenetic typing, and management of the German cases. Together with other international partners we conducted studies on the molecular epidemiology of the obtained isolates, revealing common sources of the causative



strains for both epidemics and a case that occurred several years before. As *B. anthracis* forms very resistant spores, ZBS 2 conducted intensive research on proper inactivation and decontamination approaches for situations of natural and intentional release of these spores.

Tularemia caused by *Francisella tularensis* is a relatively rare zoonosis in Germany, although ZBS 2 contributed in showing that it is probably highly underestimated in the human and wild animal population. Therefore, the unit conducts studies on the natural prevalence, possible reservoirs, and environmental resistance of this pathogen. Several isolates of this bacterium obtained from wild animals were studied together with national and international partners by whole genome sequencing and modern genetic analyses, revealing a relatively high genetic diversity of *F. tularensis* in the study region. From this the introduction of the pathogen from other parts of Europe can be deduced. Besides these observations, ZBS 2 (working group "Cellular Interactions of Bacterial Pathogens") together with national collaborators discovered a new *Francisella* species in Germany, underlining the diversity of this pathogen in nature. It is of special interest to study the mechanisms of the pathogen-host interactions and pathogenicity of the facultative intracellular bacterium *F. tularensis* which is conducted in comparison with other intracellular pathogens like *Legionella pneumophila*. This also includes attempts to discover unknown cellular reservoirs for *F. tularensis* including Amoeba.

ZBS 2 has acquired special knowledge in laboratory bio-risk management which is applied for own purposes but

also disseminated on national level and to international partners in the framework of scientific projects and international initiatives including those supported by the German Federal Foreign Office.

Overall, ZBS 2 is keeping and considering in our work the historical traces by Robert Koch on diseases like anthrax and cholera, but certainly Robert Koch would also be interested in all other bacterial diseases we are dealing with.

www.rki.de/zbs2-en

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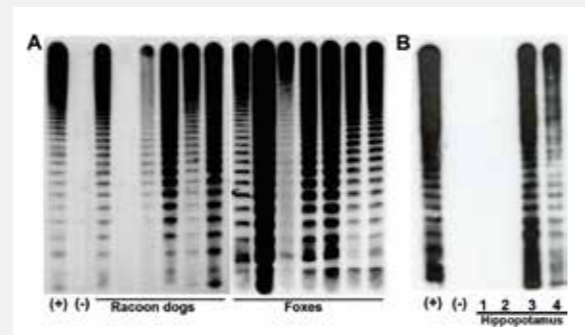
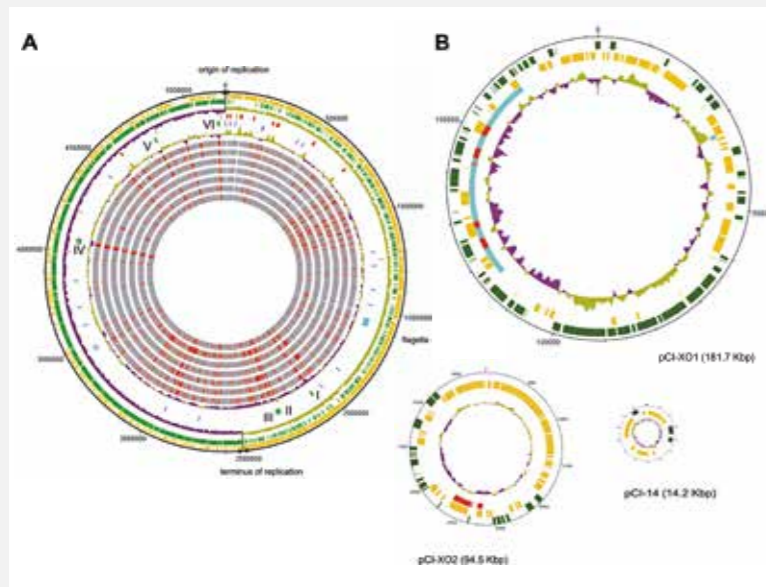


Figure 1 (left): Circular maps of "*B. cereus* bv *anthracis*" chromosome (A) and plasmids (B). [Klee SR et al., *PLoS One*. 2010 Jul 9; 5(7): e10986]

Figure 2: Detection of antibodies against *F. tularensis* in wild animals. A: Examples of racoon dogs and foxes. B: Documentation of seroconversion in a hippopotamus by sera from 2001 (1), 2003 (2), 2004 (3), and 2006 (4). [Kuehn A, Schulze C, Kutzer P, Probst C, Hlinak A, Ochs A, Grunow R. Tularemia seroprevalence of captured and wild animals in Germany: the fox (*Vulpes vulpes*) as a biological indicator. *Epidemiol Infect.* 2013 Apr; 141(4): 833–840.]

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ZBS 3: Biological Toxins

ZBS 3 conducts research into biological toxins of bacterial and plant origin which are classified as potential agents of bioterrorism. Among the proteotoxins investigated are the plant toxins ricin from *Ricinus communis* and abrin from *Abrus precatorius* as well as the bacterial botulinum neurotoxins (BoNT) from *Clostridium botulinum* and staphylococcal enterotoxins (SE) from *Staphylococcus aureus*. Based on their characteristics, biological toxins are at the interface of classical biological and chemical agents: they are substances produced by living organisms, but they are not living, hence unable to reproduce, propagate or spread from person to person. Therefore, they share many of the characteristics of classical chemical agents. However, since high molecular weight proteins like ricin or BoNT exert an enzymatic function within the body amplifying their potency, they are clearly different from low-molecular-weight chemical agents and, additionally, they display orders of magnitude of higher specific toxicity to humans.

Generally, biological toxins are relevant in the health and food sector as well as in the security sector. On the one hand, biological toxins are linked with natural intoxications worldwide and some of them cause severe and recurrent diseases (e.g., food poisoning induced by SE or the life-threatening neuromuscular disease botulism induced by BoNT). On the other hand, the relative ease in preparing some of the mentioned toxins and the world-wide availability of the biological sources qualify them as potential agents of bioterrorism (e.g. the ricin threat letters in the US in 2003 and 2013). In recognizing that biological toxins are a source of natural intoxications as well as potential agents of bioterrorism, it is necessary to develop strategies for their rapid and sensitive detection as well as precise and unambiguous identification in order to enable adequate management decisions on countermeasures.

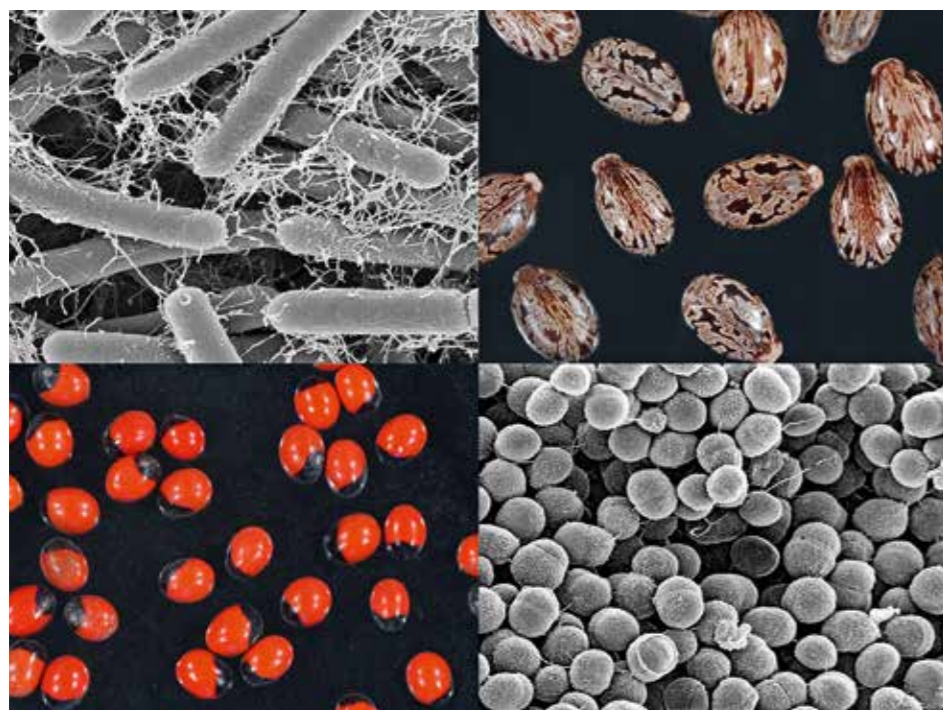
- In this context, the work performed in ZBS 3 focuses on
- ▶ the detection of proteotoxins, using modern immunological, functional, mass spectrometric and molecular biological techniques;
 - ▶ the prevalence, variability as well as epidemiology of biological toxins, especially toxins produced by *C. botulinum* (Consultant Laboratory for *C. botulinum*), as well as
 - ▶ mechanisms affecting pathogenicity of the underlying organisms.

“Biological toxins are relevant in the health sector as molecules inducing severe and recurrent intoxications worldwide. In the security sector selected biological toxins are known as potential agents of bioterrorism. Nevertheless, dissecting the toxins’ mechanism of function within the body teaches us a lot about the physiological process of life.”

Dr. Brigitte Dorner

Diagnostics

Based on its specific expertise, the group has developed a portfolio of highly specific monoclonal antibodies directed against proteotoxins that are now implemented in different complementary detection approaches and commercial platforms,



Sources of highly potent biological toxins: *Clostridium botulinum* (top left), *Ricinus communis* (top right), *Abrus precatorius* (bottom left), *Staphylococcus aureus* (bottom right)



among them mobile array-based technologies, suspension arrays and surface plasmon resonance sensors. In order to foster the identification of best practices for toxin detection, ZBS 3 coordinated a large European project called EQUATox (Establishment of Quality Assurances for the Detection of Biological Toxins of Potential Bioterrorism Risk; www.EQUATox.eu) from 2012 to 2014, joining 35 laboratories from 20 countries. EQUATox focused in-depth on biological toxins and their intricacies with respect to detection, identification and reference materials – topics that are relevant for an efficient management of natural or man-made incidents involving biological toxins. By building a network of expert laboratories and strengthening their technical exchange, the project helped to improve the analytical capabilities present in European countries and to minimise health and security threats posed by biological toxins.

Consultant Laboratory for Clostridium botulinum Prevalence, variability and epidemiology

ZBS 3 is involved in national and international outbreak analysis as well as in criminal investigations and provides diagnostic services, scientific consultation and advice to clinicians and public health authorities. In 2014, the group has been assigned as Consultant Laboratory for *C. botulinum*. In this context, ZBS 3 conducts research on the molecular and functional variability of BoNT and the identification and characterization of novel BoNT subtypes.

Mechanisms of pathogenicity

Together with leading scientists in the field, ZBS 3 addresses the question how botulinum neurotoxins are absorbed by the intestinal epithelium within the body. Understanding the mechanism of toxin action *in vivo* might pave the way for the development of novel therapeutics and tailor-made antitoxins.

www.rki.de/zbs3-en

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ZBS 4: Advanced Light and Electron Microscopy

ZBS 4 serves as the central microscopy unit of the institute and fulfills the following major tasks:

- ▶ Diagnostics (Consultant laboratory for Electron Microscopic Diagnostics in Infectious Diseases)
- ▶ Core facility for microscopy and photography
- ▶ Research on special pathogens

Diagnostics

Diagnostic electron microscopy is a powerful method for the rapid screening of samples for pathogens. Its “open view” allows a direct detection of infectious entities (viruses, bacteria, parasites) in their respective setting, which provides valuable information, and leads to an expedited diagnosis or risk assessment. For this reason, diagnostic electron microscopy is used as a scouting method and independent control in emergencies, like outbreaks or patient cases of severe diseases with unknown cause (Fig. 1). In our role as the consultant laboratory for diagnostic electron microscopy of infectious pathogens we provide advice, second opinion, test material and advanced training for colleagues worldwide.

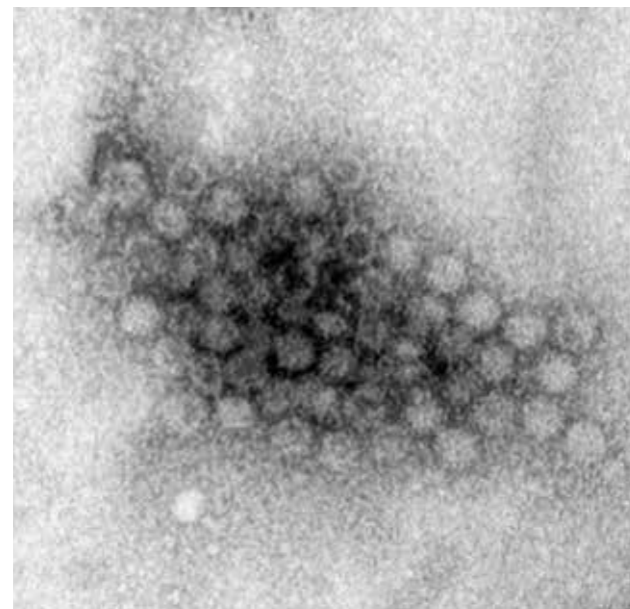


Figure 1: Transmission electron microscopy of *Norovirus* from a diagnostic sample of the large gastroenteritis outbreak in 2012. Diagnostic electron microscopy was used as an independent control for the diagnosis based on nucleic acid amplification techniques and to exclude other viruses involved. Width of a single virus particle is about 30 nm

Core facilities

The microscopy facility hosts a couple of special microscopes (laser, electron and live cell imaging microscopes) and related sample preparation equipment and, most importantly, people who are specialists in the various types of microscopy. The basic goal of the microscopy core facility is to provide optimal support for all lab-based scientists of the institute.

The photography facility provides imaging services for the entire institute: from the photography of bacteria or fungi on agar plates and other objects of interest, over digital image-processing and pre-print preparations, up to the documentation of special occasions of the institute or the Federal Ministry of Health.

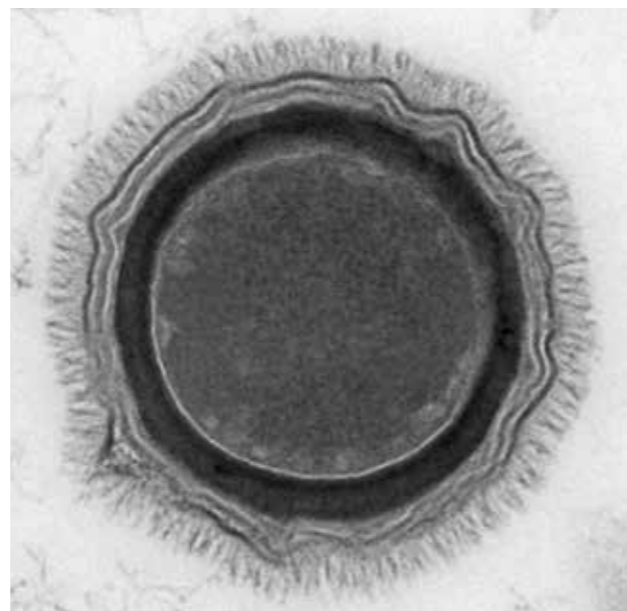


Figure 2: Transmission electron microscopy of a cross section through a spore of *Bacillus anthracis* (anthrax) which reveals the different coat layers including the hairy exosporium. Width of the spore is about 500 nm

“The reasons for using microscopy at the Robert Koch Institute have not changed much during the last 125 years: We visualize microorganisms to find the cause of an infectious disease and to examine how they live and perform.”

Dr. Michael Laue



Research

The research of the group follows two major lines: (1) Improvement of diagnostic electron microscopy and microscopic methods to study pathogenic microorganisms and (2) basic and applied research on bacterial endospores and pathogenic biofilms, which both represent special forms of pathogenic microorganisms.

Improvements in diagnostic electron microscopy focuses on speeding up procedures, increasing specificity, decreasing the detection limit and providing better biosafety, which finally results in a quicker and superior diagnosis.

Bacterial endospores (Fig. 2) and bacterial biofilm are both special forms of bacterial life, which are characterized by an increased resistance against environmental stress and disinfectants. Our goal is to explore the mechanisms behind this remarkable resistance and how these forms can be treated, whenever they pose a problem to public health, as in the transmission of *Clostridia* or biofilm in wound infections.

www.rki.de/zbs4-en; www.rki.de/cl-em

Publications

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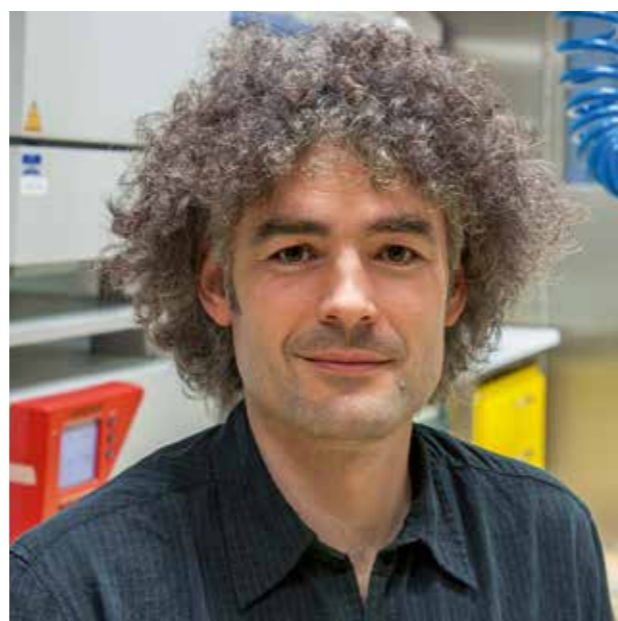
ZBS 5: Biosafety Level 4-Laboratory

The Centre for Biological Threats and Special Pathogens 5 (ZBS5) was established in 2012. Situated within the Robert Koch Institute, ZBS5 was appointed to operate a biosafety level 4 (BSL-4) laboratory to prioritize research of emerging and re-emerging viral pathogens, in particular those that cause severe haemorrhagic fever in humans. The agents include risk group 4 pathogens such as Ebola virus, Crimean Congo haemorrhagic fever virus, Lassa virus, and Nipah virus, and many of these agents are considered to be the emerging diseases most likely to cause major epidemics by the World Health Organization, for which preventive or therapeutic interventions are not available.

Upon commission of the BSL-4 laboratory in 2016 the group will investigate viral persistence in biological and environmental samples, which will lead to the development and establishment of diagnostic methods for risk group 4 pathogens. As part of a global call for more detailed research into dangerous pathogens, ZBS5 will further develop strategies for the prevention and control of highly pathogenic viruses together with the Federal Information Centre for Biological Threats and Special Pathogens and ZBS1. The research group will implement cutting edge technologies to study viral transmission in reservoir hosts, viral ecology, viral pathogenesis, and host immune response to infection.

ZBS5 works closely together with other BSL-4 laboratories in Germany and worldwide and is partner of several international EU projects including EVIDENT (Ebola Virus Disease – correlates of protection, determinants of outcome, and clinical management) and EMLab (European Mobile Laboratory). Within the latter project, diagnostic investigations have been repeatedly performed during the Ebola outbreak in West Africa in 2014/2015. ZBS5 also implements its expertise for the Technical Rules for Biological Agents (TRBA) established by the Committee for Biological Agents (ABAS).

www.rki.de/zbs5-en



“One of the few good news from the tragic Ebola epidemic in West Africa is that it stresses the wake-up call: we must prepare for future outbreaks of deadly diseases that may spread more effectively than Ebola.”

Dr. Andreas Kurth

Test operation of the new biosafety level 4 (BSL-4) laboratory at the Robert Koch Institute.

The BSL-4 laboratory allows a safe handling of pathogens of the highest risk group such as Ebola, Marburg and Lassa viruses. The laboratories have their own air, power and water supply; multi-tiered security systems prevent pathogens from being released



Publications

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ZBS 6: Proteomics and Spectroscopy

Main contribution

The core expertise of the unit “Proteomics and Spectroscopy” (ZBS 6) is on the use of proteomics and modern vibrational, i.e. infrared (IR) and Raman, spectroscopy for the characterization of biological agents such as intact microorganisms, cells and proteins. ZBS 6 conducts research projects in the fields of rapid diagnostics of microbial pathogens and the pathogenesis of protein misfolding diseases such as prion diseases, Alzheimer’s disease (AD) and Parkinson’s disease (PD). In addition, investigations are performed regarding the inactivation of highly pathogenic bacteria and the decontamination of surgical instruments.

ZBS 6 has extensive expertise in conducting research projects on the development of Raman- and IR spectroscopy-based methods for the detection, differentiation and identification of pathogenic microorganisms. In particular, Raman and IR microspectroscopy are extensively used to identify and classify bacteria down to the strain level. Raman and IR microspectroscopy, and vibrational spectroscopic imaging techniques are employed in concert with modern methods of bioinformatics to characterize risk group 3 (RG3) pathogens also in the context of bioterror diagnostics.

To identify pathogenic microorganisms we employ also proteomic techniques such as matrix-assisted laser/desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) or electrospray-ionisations mass spectrometry in combination with separation techniques (HPLC, 2D PAGE). Specifically MALDI-TOF MS has been widely used as a tool for objective, simple, rapid and cost-effective identification

“It is necessary to look at the results of observation objectively, because you, the experimenter, might like one result better than another.”

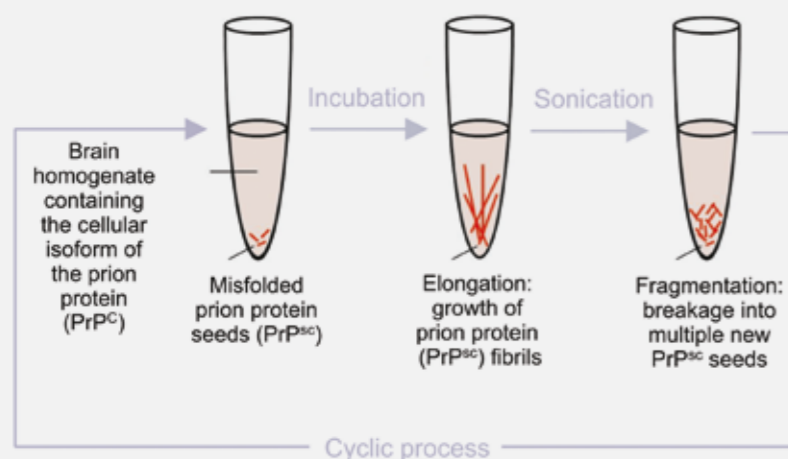
Richard P. Feynman

of bacteria. In the past ZBS 6 has developed a MALDI-TOF MS compatible inactivation protocol for RG3 pathogens.

The scientific and technical staff of ZBS 6 combines furthermore long-standing expertise and research experience in the field of neurodegenerative protein aggregation diseases (proteinopathies). The pathological aggregation of proteins such as amyloid-beta ($A\beta$) and tau in AD, alpha-synuclein (αS) in PD and prion protein (PrP) in prion diseases constitute an important research focus of ZBS 6.

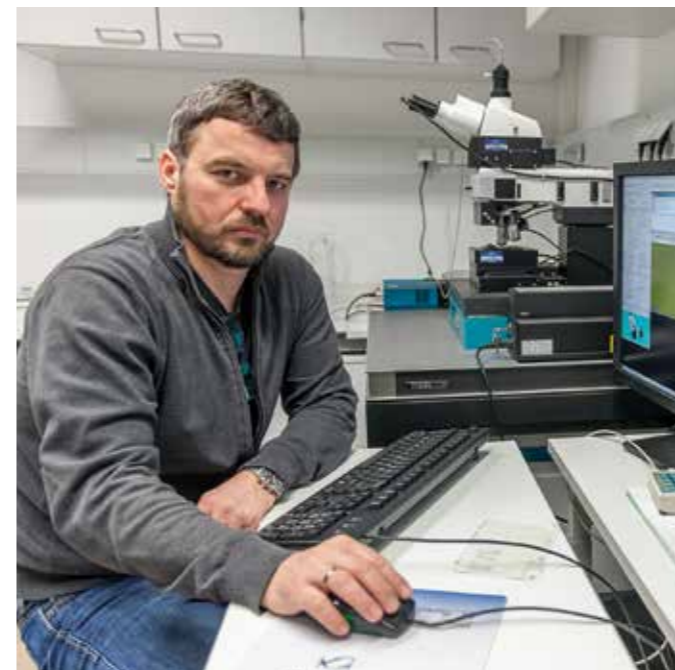
Experimental studies in mouse models indicated that AD- and PD-associated pathologies may be transmissible. In other words, in AD or PD as well as in other neurodegenerative proteinopathies misfolded protein assemblies could act as “seeds”

Protein Misfolding Cyclic Amplification (PMCA)



Proteomic equipment available at ZBS 6.
A: AutoFlex Speed MALDI-TOF mass spectrometer (Bruker Daltonics). B: EASY-nLC Liquid Chromatograph (Thermo Scientific). C: LTQ Orbitrap ESI mass spectrometer (Thermo)

Principle of protein misfolding cyclic amplification (PMCA) for the cell-free propagation in vitro of the infectious, pathological isoform of the prion protein (PrP^{Sc})



to trigger further protein misfolding in a manner reminiscent of prion diseases. Importantly, the potential transmissibility of AD or PD pathologies may also represent an issue in regard of the safety of blood, blood products, and surgical instruments. To address these concerns we are studying the presence of seeding activity in tissues obtained from human AD and PD patients in transgenic mouse models which are permissive for the propagation of AD- or PD-associated pathologies.

Finally, we explore the molecular and structural basis of conformational templating of $A\beta$, tau, αS and PrP by combining biochemical approaches, such as the protein misfolding cyclic amplification (PMCA), with biophysical methods such as IR microspectroscopy. This is expected to further elucidate the commonalities and discrepancies of AD, PD and prion diseases in terms of the infectivity, pathogenicity and association with heterogeneous disease phenotypes of different $A\beta$, tau, αS or PrP conformers.

www.rki.de/zbs6-en

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Project Groups

First established in 1998 following a recommendation of the German Council of Science and Humanities, the project groups complement the scientific departments of the RKI by concentrating on acute research topics. The German Council of Science and Humanities noted that such structures are particularly suited to focus research activities and create synergistic effects. The project groups are therefore widely exempt from official duties but it is expected that the project groups acquire third-party funding.

An evaluation of the groups is done regularly by the Scientific Advisory Board of the RKI, normally every three years. Depending on the verdict of the evaluation process the project groups can be prolonged, changed in the research direction, or the staff can be integrated back into the scientific departments.

Currently, there are five project groups. The research topics range from immune defense mechanisms to virulence and pathogenicity of *Acinetobacter baumannii* and *Salmonella*. These bacteria are good examples of special pathogens with high impact on public health. One project group deals with the epidemiology of highly pathogenic microorganisms; the current Ebola outbreak proved the importance for the RKI to maintain groups which work in this area. Another group dedicates its efforts to the modelling of infectious diseases.

The work of this group was also urgently needed during the Ebola outbreak. The research results contributed considerably to a substantiated risk assessment of a possible spread of Ebola from Africa to Europe.

In summary, the project groups serve as an effective tool for basic research and contribute significantly to RKI's task as an "antenna" for health risks and emerging threats.

www.rki.de/p-en

The following project groups are going to be introduced subsequently:

- ▶ P 1: Immune Defense Mechanisms
- ▶ P 2: *Acinetobacter baumannii* – Biology of a Nosocomial Pathogen
- ▶ P 3: Epidemiology of Highly Pathogenic Microorganisms
- ▶ P 4: Epidemiological Modelling of Infectious Diseases
- ▶ P 5: Virulence Factors in *Salmonella* and *Campylobacter*



P 1: Immune Defense Mechanisms

In our unit we try to understand how T cells, which constitute a major part of the memory-bearing adaptive immune system, contribute to fighting infections. Initially, we searched for essential molecules initiating and driving activation of T cells in humans. Thus, we originally cloned CD40L and ICOS, described the function of these T cell-specific surface molecules, and identified human diseases associated with their loss at the genetic level ("Immunodeficiency with Hyper-IgM", "ICOS-deficiency").

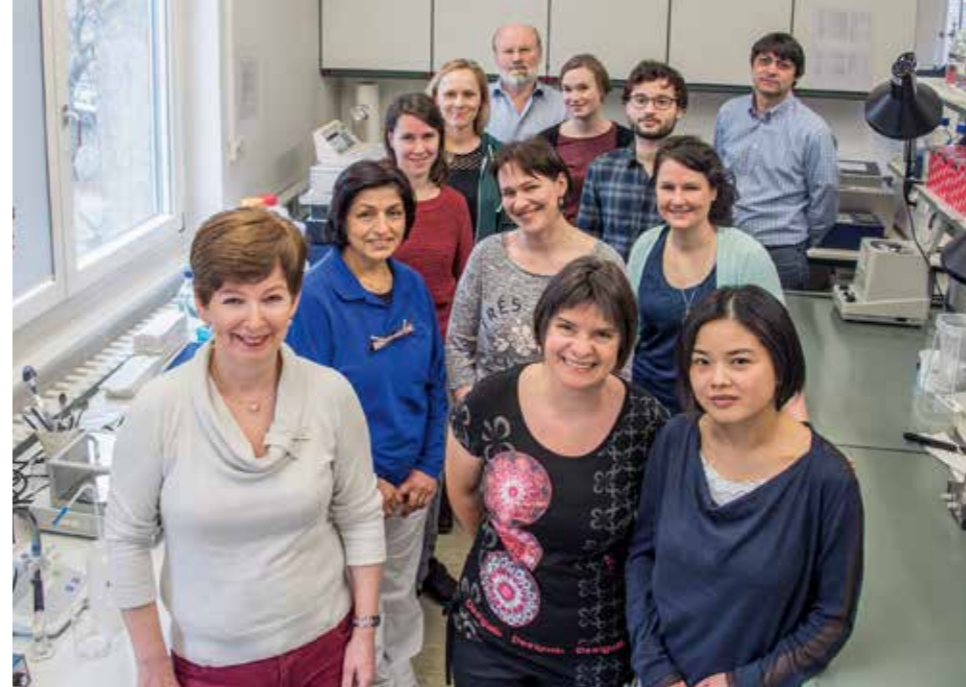
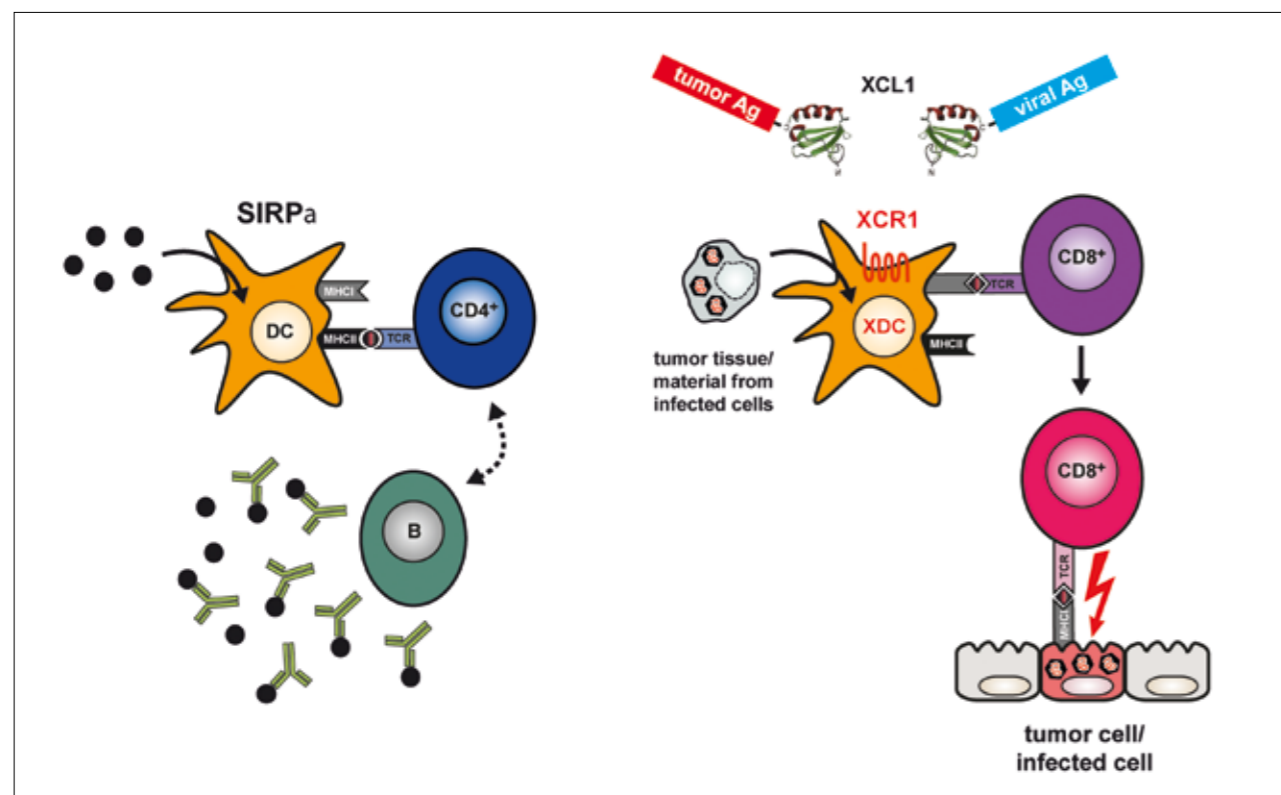
Later, we turned to in vivo experiments in the mouse model in order to better understand how T cells respond to infectious challenge. There, we studied the very early activation of T cells following recognition of antigen. Self-proteins (self-antigens) are constantly being taken up by highly specialized phagocytic cells, the dendritic cells (DC), and "presented" to T cells. This is how tolerance to "self" is established and maintained, preventing the occurrence of autoimmune diseases. Proteins from infectious agents are also taken up by DC and presented to T cells, but this occurs in an inflammatory context and thus results in a strong activation of T cells, which expand and acquire effector functions (cytokine release, kill). We investigated the difference in the programming of T cells for tolerance versus effector immune response in appropriate models and could identify some central elements in this pivotal decision.

More recently, we turned our attention to DC themselves, since these cells distinguish harmless (self-) proteins from proteins originating from infectious agents, and instruct T cells to respond appropriately. In a first step, we realized that XCR1, a surface molecule, is uniquely expressed on a subset of DC in the mouse, which was known to mainly interact with CD8⁺ T cells (1). Later, we could demonstrate that in humans too, XCR1 is uniquely expressed on the corresponding DC subset (2). Extending previous work from other groups, we then could show that DC can generally be subdivided into two functional types. The SIRPα⁺ DC mainly take up antigens flowing freely in the blood (e.g. viral particles) and present them to CD4⁺ T cells. The activated CD4⁺ T cells then direct B cells to generate antibodies neutralizing these blood antigens (Figure). In contrast, XCR1⁺ DC are specialized on the uptake of cell-associated proteins, which are then presented mainly to CD8⁺ T cells (3). If cells taken up by XCR1⁺ DC are infected, CD8⁺ T cells recognize the foreign proteins originating from the pathogen, become activated, and differentiate into cytotoxic cells capable of eliminating cells infected by this pathogen all over the body (Figure).

In our most recent work, we attempt to exploit this division of labour between different subtypes of DC into a new vaccination principle. It is apparent today that classical prophylactic vaccines are mainly addressing SIRPα⁺ DC and thus induce an efficient antibody response. In order to utilize the second, the cytotoxic arm of adaptive immunity, we have developed

Division of labour between two different types of dendritic cells.

Soluble antigens (e.g. viral particles) in the blood flow are taken up by SIRPα⁺ dendritic cells and presented to CD4⁺ T cells. This results in the activation of the B cell system and production of protective antibodies. In contrast, infected cell material/tumour tissue is taken up by XCR1⁺ dendritic cells and mainly presented to CD8⁺ T cells. These become activated and differentiate into cytotoxic T cells, now capable of eliminating infected/tumour cells all over the body



“We are attempting to translate basic immunological knowledge into a novel vaccination system inducing cytotoxic CD8⁺ T cells.”

Prof. Dr. Richard Kroczeck

a system which allows to target antigens into XCR1⁺ DC in vivo. To this end, we utilize XCL1, the natural small soluble ligand of the XCR1 receptor, as a transporter molecule. Proteins of choice are recombinantly attached to XCL1 and injected in vivo. After binding to XCR1, the proteins are taken up by XCR1⁺ DC, presented to CD8⁺ T cells, which then become cytotoxic effector T cells. We could recently demonstrate that this approach generates effective cytotoxic immunity capable of preventing disease after exposure to certain pathogens, and also preventing the establishment of cancerous tissue in model systems (4). Further, we have developed procedures which dramatically amplify this initial cytotoxic CD8⁺ T cell response (unpublished). As a result, targeting of a protein into XCR1⁺ DC, followed by the amplification steps, induces a massive T cell cytotoxic protection against highly lethal doses of certain pathogens in the mouse. The same approach can be used to instruct the T cell immune system to develop massive cytotoxicity against altered proteins present in cancerous tissue.

Based on these results in the mouse, we will now attempt to translate this knowledge into therapeutic and prophylactic vaccines applicable in humans. We hope that we can develop prophylactic vaccines against infectious agents to which currently no protection exists. At the same time, we hope to establish therapeutic vaccines capable of eradicating various types of cancer.

Finally, in close collaboration with the group of Dr. Andreas Hutloff of the German Rheumatism Centre in Berlin, we have in recent years made some contributions to the understanding of the communication between CD4⁺ T cells and B cells in inflamed tissues (5). www.rki.de/pi-en

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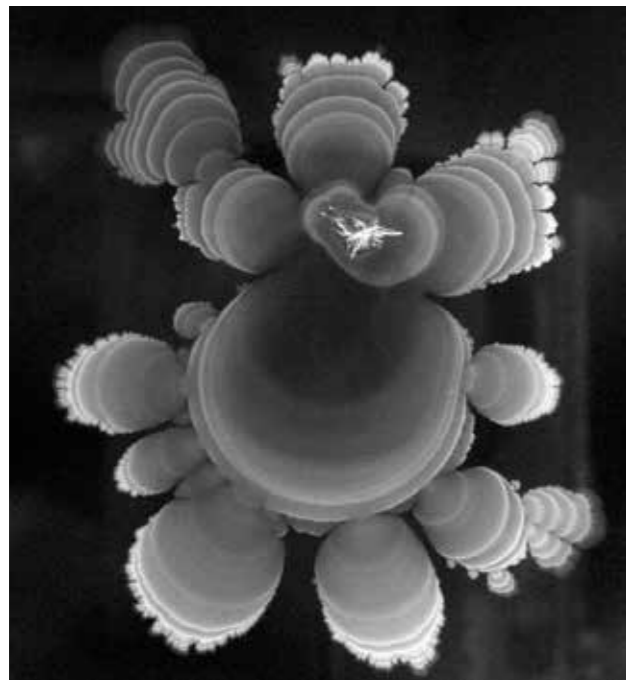
P 2: *Acinetobacter baumannii* – Biology of a Nosocomial Pathogen

Objective

To elucidate the biology of the nosocomial pathogen *Acinetobacter baumannii* in order to contribute to prevention and therapy.

Why working on *Acinetobacter baumannii*?

Nosocomial infections caused by multi-drug resistant pathogens are among the major public health concerns, especially in the light of an ageing population. *Acinetobacter baumannii* is a Gram-negative bacterium which causes nosocomial infections worldwide and progressively develops antibiotic resistance. *A. baumannii* and some other *Acinetobacter* species including *A. pittii* and *A. nosocomialis* are implicated in infections such as ventilator-associated pneumonia, bloodstream infections, meningitis and wound infections, mostly in debilitated patients. Several antibiotic resistance genes found in different Gram-negative pathogens worldwide have originated in *Acinetobacter* spp. illustrating the global interrelatedness of



A colony of *Acinetobacter baumannii* moving along a wet surface

resistance gene pools. While the epidemiology of *Acinetobacter* spp. and their resistance determinants are increasingly studied today, fundamental questions on the biology of these species remain unresolved the answers to which could help significantly in setting up better measures of prevention, surveillance and therapy.

Where does *Acinetobacter baumannii* originally come from?

Most members of the genus *Acinetobacter* are ubiquitous environmental bacteria found in water and soil. By contrast, the natural reservoirs of *A. baumannii* and of other clinically relevant *Acinetobacter* species are poorly defined. Healthy humans only rarely carry *A. baumannii* on their skin, at least

in temperate climates. In order to understand the biology of pathogens, it is however important to study them within their natural “training area”. Only with this knowledge will we be able to deduce optimal prevention strategies, improve diagnostics and possibly develop novel therapeutic options. We are currently studying a number of potential zoonotic reservoirs including livestock from which we have isolated *A. baumannii* at considerable rates. Whole genome sequencing of animal isolates in cooperation with unit 13 and the junior research group “Microbial Genomics” allows us to assess the relevance of these reservoirs for transmission to humans.

What are the secrets of success of this pathogen?

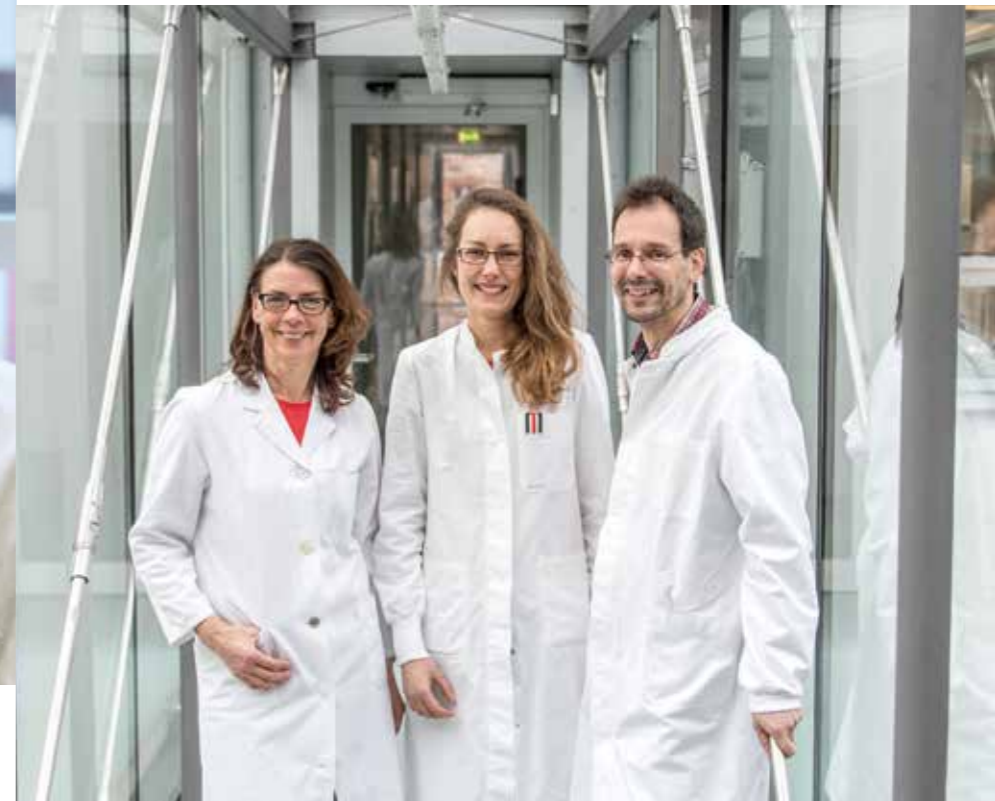
There is a worldwide spread of a few successful clonal lineages of *A. baumannii* in hospitals but also a perpetual influx of novel lineages from unknown reservoirs into the clinical setting. Basically, the clonal lineage isolates show a higher degree of antibiotic resistance compared to non-clonal sporadic isolates consistent with a more recent entry into the hospital environment of the latter. In general, *A. baumannii* is considered highly resistant to desiccation stress and disinfectants. Furthermore, an enhanced capability to form biofilms has been identified in the most successful clonal lineage. Colonization of surface environments is of the utmost importance in the bacterial world, notably also during infection. Motility facilitates initial stages of biofilm formation resulting in increased persistence and antibiotic resistance as well as protection from immune responses. In previous work, we found surface-associated motility to be a common trait of clinical isolates of *A. baumannii* (see Fig. 1) suggesting an important role during colonization and infection of patients and/or persistence in the hospital environment. Therefore, we presently seek to elucidate the molecular basis of motility and biofilm formation in *A. baumannii* in cooperation with colleagues from ZBS4 and DFG Research Unit FOR2251. Within biofilms individual *Acinetobacter* cells communicate in a complex manner including physical and chemical interactions. We are particularly interested in studying how gaseous signalling molecules contribute to biofilm formation and resistance development.

“To really understand *Acinetobacter baumannii* we need to identify its natural reservoirs.”

PD Dr. Gottfried Wilharm

How does *Acinetobacter baumannii* acquire resistance genes?

The development of multi-drug resistance (MDR) is one of the most awesome features of *A. baumannii* and facilitated by horizontal gene transfer (HGT). HGT not only occurs extensively among members of the genus *Acinetobacter*, but also in exchange with *Pseudomonas* spp. and *Enterobacteriaceae*. The global spread of the New Delhi metallo- β -lactamase gene (*bla_{NDM-1}*) exemplifies the existence of “genetic exchange



communities”. The *bla_{NDM-1}* gene was first described in *Enterobacteriaceae*, but its genetic analysis later revealed that it most probably originated in *A. baumannii*. Co-infection involving carbapenem-resistant strains of *A. baumannii*, *Pseudomonas aeruginosa* and/or *Enterobacteriaceae* is a common phenomenon facilitating HGT. However, the modes and conditions of HGT are poorly defined. We could recently demonstrate that many clinical isolates of *A. baumannii* become naturally competent while they move along wet surfaces in a type 4 pilus-dependent manner. The transformability of cells moving along surfaces might thus lead to an acquisition of novel genetic traits thereby increasing persistence, virulence and resistance of *A. baumannii*.

Funding

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www.rki.de/p2-en

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P 3: Epidemiology of Highly Pathogenic Microorganisms

Research

Among the pathogens causing infectious diseases in humans, those originating from animals (so-called zoonoses) are exceptionally important in terms of their number and pathogenicity. They can represent a serious threat to public health. Our group combines different approaches to investigate the sources and reservoirs of such zoonotic microorganisms, mechanisms of their transmission to humans and their evolutionary pathways. We hereby focus mainly on sub-Saharan Africa, which bears a disproportionately high burden of morbidity and mortality due to infectious diseases and is a hotspot for zoonotic disease emergence. Ever growing globalisation leads to fast regional but also international spread of pathogens, as demonstrated by HIV, SARS-Coronavirus, Ebolavirus and H5N1. Therefore, understanding mechanisms of disease emergence in high risk areas is of direct relevance for global public health.

I. Zoonotic pathogens in tropical wildlife and livestock

Group lead: Dr. Fabian Leendertz

We examine the presence of various zoonotic pathogens as well as potential risk factors associated with transmission in humans and animals in several sub-Saharan African countries. All studies are performed in close collaboration with partners in the according countries to foster local capacities for disease detection and control. Our focus is on non-human primates since pathogens readily cross the species barrier to the closely related humans. We also investigate other wildlife species, especially those which have adapted to human settlements (bats and rodents) as well as livestock as intermediate hosts.

At the same time, we collect environmental and epidemiological data in the respective regions. This multifactorial approach enables us to reconstruct potential transmission cycles between humans and animals and to pinpoint sources of pathogen outbreaks.

II. Viral Evolution

Group lead: Dr. Sébastien Calvignac-Spencer

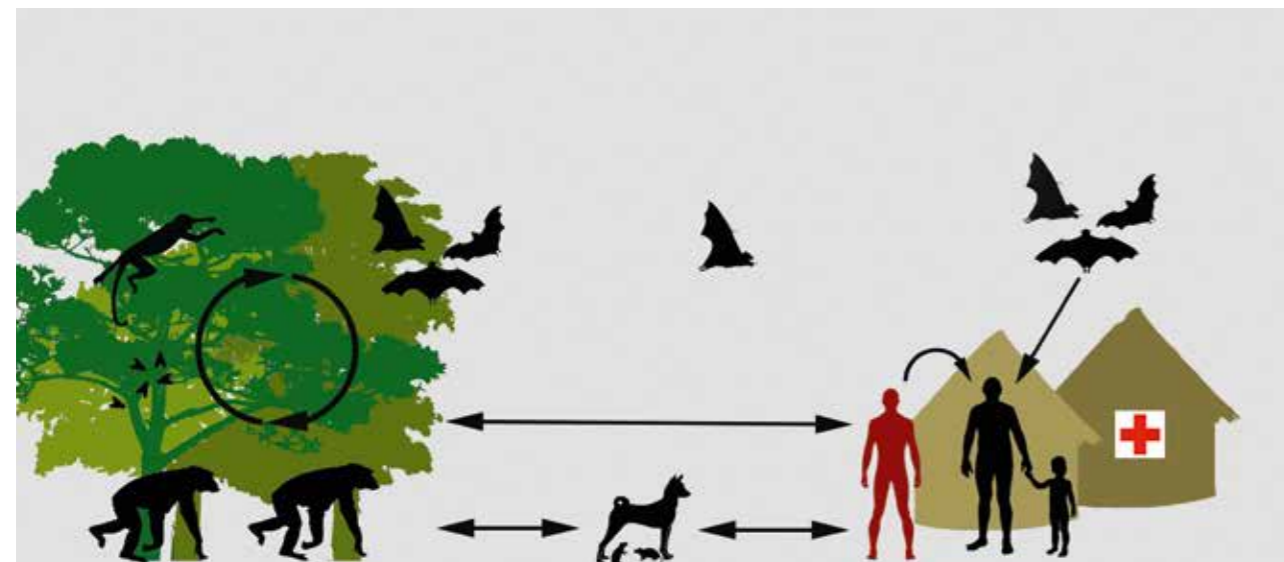
The last decade witnessed the simultaneous development of powerful sequencing and statistical methods. This was particularly profitable to our understanding of the biology, spread and recent evolutionary history of measurably evolving viruses, i.e. RNA viruses, including influenza and Ebola viruses. The deep evolutionary history of many viruses was also considerably clarified. It now seems clear that a number of viral lineages have been associated to their hosts for much longer than previously thought. However, such progresses in our understanding of the long-term evolution of viruses (whether fast or slow evolving) have only rarely been leveraged to investigate public health-related questions.

Our work precisely aims at deriving public health-relevant predictions from the study of the deep evolution of viruses. We do this by focusing on African great apes and bats, and investigating all conceivable sources of information on their co-evolution with viruses – from their own genomes to the genomes of their exogenous viruses, using contemporaneous and historical samples. We use this information to identify ancient host-virus associations and the processes that shaped these associations, e.g. co-divergence, host switches, etc. We expect this will ultimately allow us to pinpoint viral lineages more likely to commit into cross-species jumps, to predict the existence of yet-to-be-discovered human viruses and to identify natural hosts of “orphan” viruses.

III. Surveillance of zoonotic infections in rural Africa

Group lead: Dr. Grit Schubert

Through the transnational project ANDEMIA (African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents) we aim to research and combat acute respiratory tract and gastrointestinal infections, the emergence of antimicrobial resistance and acute febrile disease of unknown cause in sub-Saharan Africa. While this project is a collaborative effort between many units at RKI and several African partners, our group focuses on pathogens of animal



Transmission cycles of zoonotic pathogens among wildlife (e.g. non-human primates), domestic animals (e.g. dogs) and humans in a rural setting in tropical Africa



origin. Rarely have international consortia focused on such common disease syndromes. This is a significant public health oversight because recent studies demonstrate that they are a main cause of morbidity and mortality in sub-Saharan Africa, but are not sufficiently addressed by vertical disease programs.

After identifying the pathogens underlying the above syndromes, we aim to guide appropriate interventions, such as implementing rapid diagnostic tests where appropriate and

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“Understanding mechanisms of disease emergence in high risk areas is of direct relevance for global public health.”

Dr. Fabian Leendertz

introducing infection control measures (e.g. vector control) and outbreak management. Our hypothesis is that locally adopted interventions based on integrated surveillance data (using clinical and laboratory data gathered at various “sentinel” hospital sites) are more effective in improving patient outcomes and disease prevention than vertical disease programs.

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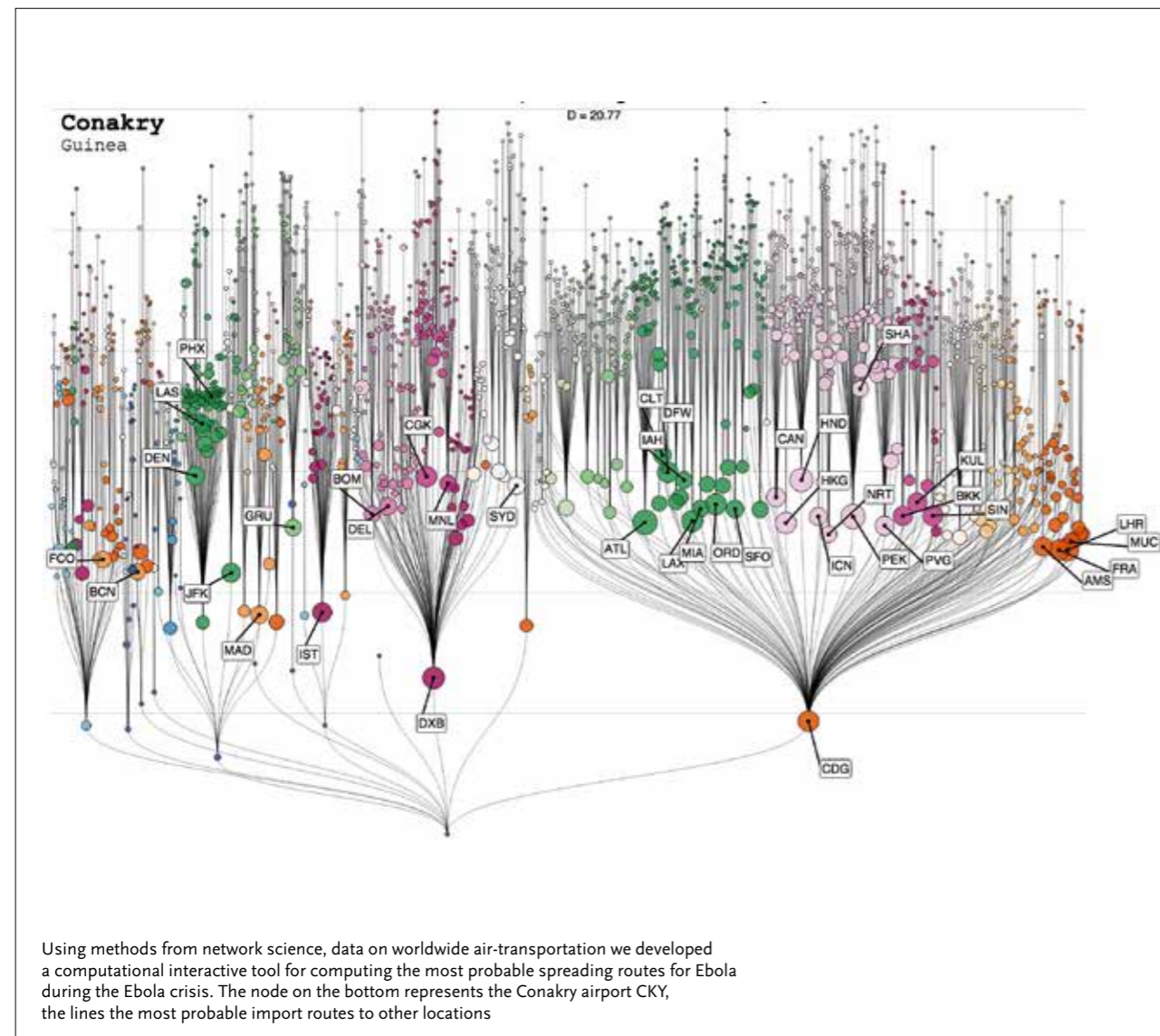
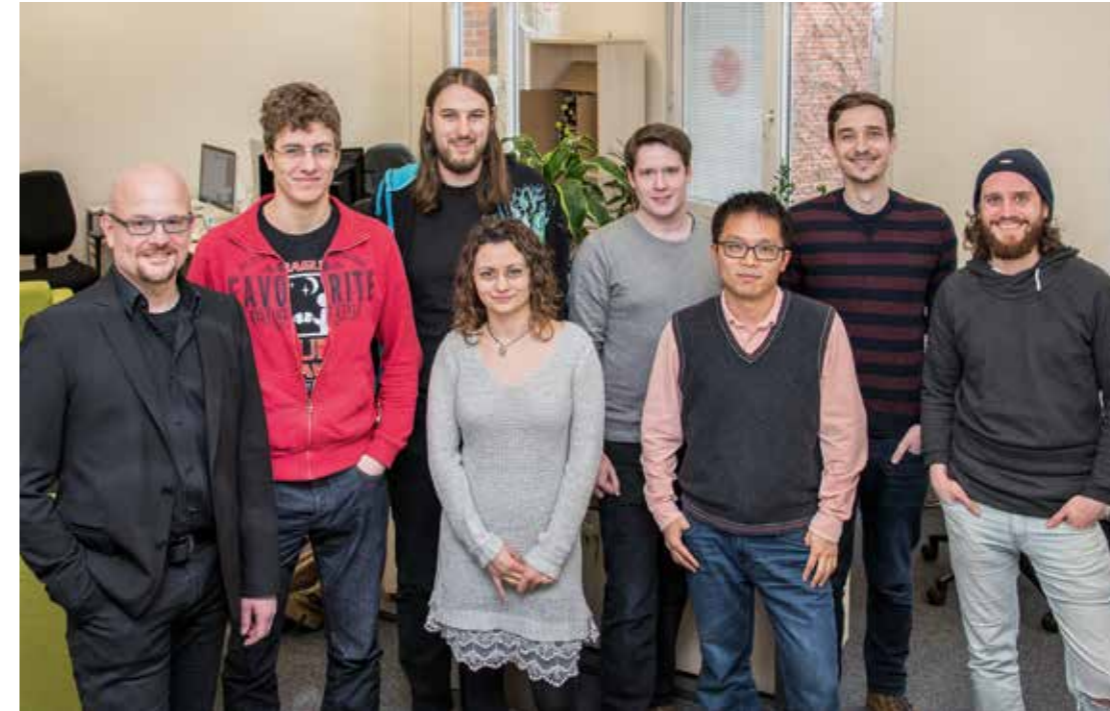
P4: Epidemiological Modelling of Infectious Diseases

Research

Using computational, theoretical and data-driven techniques from physics, computer science, dynamical systems theory, complex networks theory and complexity science we develop computational and theoretical models to improve our understanding of the dynamics, proliferation and evolution of infectious diseases. These models are designed to advance our understanding of basic mechanism and observed phenomena on a fundamental level. Based on mechanistic, data-driven models we design and build large scale computational models and forecast infrastructures that serve as predictive tools in the context of emergent outbreak scenarios. We develop models with a wide range of applications and scales.

Global mobility and emergent infectious diseases

On one end of the spectrum we develop large-scale computational models that target global aspects of disease dynamics, predominantly the geographic spread of diseases or how relative import risks are globally distributed as a function of outbreak locations. For instance, we have developed a class of models that incorporate the entire global air-transportation system including the passenger flux along more than 25,000 connections between 4,000 airports worldwide, amounting to a global traffic of over three billion passengers per year. Because mobility is a key factor in global dissemination of emergent diseases we apply new techniques from network theory to understand how hidden structural features of global mobility networks shape the expected spread or distribution of import risks across the globe. These quantitative, early risk-assessment methods are extremely useful in the early phase of an outbreak when little information on the specific situation is available in order to get a holistic approximate assessment of what is expected concerning the time-course of an outbreak.



Big Data and digital epidemiology

Currently, novel technological developments, trackable items, social media, personal health monitors, and smart devices open new possibilities and opportunities for measuring contact patterns in large scale populations. The collection and assessment of very precise data obtained by these methods is a major shift in epidemiological analysis because data of this resolution is generally not accessible by traditional surveys or cohort studies. Digital epidemiology, the measurement of individual-based contact patterns with a very high spatiotemporal precision embedded in large scale natural experiments, for instance electronic contact tracing using RFID technology in hospital settings, has become a powerful technique for understanding transmission pathways in the context of hospital acquired diseases. Using this type of Big Data we reconstruct temporal contact networks, applying methods from complex network theory to unravel structural patterns and to identify which types of networks are particularly susceptible to spreading a disease. In combination with sequence data obtained by next generation sequencing technology we develop techniques that improve our understanding of transmission mechanisms in hospitals and other contexts. Based on this data we develop mechanistic models for disease dynamics on temporal contact networks in order to improve predictive and complement statistical models usually applied in traditional epidemiology.

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P 5: Virulence Factors in Salmonella and Campylobacter

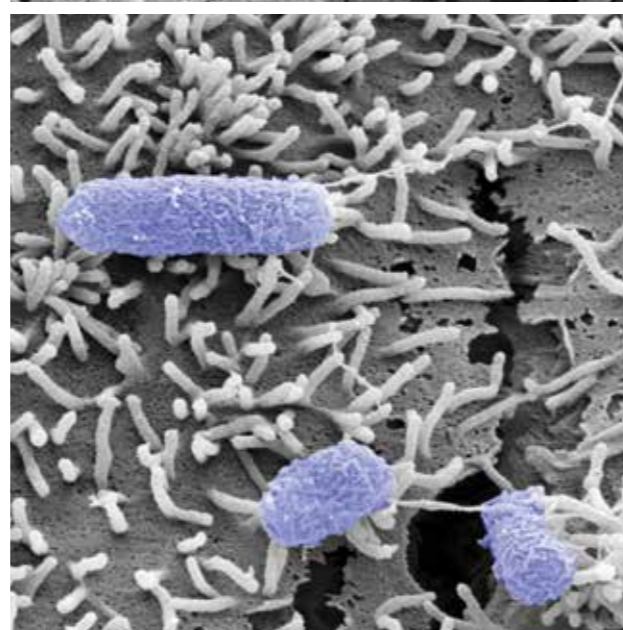
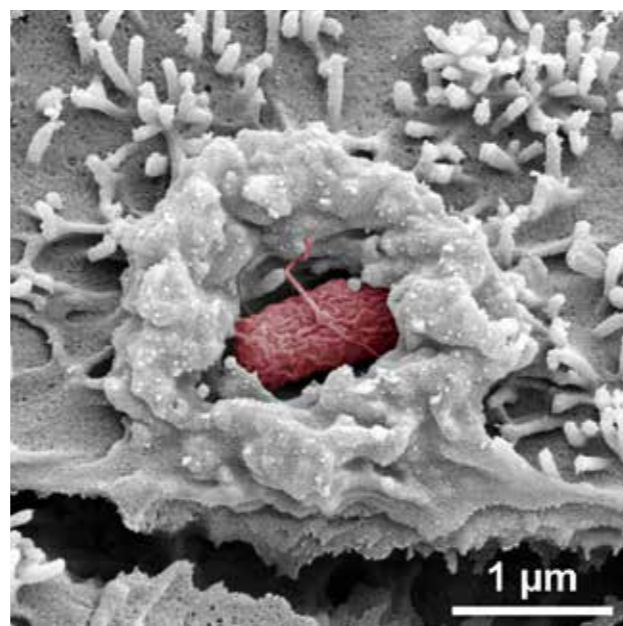
Significance of our research

Salmonella and *Campylobacter* are pathogens in the highest priority group when numbers of cases, severity of disease and costs for the public health system are considered. With more than 69,800 and 13,700 cases in 2015, *Campylobacter* and *Salmonella* respectively were responsible for over 85 % of all reported bacterial intestinal infections in Germany. The actual incidences are probably far higher as mild courses of the diseases are not recorded. In most cases contaminated food is the source of infection since both pathogens are considered classical zoonoses and livestock in particular constitutes a readily available natural reservoir for these bacteria. As a consequence there is an urgent need for further research to understand the virulence mechanisms leading to pathogenicity in humans. The focus of our work is the characterisation of known virulence factors as well as the identification of new bacterial genes with virulence function. Ultimately, our work should contribute to future strategies on how these infections can be prevented.

The trick to make them stick

Pathogenicity of *Salmonella* is largely determined by virulence factors encoded on genomic clusters called *Salmonella* Pathogenicity Islands (SPI). Several of these SPI encode for protein secretion systems which are required for direct interactions

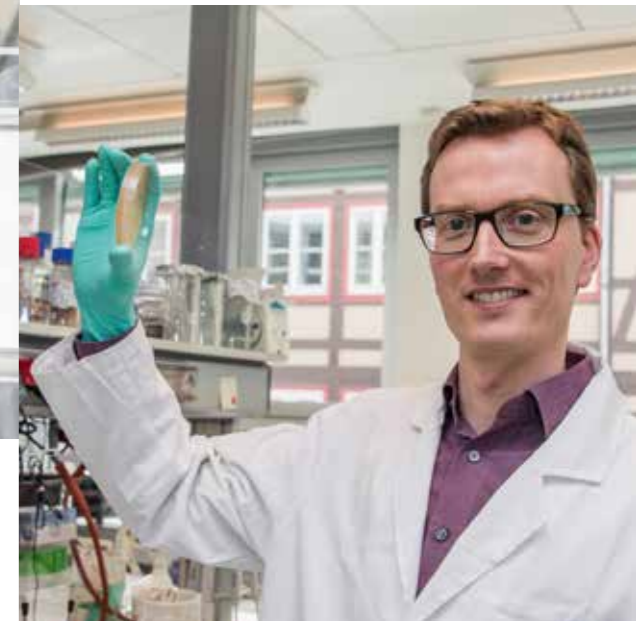
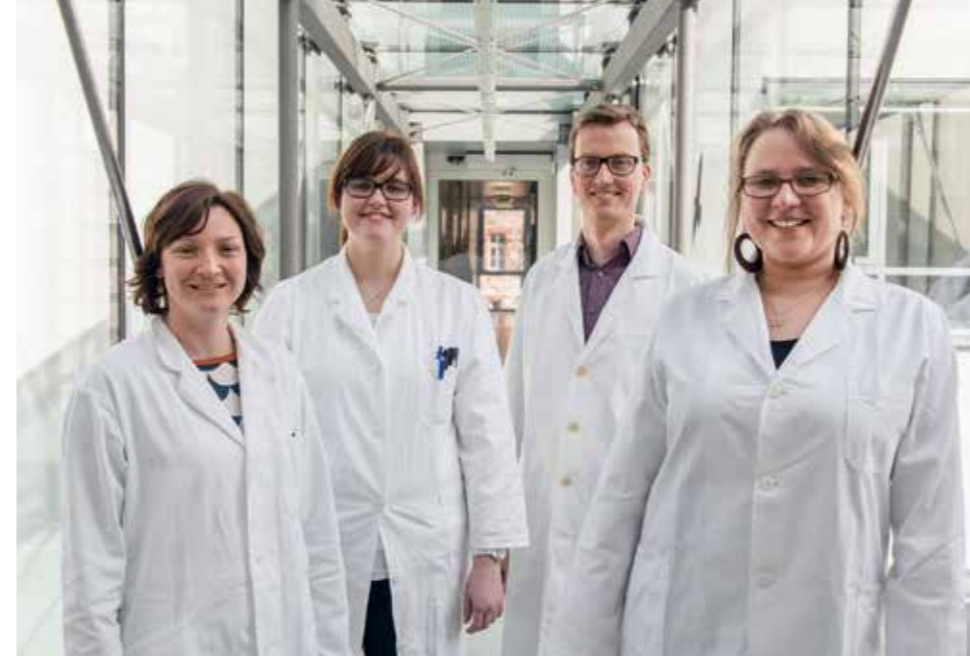
with cells of the infected host. *Salmonella* can actively enter host cells with the help of a specialized secretion system encoded on SPI-1. This so-called type III secretion system functions as a molecular injection needle for a cocktail of bacterial toxins which can manipulate the host cell for bacterial uptake. We were able to demonstrate that the function of another secretion system encoded by SPI-4 is a prerequisite for bacterial uptake (Figure). The substrate of the SPI-4 secretion system is the giant and repetitive adhesin SiiE which can mediate binding of *Salmonella* to epithelial cells. Our aim is to understand this mechanism in more detail which will provide deeper insights into the interaction between *Salmonella* and the intestinal epithelium. The latter is one of the most important barriers of the body against invasive bacteria like *Salmonella*. Here, an anti-adhesion strategy interfering with bacterial binding would help to reduce persistence and spread of the pathogen.



Wildtype *Salmonella* (red) invading an epithelial cell (upper panel) and a SPI-4 mutant (blue, lower panel)



The hypoxia workstation enables experiments under physiological oxygen concentrations



“The unexpected is the most fascinating.”

Dr. Roman G. Gerlach

Not so breathless bacteria

Bacterial pathogens have to adapt in order to survive and replicate in the challenging environments of the human body. Low oxygen concentration (hypoxia) is one of the key environmental signals to which enteric pathogens are exposed to *in vivo*. Physiological oxygen levels of the gut epithelium range between 3 and 5 % and can be even lower under pathological conditions such as infection and inflammation. A hypoxia workstation (Figure) enables us to reproduce these *in vivo* oxygen levels *in vitro*. With this experimental setup we were able to show that under low oxygen conditions *Salmonella* can replicate much better within macrophages as a result of an increased virulence of the bacteria in combination with a decrease in antimicrobial activity of the macrophages. This is just one example how low oxygen can tip the balance of host-pathogen interactions. We will continue to characterize virulence functions of *Salmonella* under hypoxia to learn more about how control of oxygen availability might be used as a part of anti-infective strategies.

Warrior without weapons?

Campylobacter is a very successful pathogen; however, only a few classical virulence factors have been described. In this respect *Campylobacter* is comparable with opportunistic pathogens which cause disease only when the host immune system is weakened or colonization resistance is otherwise disturbed. Here we investigate possible resistance mechanisms of *Campylobacter* against host-derived antimicrobial peptides. In combination with other factors, resistance might be one component ultimately resulting in a colonization advantage in the gut. Our work should shed some light on the early steps of *Campylobacter* pathogenesis and identify opportunities for interference.

www.rki.de/p5-en

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Junior Research Groups

Like the project groups, the junior research groups are a consequence of the report of the German Council for Science and Humanities in 1997. Young and talented scientists shall have the possibility to conduct high-level research on a self-chosen topic without being obliged to contribute to the daily work of the institute. The field of research should complement the work of the scientific departments, meet new health challenges or introduce new methods. Usually a Junior Research Group consists of one group leader, one technician and two PhD-students. Additional staff must be financed by raising external funds. Regular evaluations of the success of the Junior Research Groups are performed by the Scientific Advisory Board with the help of external experts. The period of time for the groups is limited to five years. In this time, the group leader is expected to qualify for higher functions, i.e. to be appointed as a university professor. Only in rare cases the career should be continued within the RKI.

Up to now the introduction of the junior research groups was a success story for the RKI. A considerable number of high quality publications were compiled by the groups which helped to establish the reputation of the RKI as a qualified research facility. Several of the former junior group leaders now hold positions as university professors, or lead large scientific departments in research institutions.

www.rki.de/ng-en

The following junior research groups are going to be introduced subsequently:

- ▶ Microbial Genomics
- ▶ Bioinformatics
- ▶ Sexually Transmitted Bacterial Pathogens



Microbial Genomics

At the junior research group “Microbial Genomics” we focus on the mechanisms of the evolution and spread of bacterial pathogens in humans as well as in animals. Most methods that we use are genomic approaches that are combined with phenotypic analyses to understand the virulence, transmission and host-interactions of the bacteria.

An important theme of our research activities is the understanding of anti-microbial resistance (AMR) which is one of the most essential evolutionary forces in the development of the bacteria in the presence.

The group is following two approaches to increase the knowledge, one is to investigate a wide variety of human and animal pathogens to study and compare the diversity of mechanisms that are responsible for the virulence of a strain and its ability to infect various hosts. In this context we also characterize the whole population of a species to identify certain evolutionary successful phylogenetic groups or groups that are characterized by an increase in their pathogenicity and/or an extended antimicrobial resistance and try to find the molecular source for this. We identify orthologous genes, present in all members of the population which will be used to compare the strains and their shared molecular characteristics and genes that are accessory for example responsible

for interaction with specific hosts, or for specific pathogenic mechanisms. We often find associations here. For example in *Escherichia coli* strains of the phylogenetic group B2 are more likely associated with pathogenicity and show on the genomic level a decreased diversity together with an increased recombination rate. Another example where we look into the details of the genomes of a whole population is the emergence of drug resistant strains and their global spread. This enables us to track how resistant strains like extended-spectrum beta-lactamases *E. coli* (ESBL) and methicillin-resistant *Staphylococcus aureus* (MRSA) are on the rise and what are the mechanisms behind this trend.

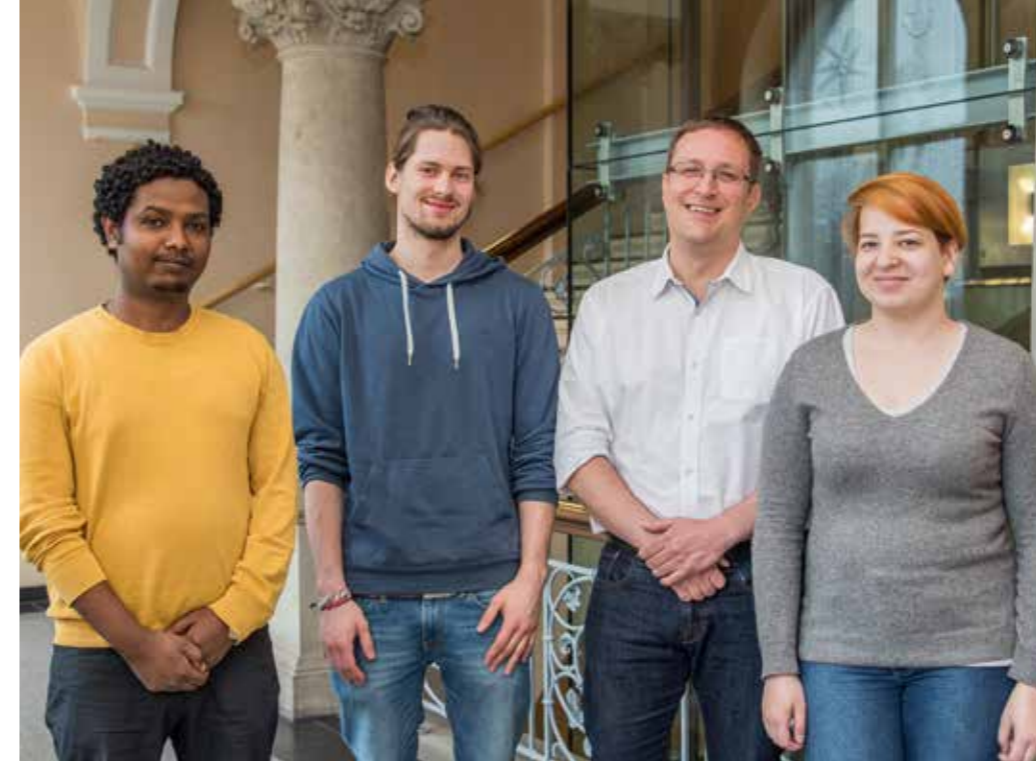
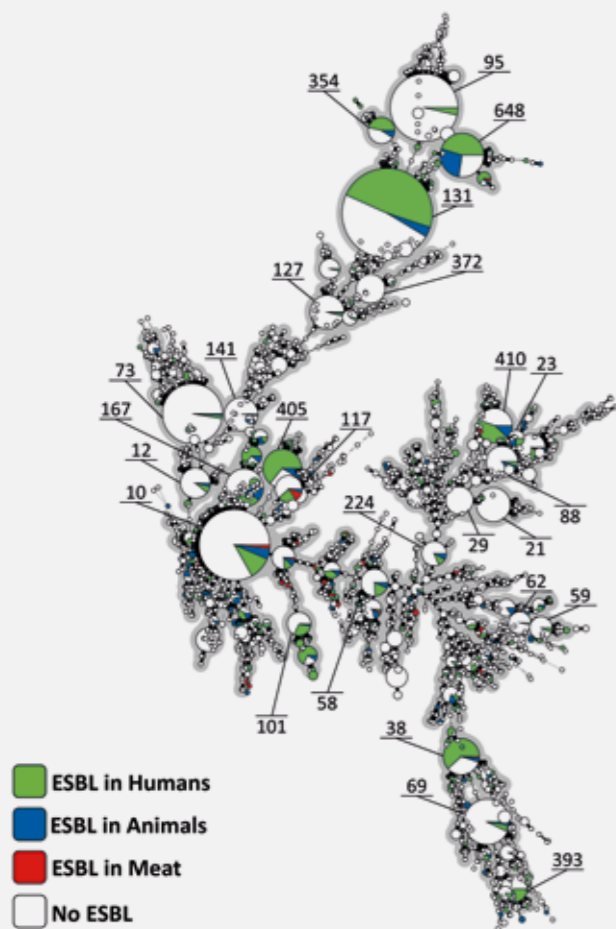
“Everything must be
made as simple
as possible.
But not simpler.”

Albert Einstein (1879 – 1955)

On the other hand we also analyze and compare very closely related strains of one species. Such comparisons allow us to track the microevolution within evolutionary successful lineages and ancient origins of a species. For example we are able to determine the genomic factors that are responsible for the emergence and worldwide spread of *E. coli* ST131, ST648, and ST410 focusing on their high zoonotic potential as well as their increased AMR prevalence. We also get an insight into the *E. coli* ST10 group where the evolutionary origin of *E. coli* is assumed and which contains commensal strains as well as pathogenic ones with the same evolutionary background giving us the opportunity to find the driving forces for the transformation of commensals into pathogens. Combined with analyses of metabolic pathways this will make it possible to identify potential vaccination or drug targets. In methicillin-resistant *Staphylococcus pseudintermedius* (MRSP), which is another typical nosocomial pathogen and an evolutionarily very young species, the absolutely predominant clone is ST71. Based on a high-resolution comparison of the whole genomes, distinct factors can be identified that differentiates this clone from the rest of the population and may be the key to success for this lineage.

Infectious diseases are still a global and local threat. On the one hand the causing bacteria are evolving very quickly and on the other hand these bacteria can be resistant to almost all antibiotics. This can have fatal consequences, particularly in developing countries. Mechanisms of adaptations on the pathogen side as well as on the host side and their interaction are supposed to play an important role in the spread of infectious agents. In the case of enterotoxigenic *Escherichia coli* (ETEC), a major cause of infectious diarrhoea, it could be shown on the basis of whole genome analyses that although

Prevalence of ESBL in the *E. coli* population based on the data of 7766 strains from different epidemiological background



the different global lineages have clade specific distinct toxin profiles and colonization factors they might harbour chromosome and plasmid combinations that optimize fitness and transmissibility.

Infectious events, especially in the gut as well as their anti-biotic treatment, which is mostly oral, have a huge impact on the human microbiome. While only very little is known about the mechanisms that lead to the functional consequences in an event of disruption of the equilibrium in the composition of the microbiome in the gut, the variety of effects to the health of the host is impressive. But it is not only humans that have to be considered. The gut of animals, livestock as well as wildlife, is an important reservoir for zoonotic pathogens and the development of anti-microbial resistances, both having influence on public health either directly or via the environment.

We therefore also focus on the development of new algorithms for species identification and a quantification of the resistome and virulome in shotgun metagenomics datasets and their application in medical and veterinary setups.

www.rki.de/ng1-en

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Bioinformatics

Technological advances in high-throughput processes are allowing previously unimagined insights into biomedical contexts. Today, billions of genetic bases can be sequenced and millions of mass positions for protein identification can be analyzed in a single experiment. The ongoing, rapid growth of technical possibilities can thus generate datasets for single experiments that fill entire computer hard drives. The growth of data acquisition capacities for the example of genome sequencing at RKI is highlighted in Figure 1. The risk is, however, that the process of data analysis will be unable to keep up with the pace of data acquisition.

Our work focuses on developing and applying fast and robust bioinformatics procedures for high-throughput experiments, the main aim being to clarify issues related to diagnosing and characterizing pathogens. The scope of our work ranges from formulating the respective question in mathematical terms to developing or adapting algorithms, evaluating biomedical data, and, finally, to implementing and publishing open-source software.

The main challenge with high-throughput experiments, therefore, is not so much the actual collection of information as data analysis and the automated extraction as well as interconnection of relevant information. In view of the huge amount of data and their structures, we require tailor-made algorithms to obtain prompt and reliable results.

Our work focuses on next-generation sequencing data for analyzing DNA and RNA sequences, as well as on mass spectrometry measurements for protein identification and structure predictions. In this context, we are especially interested in the integration of complementary data sources. It is also essential for our bioinformatics procedures and data analysis to consider the statistical effects of high-dimensional data and to determine accurate error rates to avoid potentially misleading interpretations. While we develop novel bioinformatics procedures and tools, we are persistently interested in putting them to use in cooperation with experimental groups

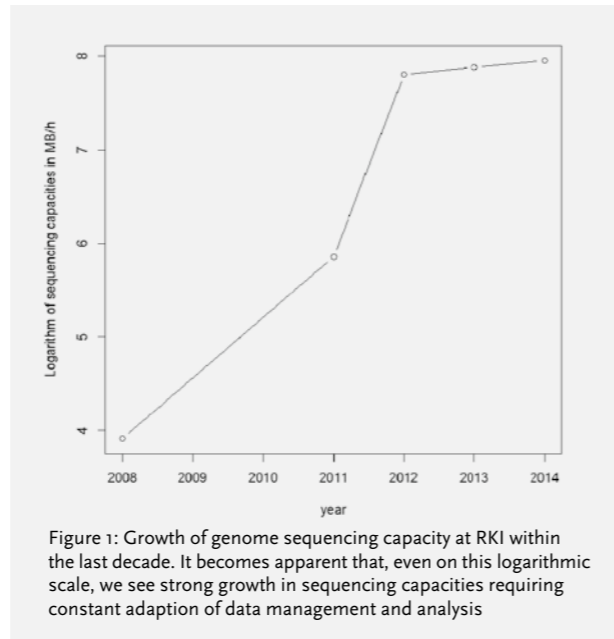


Figure 1: Growth of genome sequencing capacity at RKI within the last decade. It becomes apparent that, even on this logarithmic scale, we see strong growth in sequencing capacities requiring constant adaption of data management and analysis

both within and outside the Robert Koch Institute. Applications are manifold and include fundamental molecular research such as identifying driving factors for pathogenicity, resistance or persistence of pathogens (e.g. [1, 2]) as well as diagnostics (e.g. [3, 4]). Also, we cover a wide variety of pathogens from viruses to bacteria, amoeba and parasitic nematodes.

We have a particular interest in complex, environmental samples that are studied to determine their microbial constituents, for instance the bacteria or viruses populating a human gut or skin. Metagenomic or metaproteomic approaches allow direct analyses of these samples without prior cultivation and give a detailed insight into their composition. Here, we developed algorithms and software to differentiate on the species or strain level [3] and applied them to distinguish closely related cowpox virus strains in collaboration with the unit for highly pathogenic viruses (ZBS 1) [4].

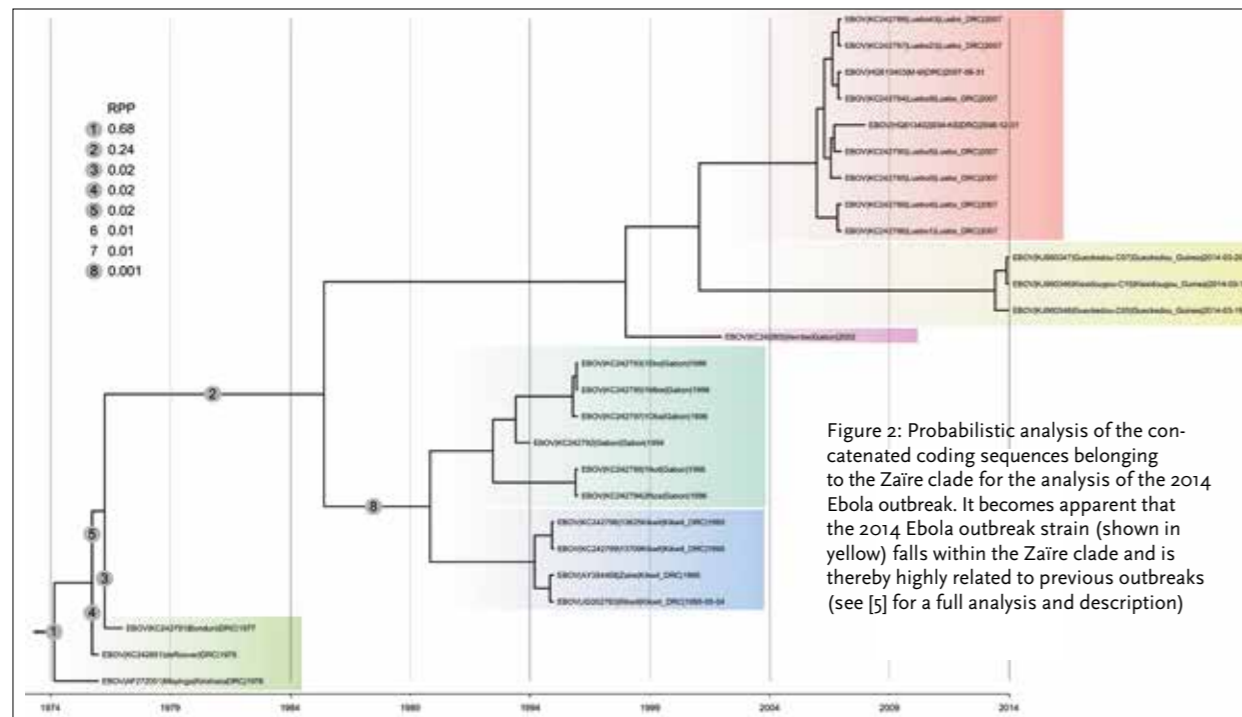


Figure 2: Probabilistic analysis of the concatenated coding sequences belonging to the Zaire clade for the analysis of the 2014 Ebola outbreak. It becomes apparent that the 2014 Ebola outbreak strain (shown in yellow) falls within the Zaire clade and is thereby highly related to previous outbreaks (see [5] for a full analysis and description)



“Infectious disease research nowadays commonly implies the analysis of big, complex data volumes.”

PD Dr. Bernhard Renard



One recent disease focused example of our work is the analysis of the 2014 Ebola outbreak in West Africa [5]. Here, we could apply our software RootAnnotator that was developed in collaboration with members of the research group on Epidemiology of Highly Pathogenic Microorganisms (P3). Our analysis of available Ebola genomes unambiguously supported the 2014 outbreak strain as a member of the Zaire lineage rather than a novel lineage. In addition, we also showed that some uncertainty exists concerning the location of the root of the genus *Ebolavirus* (compare Figure 2), but could pinpoint the likely time point of separation of the 2014 outbreak from previous outbreaks.

In addition to our research, we provide a centralized bioinformatics support for users within the Robert Koch Institute, with a major focus on analyzing next generation sequencing data. Here, we build computational infrastructure for large-scale data management and automated computational analyses of sequencing experiments. This is supported by constant feedback from users regarding priorities and needs. Thereby, we contribute to establishing genome sequencing as a major workhorse within the RKI for outbreak detection and molecular surveillance and fundamental research in close cooperation with others units such as ZBS 1, FG13, or NG1.

We expect constant growth of high-throughput experiments and resulting data. Thus, we particularly focus on the fast translation of data into actionable information and the integration of knowledge across experimental platforms and constantly growing databases.

www.rki.de/ng4-en

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Sexually Transmitted Bacterial Pathogens

Sexually transmitted infections (STI) are caused by a heterogeneous group of bacterial, viral and parasitic pathogens. Untreated, these infections can develop into devastating diseases that can result in severe sequelae including infertility or may have even fatal outcomes.

The junior research group “Sexually Transmitted Bacterial Pathogens” focuses on the obligate intracellular bacterium *Chlamydia trachomatis* which is among the most frequently sexually transmitted bacteria worldwide. About 5% of young adults worldwide have *C. trachomatis*-based genital infections, which can potentially result in female infertility. Despite great efforts vaccines are not available to date. *C. trachomatis* is

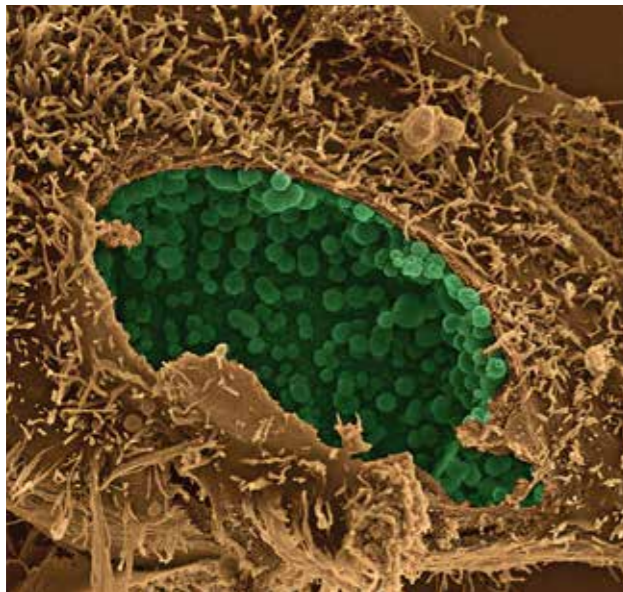


Figure 1: Colored scanning electron micrograph of an epithelial cell harboring a *C. trachomatis* inclusion. HeLa cells were infected with *C. trachomatis* L2 (MOI 2), fixed at 24 h post infectionem and further processed for scanning electron microscopy. During to the preparation process inclusions occasionally break open, allowing a view into the inclusion lumen. Scale bar, 5 μ m

sensitive to antibiotics, but these do not prevent re-infection, cannot fight asymptomatic cases. Thus, current control measures are inadequate, and new and more effective approaches are required. The group aims to understand the mechanisms *Chlamydia* uses to infect and grow inside the eukaryotic host cell, which will potentially lead to the identification of new targets that can be exploited for the development of novel anti-chlamydial strategies.

Chlamydia has a unique cycle of development that takes place exclusively inside a membrane-bound intracellular compartment, the inclusion and is characterized by the presence of two distinct bacterial forms, the infectious extracellular elementary body (EB) and the metabolically active reticulate body (RB). After internalization of the EB, the bacteria are found inside the inclusion (Fig. 1), which is segregated from the lysosomal degradation pathway. The surrounding inclusion membrane is the interface between the bacteria and the host cell and is modified by insertion of bacterial proteins. We exploit global and hypothesis-driven approaches to under-

stand the fundamental processes that enable *Chlamydia* to establish and maintain this unique compartment and permit the intracellular growth of the pathogen. One major obstacle in *Chlamydia* biology and research is due to the intricate interconnection between *Chlamydia* spp. and their host cells.

The inability to isolate *Chlamydia* inclusions brought about severe experimental constraints and impeded progression in the comprehension of virulence mechanisms and the development of novel anti-chlamydial therapies. We have successfully developed and established a method to isolate *C. trachomatis* inclusions from infected HeLa cell cultures. Global analysis of the inclusion protein composition by shotgun high-throughput proteomics revealed *C. trachomatis* inclusions are an intracellular trafficking platform that interact with a multitude of different cellular transport routes and are enriched for sorting nexin (SNX) proteins belonging the retromer complex. Detailed analysis of these SNX proteins showed a strong recruitment to *C. trachomatis* inclusions at mid-infection time points. Interestingly, SNX proteins were also found on fibres emanating from the inclusion (Fig. 2) and seem to control development of these structures. Current experiments are being performed to describe the structure of SNX positive fibres by high-resolution microscopy and to understand the role of SNX proteins and SNX fibres during *Chlamydia* infection.

In addition to *Chlamydia*'s ability to hijack cellular proteins, *Chlamydia* also sequesters lipids from the host cell. Especially sphingolipids play a pivotal role in *Chlamydia* development. Sphingolipids are a family of lipids including ceramide, sphingomyelin and different glycosphingolipids that contain a characteristic eighteen carbon amino-alcohol backbone. Modification of this core structure results in the diverse sphingolipid family. These lipids are building blocks of the eukaryotic cell membranes and evidence accumulates that they regulate different cellular processes that are important in inflammation and immunity. Interestingly, sphingomyelin

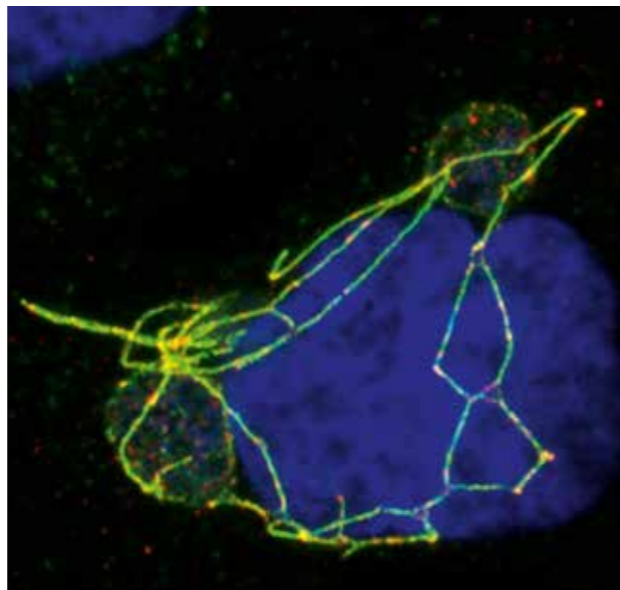
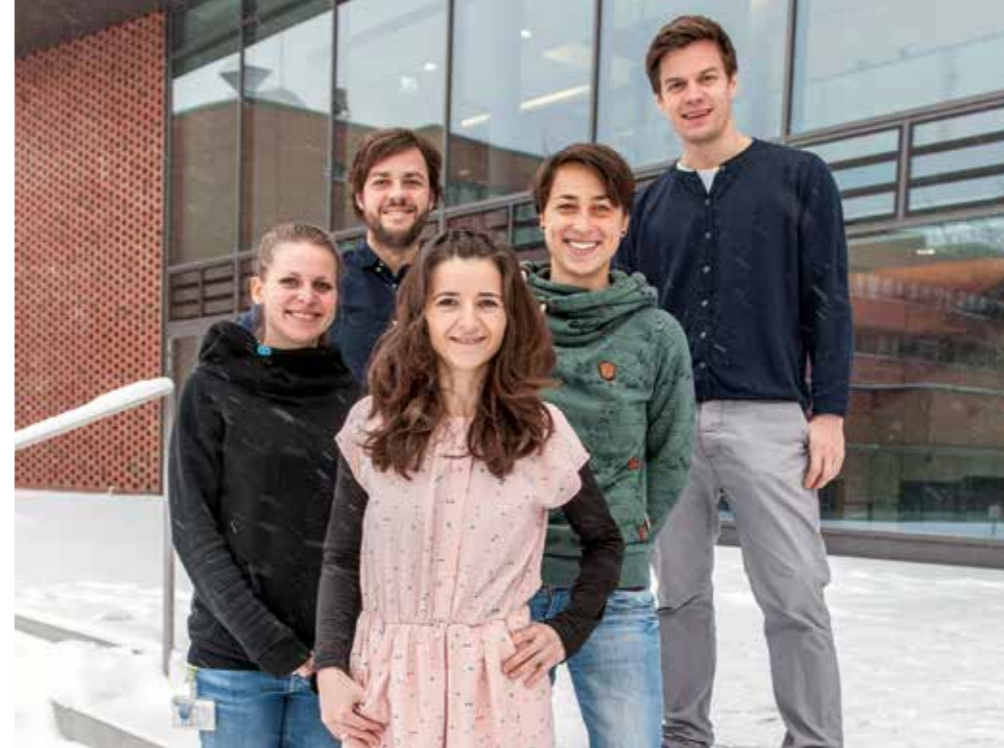


Figure 2: SNX proteins are recruited to the *C. trachomatis* inclusion and to fibers protruding into the host cell. Confocal immunofluorescence images showing fibers positive for SNX1 and IncA in *C. trachomatis* L2 infected HeLa cells (MOI 2). Cells were fixed at 24 h post infectionem and stained with antibodies against SNX1 (green) and IncA (red); DNA was stained with DAPI (blue). Images show a maximum intensity projection of a z-stack, arrows indicate SNX1/IncA fibers. Scale bar, 10 μ m



“*Chlamydia trachomatis* is among the most frequently sexually transmitted bacteria worldwide.”

Dr. Dagmar Heuer

is also found in *Chlamydia*. We study how sphingomyelin is transported to *Chlamydia* and its function for different *Chlamydia* species. We apply and establish techniques including classical cell biological, microscopy-based assays and state-of-the-art sphingolipidomics approaches to understand localization, transport and metabolism of sphingolipids before and after infection with different *Chlamydia* species. These studies already revealed that C-16-1-O-methyl-NBD ceramide is a lead compound to inhibit the growth of different *Chlamydia* species in cell culture and we currently dissect its mode of action. Progress in understanding these fundamental processes will shed light onto *Chlamydia*'s unique biology and will hopefully pave the way for the development of new anti-chlamydial strategies.

www.rki.de/ng5-en

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Trainings and Education

Postgraduate Training for Applied Epidemiology (PAE)

The Postgraduate Training for Applied Epidemiology (PAE) was founded in 1996. The main goal of this unit is to offer competency-based training in infectious disease epidemiology in order to strengthen the public health workforce in Germany. The two-year fellowship programme is based at the Department of Infectious Disease Epidemiology at RKI (see p. 54 ff.) and provides training and practical experience using the 'learning by service' approach. Every year, five motivated professionals who want to dedicate their career to public health are enrolled as PAE fellows.

All aspects of the training are aimed at identifying and implementing appropriate actions to prevent and control infectious diseases. The programme provides valuable practical experience as a large portion of the training period is spent on independent work under close expert supervision. The training objectives include the analysis of infectious disease surveillance data, the evaluation of surveillance systems as well as the development and implementation of research projects in applied epidemiology. PAE fellows communicate their findings at national and international scientific public health conferences and through scientific publications. Thus, the scientific community and public health decision-makers receive essential information for permanently improving the public health system in Germany and beyond.

Another key training objective of the programme is outbreak response. As such, PAE fellows are an essential resource for the German public health service in the investigation and control of outbreaks and other infectious disease threats. They also take responsibility as duty officers of the RKI 24/7 hotline for national public health emergencies. As part of RKI's epidemic intelligence they are involved in screening the Rapid Alert System for Food and Feed (RASFF) in order to identify and communicate potential threats for Germany and participate in the weekly Epidemic Telephone Conference with infectious disease epidemiologists from the federal states. Additionally, they participate in Epikurs@RKI offering training in outbreak investigations to German public health officers at the sub-national level.

Since 2006, ten of the authorities responsible for infectious disease control in the German federal states have taken part as training sites. The PAE fellows who are seconded to a federal state enhance the capacities for outbreak investigation, public

health surveillance, and applied research at state and local level. Through their engagement in these activities, the PAE fellows help to strengthen the ties between the different levels of the German national public health system network.

In 2009 a Master of Science programme in Applied Epidemiology (MSAE) has been established in cooperation with Charité in Berlin and the Berlin School of Public Health. The two-year fulltime course of 120 ECTS credit points is integrated into the PAE and allows PAE fellows to obtain a master degree in applied epidemiology.

In the international context, PAE is a part of the TEPHINET network which allows exchange with fellows from other international field epidemiology programmes across the world. On the European level, PAE collaborates with the European Programme for Intervention Epidemiology Training (EPIET) sharing the same training activities and curriculum. Most of the theoretical modules are jointly organised by both programmes. This close connection between PAE and EPIET is an important basis for the exchange between RKI and other players in the European public health system and helps building a strong European network of epidemiologists who share common objectives. Through these international networks PAE fellows also have the opportunity to take part in outbreak responses at the international level. By way of example, nine fellows have participated in the fight against the 2014/2015 Ebola outbreak in West Africa.

The PAE graduates are experts at applying epidemiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. Continued training efforts form an essential foundation for maintaining and further improving the surveillance and response capacities in the German public health system. www.rki.de/pae-en

ECDC fellowship training programmes: EPIET and EUPHEM

RKI is collaborating with the European Centre for Disease Prevention and Control (ECDC) hosting fellows and coordinators for the European Programme for Intervention Epidemiology Training (EPIET) and the Public Health Microbiology Training (EUPHEM). The EPIET path offers a curriculum that trains public health experts in competencies for intervention epidemiology and the EUPHEM path provides microbiologists with training in competencies for public health microbiology. After the two-year

“We strengthen the public health workforce in Germany and Europe by training experts in communicable disease surveillance and response.”

Dr. Katharina Alpers



training EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control.

Epikurs@RKI

The department for infectious disease epidemiology (see p. 54 ff.) also organizes a training course for the staff working in the German Public Health Service (Öffentlicher Gesundheitsdienst) on local and state level. The course consists of two modules which are both organized once a year. It aims at teaching basic epidemiological knowledge and skills, as well as at providing a platform for exchange between participants and trainers. The first module focuses on analysis of surveillance data to identify health problems and develop targeted interventions; the second module teaches outbreak investigations with focus on foodborne outbreaks.

Robert Koch Doktoranden Kolleg (RoKoDoKo)

Based on cooperation agreements with a number of universities and the fact that many scientists of the RKI are also academic lecturers, students from various faculties carry out their bachelor or master thesis at RKI laboratories. At the moment there are about 80 PhD-students working at the RKI. Most of these students are members of the Robert-Koch-Doktoranden-Kolleg (RoKoDoKo). This doctoral degree programme is self-organized by the students but gets support from the unit Research Coordination. It is intended to merge this programme in the near future with the doctoral programmes of the Berlin universities in order to ensure a high quality of education.

Twinning and training of foreign scientists

In the last years the number of scientific personnel from abroad that comes to the RKI to learn special skills has increased steadily. In some cases specialised funds can be raised for these purposes, like from EU twinning programmes or financial contributions from national and international organisations like the World Health Organization to allow the realisation of such an education. The RKI also runs several programmes that

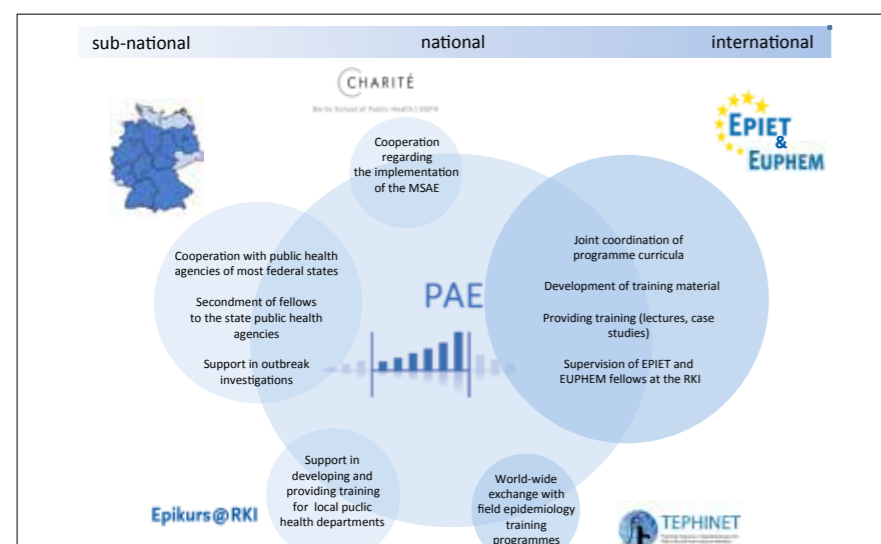
train people in their home countries. For instance one project, organized as a “train the trainers” project, aims to instruct physicians and nurses on the appropriate handling of patients suspected to be Ebola-infected. Other projects financed by the German Federal Foreign Office deal with the training of biological security in selected partner countries.

Vocational training

In the past, vocational training was limited to the vocational training as office clerk, chemical lab technician or animal keeper. Today a wide range of apprenticeships are offered. Besides the above mentioned professions young people are trained to become assistant for office communications, administrative assistant, specialist for office management or skilled employee for media and information services. It is also possible to graduate in technical professions like IT specialist, software developer or mechatronics technician.

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The PAE has interfaces with many national and international players of the public health sector. On the international level it is part of both the EPIET and the TEPHINET network. It offers a joint master degree with Charité and collaborates with the sub-national public health sector in Germany by supporting the EpiKurs@RKI and the secondment of fellows to the federal states. So far 10 states (shown in darkblue) have been a PAE training sites

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Public Health Laboratories and Collaborating Centres

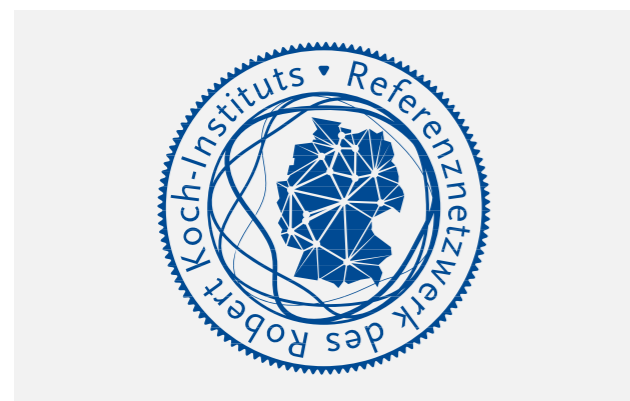
National Reference Centres and Consultant Laboratories

Public health microbiology laboratories play a central role in detecting infectious diseases, monitoring outbreak response and providing scientific evidence to prevent and control diseases. In 1995, in agreement with the German Federal Ministry of Health, the Robert Koch Institute established a public health microbiology network consisting of national reference centres (NRCs) and consultant laboratories (CLs).

The general goal of this network is to improve the efficiency of infection protection by advising the authorities on possible measures and to supplement infectious disease surveillance by monitoring selected pathogens that have high public health relevance.

Currently, there are 19 NRCs and 40 CLs, each appointed for three years. These laboratories are considered national centres of excellence in the field of laboratory science for a particular pathogen or group of pathogens. Of these, 5 NRCs and 9 CLs are currently situated to the RKI; the others are located at various universities, federal or state institutes, private laboratories and research facilities in Germany, with one binational CL being based in Austria.

NRCs have important roles and responsibilities associated with accurate diagnosis, resistance testing and prevention of the spread of infectious disease. They establish and use



reference methods, and can validate and verify test results from other laboratories. NRCs also produce and distribute reference materials for external quality control and quality assurance.

CLs focus primarily on guidance and advice for a specific pathogen to health professionals and the national Public Health Service ("Öffentlicher Gesundheitsdienst," ÖGD). Additionally, specific diagnostic methods are available.

Owing to the high level of expertise, resources and infrastructure, both NRCs and CLs are involved in training and in providing expert advice to national health authorities and other laboratories. Moreover, these laboratory scientists work closely together with their epidemiologist counterparts at the RKI as well as those at federal, state and local levels. The NRCs focus on outbreak detection and response, and advise RKI in the preparation of case definitions according to the Protection against Infection Act (IfSG). Furthermore, the reference laboratories conduct or are involved in laboratory surveillance systems which provide additional information

complementing statutory notifications. NRCs and CLs are also involved in the development of RKI's fact sheets for physicians ("Ratgeber für Ärzte") as well as investigating outbreaks, conducting epidemiological studies, evaluating implemented vaccination recommendations and analyzing the effectiveness of the vaccines.

The high relevance of NRC and CL work for the surveillance of infectious diseases is evident by the wide range of national and international publications.

For which pathogen a reference laboratory is to be established is decided based on the public health relevance of the pathogen as appraised by the RKI and on the needs expressed by the national Public Health Service. In a next step, the Advisory Board for Public Health Microbiology assesses the proposal and provides the RKI with a recommendation on whether to set up a new laboratory. The decision to establish or continue a NRC or a CL is made by the RKI, which considers recommendations given by the Scientific Advisory Board for Public Health Microbiology, and must be confirmed by the Federal Ministry of Health. Appointments are restricted to three-year periods. At the end of each appointment period, an evaluation of the laboratories is performed by the RKI in cooperation with the Scientific Advisory Board for Public Health Microbiology, which again consults national and international professional societies and experts. Based on these evaluation results, the president of the RKI, in cooperation with the Federal Ministry of Health, appoints and reappoints the NRCs and CLs. Besides, every replacement of the appointed head of a NRC or CL leads to a call for tenders.

In general, public funding does not and cannot cover the total costs of the reference laboratories. Hence, an own contribution of appointed reference laboratories is anticipated. Since 2010, the available funding stayed at 2.6 Mio €, where the NRCs receive between 60,000 and 253,000 € per year and the CLs receive between 10,200 and 16,000 € per year depending on the number of samples and extraordinary public health relevance of the pathogen received.

In 2009, a system of national networks of NRCs and CLs was set up in order to enhance effectiveness and cooperation within the national reference laboratory system. The aim of these networks is to advance exchange in diagnostic methods and prevention concepts among reference laboratories and to develop geographic coverage of services.

The public health microbiology network consisting of NRCs and CLs is coordinated by Dr. Osamah Hamouda, Dr. Sandra Beermann and Dr. Markus Kirchner, Department of Infectious Disease Epidemiology. www.rki.de/nrc

Publications

1. Beermann S, Allerberger F, Wirtz A, Burger R, Hamouda H: Public health microbiology in Germany: 20 years of national reference centres and consultant laboratories. *Int J Med Microbiol* 2015; 305(7): 595–600.
2. Vogel U, Beermann S, Gerlich W, et al.: Twenty years of National Reference and Consultant laboratories for infectious diseases in Germany. *Int J Med Microbiol*. 2015; 305(7): 591–594.
3. Laude G, Kist M, Krause G: Referenznetzwerke aus Nationalen Referenzzentren mit assoziierten Konsiliarlaboratorien in Deutschland. *Bundesgesundheitsbl* 2012; 55: 223–230.



National Reference Centres at the RKI

- ▶ Influenza (unit 17)
- ▶ Measles, mumps, rubella (unit 12)
- ▶ Poliomyelitis and enteroviruses (unit 15)
- ▶ Salmonella and other enteric pathogens (unit 11)
- ▶ Staphylococci and enterococci (unit 13)

Consultant Laboratories at the RKI

- ▶ Bacillus anthracis (unit ZBS 2)
- ▶ Clostridium botulinum (unit ZBS 3)
- ▶ Electron microscopic diagnostics in infectious diseases (unit ZBS 4)
- ▶ Cryptococcosis, Scedosporiosis, and imported systemic mycoses (unit 16)
- ▶ Listeria (unit 11)
- ▶ Noroviruses (unit 15)
- ▶ Respiratory syncytial viruses, parainfluenza viruses and Metapneumoviruses (unit 17)
- ▶ Poxviruses (unit ZBS 1)
- ▶ Rotaviruses (unit 15)
- ▶ Tularemia (unit ZBS 2)

WHO/EURO Regional reference laboratories at the RKI

- ▶ Poliomyelitis (unit 15)
- ▶ Measles and rubella (unit 12)

WHO Collaborating Centre for Emerging Infections and Biological Threats

The Robert Koch Institute (RKI) has been granted by the World Health Organization (WHO) the status of a collaborating centre for Emerging Infections and Biological Threats. The status was agreed upon by the German Federal Ministry of Health and WHO at the World Health Assembly in Geneva in May 2016 and is initially granted for four years.

The WHO collaborating centre at RKI is part of an international cooperation that aims to support WHO and its member states in preparing for and responding to emerging infections and biological threats with specific tasks. These supportive activities are structured in four terms of reference:

- ▶ Support WHO in its function to prepare for alert and response to outbreaks of international importance by building laboratory capacities.
- ▶ Provide expertise in event investigation and outbreak response and preparedness including laboratory diagnostics, epidemiology, infection control measures, and clinical management.
- ▶ Support WHO's epidemiology and surveillance activities including training in outbreak response, applied research, data analysis and modelling, when requested.
- ▶ Support the implementation of the International Health Regulations (IHR) (2005) regarding emerging infections and biological threats.

The collaborating centre at RKI is a cooperation between the Centre for Biological Threats and Special Pathogens (ZBS), the Department of Infectious Disease Epidemiology and the Department of Infectious Diseases.

www.rki.de/whocc-biothreat-en

Scientific Committees

The Robert Koch Institute gets advised by a number of scientific committees in order to fulfil its regulatory and technical duties at the highest level. Members of the individual committees are experts from various related disciplines which are appointed by RKI and the Federal Ministry of Health, respectively. According to their individual rules of procedure, the periods of appointment range from three to four years. The committees' offices are located at the RKI and organize all aspects concerning the work of the committees, convey recommendations and implement their resolutions. www.rki.de/committees

The following committees are going to be introduced subsequently:

- ▶ Advisory Committee of the German Centre for Cancer Registry Data
- ▶ Central Ethics Committee for Stem Cell Research
- ▶ Commission for Hospital Hygiene and Infection Prevention
- ▶ Commission on Anti-Infectives, Resistance and Therapy
- ▶ Commission on Genetic Testing
- ▶ Committee for Environmental Medicine
- ▶ Committee for Health Reporting and Health Monitoring
- ▶ Competence and Treatment Centres for Highly Contagious and Life-threatening Diseases
- ▶ Editorial Board of the Bundesgesundheitsblatt
- ▶ Expert Advisory Board on Influenza
- ▶ National Advisory Committee Blood
- ▶ National Certification Committee for Poliomyelitis Eradication in Germany
- ▶ National Verification Committee for Measles and Rubella Elimination in Germany
- ▶ Scientific Advisory Board for Public Health Microbiology
- ▶ Standing Committee on Vaccination



Advisory Committee of the German Centre for Cancer Registry Data

The German Centre for Cancer Registry Data (ZfKD) is advised by a committee of experts in cancer registration, research and policy. The Advisory Committee's function is to counsel the ZfKD regarding both methodological advancements as well as dissemination of scientific findings. It further supports continuous efforts to harmonize methods for registration, exchange and analysis of cancer registry data and the collaboration between clinical and population-based registries in Germany.

In order to promote the more intensive use of cancer registry data in epidemiological research, the Centre for Cancer Registry Data – in accordance with the Federal Cancer Registry Data Act (Bundeskrebsregisterdatengesetz – BKRG) – provides the data of the epidemiological cancer registries in Germany to third parties on application. The Advisory Committee assesses the particular scientific goals and the feasibility of the proposed projects and formulates an opinion to guide the ZfKD in its decision on the application.

Members of the committee include representatives of the federal states, the associations of the German population-based and clinical cancer registries, the German childhood cancer registry as well as patient organizations. Further members are national and international experts in the fields of oncology and epidemiology. The constructive exchange with the Advisory Committee is important to the continued success of the ZfKD and ensures an ongoing dialogue among stakeholders in cancer registration. www.rki.de/ac-zkfd



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Central Ethics Committee for Stem Cell Research

The Central Ethics Committee for Stem Cell Research (Zentrale Ethik-Kommission für Stammzellenforschung, ZES) was established in 2002 as part of the German Stem Cell Act. The committee is an independent and interdisciplinary expert body whose activities are governed by this law, the Act ensuring the protection of embryos in conjunction with the import and use of human embryonic stem cells (Stem Cell Act – StZG) dated 28 June 2002 and by the Regulation concerning the Central Ethics Committee for Stem Cell Research and the competent authority pursuant to the Stem Cell Act (ZES Regulation – ZESV) dated 18 July 2002. The commission, which performs its duties on a voluntary basis, comprises 18 members and deputy members appointed by the Federal Government for a term of three years. The members represent the fields of biology, medicine and philosophical, medical and theological ethics.

The committee's remit is to review and assess applications for the import and use of human embryonic stem cells (hESCs). For every application submitted, the committee issues an opinion which is then sent to the Robert Koch Institute (RKI), the competent authority under the Stem Cell Act. The committee reviews the ethical acceptability of the applications according to the requirements stipulated in the Stem Cell Act. An application must demonstrate in a scientifically substantiated manner (a) that the research project

pursues objectives of outstanding interest for the advance of scientific knowledge, (b) that the scientific issues have already been addressed in preliminary studies using other systems such as embryonic stem cells from animals, and (c) that the targeted increase in scientific knowledge actually requires the use of hESCs. Based on the results of voting on the different scientific and ethical aspects, the commission summarises the outcome of the assessment in a written opinion.

The commission holds 5 to 7 meetings per year at which the applications for the import and use of hESCs as well as the assessments are discussed. Annual reports are submitted to the Federal Ministry of Health (BMG) and can be accessed via the websites of the BMG (www.bmg.bund.de) and the RKI (www.rki.de/zes-reports).

The executive secretariat of the ZES is located at the RKI as a staff unit of the president's office. The office of the ZES organises and supports the meetings of the ZES, assists and supports the members and deputy members of the committee in the assessment of applications according to the Stem Cell Act and coordinates the collaboration between the ZES and the RKI, the competent authority. www.rki.de/stemcell

Publications

1. Annual Activity Reports (2002/2003 to 2014). The English versions of so far 12 annual activity reports of the ZES are accessible through the RKI web page: www.rki.de/DE/Content/Kommissionen/ZES/Taetigkeitsberichte/taetigkeitsbericht_node.html.



Commission for Hospital Hygiene and Infection Prevention

The Commission for Hospital Hygiene and Infection Prevention (KRINKO) has the official mandate to develop national recommendations for the prevention of healthcare-associated infections. A precursor of the Commission developed a "Guideline for the detection, prevention and control of hospital-acquired infections" in the mid-seventies which was constantly complemented and reviewed over the next two decades and finally renamed "Commission for Hospital Hygiene and Infection Control" in 1989. The renaming was supposed to clarify that beside hospitals, the recommendations are applicable to other healthcare facilities as well, particularly emphasizing the prevention of communicable diseases. Since 2001, the commission is legally anchored in §23 of the German Protection against Infection Act.

Thus, the commission's main function is to compile national recommendations for the prevention of nosocomial infections and structural and organizational measures of hygiene in hospitals and other healthcare facilities. Basic aims of the recommendations are the decrease of infection rates and number of outbreaks as well as preventing the spread of multidrug-resistant organisms. In order to fulfil these aims, evidence-based measures are recommended, which are obliged to be based on systematic risk analysis, clinical and epidemiological studies, as well as on results of microbiological and experimental research. They are recommended by mutual consensus and published by the Robert Koch Institute. The scientific secretariat of the commission is affiliated to the unit for Hospital Hygiene, Infection Prevention and Control at the Robert Koch Institute. Commission members are appointed by the Federal Ministry of Health for a period of three years. The commission is composed of eighteen members, who are experts and specialists in different medical fields and specialties. Representatives of the Federal Ministry of

Health, the Chief Federal state authorities and the Robert Koch Institute partake in all meetings as professional consultants. Independence of members from payers, manufacturers and other important stakeholders is an essential condition. To date, the KRINKO recommendations refer to several aspects of medicine such as prevention of different healthcare-associated infections (HCAI), hygiene management in special fields such as dialysis or endoscopy, reprocessing medical equipment, disinfection and sterilization and surveillance of HCAI.

The picture shows members of the commission, permanent guests and the commission's scientific secretariat.

All recommendations and further details concerning the commission are provided at www.rki.de/krinko.

Publications

1. Kommission für Krankenhaushygiene und Infektionsprävention (2015). Infektionsprävention im Rahmen der Pflege und Behandlung von Patienten mit übertragbaren Krankheiten. Bundesgesundheitsbl (8): 1151–1170.
2. Simon A, Christiansen B (2012). Zur Fortentwicklung der Arbeiten bei den Empfehlungen der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO). Bundesgesundheitsbl (55): 1427–1431.
3. Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut (RKI) und des Bundesinstitutes für Arzneimittel und Medizinprodukte (BfArM) (2012). Anforderungen an die Hygiene bei der Aufbereitung von Medizinprodukten. Bundesgesundheitsbl (55): 1244–1310.
4. Kommission für Krankenhaushygiene und Infektionsprävention (2010). Die Kategorien der Richtlinie für Krankenhaushygiene und Infektionsprävention – Aktualisierung der Definitionen. Bundesgesundheitsbl (53): 754–756.
5. Kommission für Krankenhaushygiene und Infektionsprävention (2009). Personelle und organisatorische Voraussetzungen zur Prävention nosokomialer Infektionen. Bundesgesundheitsbl (52): 951–962.



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Commission on Anti-Infectives, Resistance and Therapy

The increasing importance of resistant pathogens is addressed in the German Antimicrobial Resistance Strategy (DART). The correct use of anti-infectives plays an important role in combatting development and spread of resistant pathogens.

In 2011, the law amending the Protection against Infection Act and other laws created the basis for the Commission on Anti-Infectives, Resistance and Therapy (ART) at the RKI, that started working in January 2013. The commission compiles up-to-date general recommendations for diagnosis and therapy, especially in the case of infections with resistant pathogens, and, in close collaboration with the Association of the Scientific Medical Societies (AWMF), it initiates the compilation of medically sound recommendations and of infectious disease guidelines on antibiotic therapy by the scientific societies. The commission has determined a need for evidence-based guidelines (especially S3 guidelines) for common and life-threatening infectious diseases. It is also involved in the discussions of the inter-ministerial working group on antibiotic resistance.

The scientific secretariat to the commission is located in the Department of Infectious Disease Epidemiology at the RKI, in the unit "Healthcare-associated Infections, Surveillance of Antimicrobial Resistance and Consumption (unit 37)". It assists and coordinates all activities of the commission, especially the preparation of scientific content for meetings and for consulting the Federal Ministry of Health.

The commission ART consists of currently 16 independent experts, appointed by the Ministry of Health for periods of three years. The members of this commission are renowned experts in the fields of clinical medicine, microbiology, virology, infection control, epidemiology and public health.

www.rki.de/art-en

Publications

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2. Kommission ART (2015) Bestandsaufnahme, Bedarfsanalyse und notwendige Verbesserungen für die Entwicklung und Überarbeitung der Leitlinien in der Infektionsmedizin in Deutschland. http://www.rki.de/DE/Content/Kommissionen/ART/Positionspapier/Positionspapier_Leitlinien-in-der-Infektionsmedizin.html. Zugriffen 12.01.2016.
3. Kommission ART (2015) Infektionserreger und ihre Resistenzen gegenüber Antiinfektiva: Surveillance-Systeme und weitere Datenquellen. http://www.rki.de/DE/Content/Kommissionen/ART/Surveillance/Surveillance_Resistenzen_gesamt.html. Zugriffen 12.01.2016.
4. Kommission ART (2014) Antiinfektiva und Resistenzen: Gesundheitsgefahren wirksam begegnen- [http://www.rki.de/DE/Content/Kommissionen/ART/Positionspapier_inhalt.html](http://www.rki.de/DE/Content/Kommissionen/ART/Positionspapier/Positionspapier_inhalt.html) – Zugriffen 12.01.2016.
5. Kommission ART (2014) Grundsätze der Antibiotika-Therapie. <http://www.rki.de/DE/Content/Kommissionen/ART/Links/Grundsätze-der-Therapie.html> . Zugriffen 12.01.2016.



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Commission on Genetic Testing

The Commission on Genetic Testing (GEKO) is an interdisciplinary, independent commission based on the Act on Genetic Testing (Gendiagnostikgesetz; GenDG). This act, effective since February 2010, stipulates the requirements of good practice with regard to safety, informed consent and free decision-making for people undergoing genetic testing. It contains general provisions and definitions for gene tests and regulates genetic examinations for medical purposes, for parentage and descent matters and genetic testing in insurance and employment sectors. The act does not cover tumour genetic diagnostics. Nor does it apply to genetic examinations and genetic analyses or the handling of genetic samples or gathering genetic data for research purposes. The GEKO, established in November 2009 by the German Federal Ministry of Health, is made up of 18 members and 18 deputy members:

- ▶ 13 experts from the specialties of medicine and biology
- ▶ two experts from the areas of ethics and law
- ▶ three representatives of nationally relevant organisations responsible for protecting the interests of patients, consumers and self-help institutions of the disabled

The commission is mainly responsible for the preparation and issuance of guidelines (§ 23 GenDG) and written opinions to novel genetic screenings. Guidelines focus on professional and qualitative requirements for the performance of genetic analyses for medical and ancestry disclosure purposes. Every three years, GEKO has the mandate to evaluate new developments in genetic diagnostics in an activity report.

The administrative office is run by PD Dr. Holger Tönnies (Head of Office), Dr. Eva Fisher, scientist, and Steffi Achilles, information specialist.

www.rki.de/geko-en

Publications

1. Gendiagnostik-Kommission beim Robert Koch-Institut (2016) Tätigkeitsbericht der Gendiagnostik-Kommission (GEKO) für den Zeitraum 01.01.2013 bis 31.12.2015. http://www.rki.de/DE/Content/Kommissionen/GendiagnostikKommission/Taetigkeitsbericht/Taetigkeitsbericht_02.html. Zugriffen: 28 Januar 2016.
2. Gendiagnostik-Kommission beim Robert Koch-Institut (2013) Richtlinie der Gendiagnostik-Kommission (GEKO) für die Anforderungen an die Durchführung der vorgeburtlichen Risikoabklärung sowie an die insoweit erforderlichen Maßnahmen zur Qualitätssicherung gemäß § 23 Abs. 2 Nr. 5 GenDG. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 56: 1023–1027.
3. Gendiagnostik-Kommission beim Robert Koch-Institut (2013) Richtlinie der Gendiagnostik-Kommission (GEKO) für die Beurteilung genetischer Eigenschaften hinsichtlich ihrer Bedeutung nach § 15 Abs. 1 Satz 1 GenDG für eine Beeinträchtigung der Gesundheit des Embryos oder des Fötus während der Schwangerschaft oder nach der Geburt gemäß § 23 Abs. 2 Nr. 1d GenDG. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 56: 1028–1029.
4. Gendiagnostik-Kommission beim Robert Koch-Institut (2013) Richtlinie der Gendiagnostik-Kommission (GEKO) für die Anforderungen an die Inhalte der Aufklärung bei genetischen Untersuchungen zu medizinischen Zwecken gemäß § 23 Abs. 2 Nr. 3 GenDG. – zuletzt geändert am 16.11.2012. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 56: 326–331.
5. Gendiagnostik-Kommission beim Robert Koch-Institut (2013) Tätigkeitsbericht der Gendiagnostik-Kommission (GEKO) für den Zeitraum 19.11.2009 bis 31.12.2012. http://www.rki.de/DE/Content/Kommissionen/GendiagnostikKommission/Taetigkeitsbericht/Taetigkeitsbericht_01.html. Zugriffen: 28 Januar 2016.

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Committee for Environmental Medicine

As an interdisciplinary research area, environmental medicine is concerned with health- and disease-determining aspects of the human-environment relationship. Environmental factors/environment exposure and their impact on human health are its major topics.

The task of the committee for Environmental Medicine, appointed by the Federal Ministry of Health (BMG) in 2012, is to advise the Robert Koch Institute (RKI) and the Federal Environment Agency (UBA) on environment-related health risks and to explore topical issues relating to environmental medicine. In this particular field of study, the focus is on population-based/preventive environmental medicine. The committee issues statements and makes recommendations to the RKI and the UBA concerning the assessment of the impact of environmental factors on public health. This includes the effects of the physical environment on the origin of health restrictions and diseases, the effects of social-ecological factors (life, work and housing conditions) on the origin of communicable and non-communicable diseases as well as the assessment of health implications caused by climate change.

The committee consists of 15 members who are recognized experts in the area of health sciences/public health, environmental epidemiology and environmental medicine. The committee is appointed for a period of four years. Appointments for a second term will be conducted in 2016. A central office, associated with RKI's unit 24, provides administrative and scientific support to the committee. www.rki.de/cem

Publications

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3. Hygienehypothese (2014). Stellungnahme der Kommission Umweltmedizin zur Hygienehypothese. Online unter: http://www.rki.de/DE/Content/Kommissionen/UmweltKommission/Aktuelle_Informationen/Downloads/stellungnahme_hygienehypothese.pdf?__blob=publicationFile. Zuletzt abgerufen 10.03.2016.
4. Klimawandel und Gesundheit Allgemeiner Rahmen zu Handlungsempfehlungen für Behörden und weitere Akteure in Deutschland (2013). Online unter: http://www.rki.de/DE/Content/Kommissionen/UmweltKommission/Aktuelle_Informationen/Downloads/klimawandel_gesundheit_handlungsempfehlungen_2013.pdf?__blob=publicationFile. Zuletzt abgerufen 10.03.2016.



Committee for Health Reporting and Health Monitoring

The Committee for Health Reporting and Health Monitoring advises the Department of Epidemiology and Health Monitoring on the development of medium- and long-term goals and on the design and conceptual development of health monitoring and health reporting. This includes advice on prioritizing relevant topics. The committee includes stakeholders from different areas of the health system who have a strong interest in using the “products” of the department or produce data of relevance for the Federal Health Reporting.

The committee consists of 19 members who are affiliated with health sciences/public health, the Public Health Service and autonomous governing bodies within the healthcare system. Equally, through their expertise, the members represent the perspectives of patients, citizens, self-help organizations and the transparency of health information. The composition of the committee ensures that health monitoring and health reporting gain impetus for further development from all key partners in the health system. www.rki.de/chrhlm

“Over the past decades, the health surveys by Robert Koch Institute have been a very successful means to improve the availability of data for health reporting. Federal Health Reports are an excellent basis to formulate recommendations for action and to monitor public health policy.”

Prof. Dr. Petra Kolip



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Competence and Treatment Centres for Highly Contagious and Life-threatening Diseases

STAKOB denotes the Permanent Working Group of Competence and Treatment Centres for Highly Infectious and Life-threatening Diseases. STAKOB brings together experts for public health preparedness and response as well as for the clinical treatment of patients with highly contagious and life-threatening diseases. The STAKOB office at the Robert Koch Institute supports the work of the working group.

Treatment centres in Germany

There are several treatment centres in Germany where patients with highly contagious and life-threatening diseases can be properly treated. These centres meet the highest standards in terms of clinical isolation, well-trained personnel and laboratory diagnostics.



Training is offered continuously both in the use of personal protective equipment and in technical measures and skills to prevent infection. Quality standards are developed to ensure that necessary requirements on technical equipment and trained staff are applied in all centres.

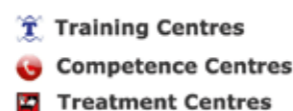
When treating highly contagious, life-threatening diseases, the medical staff is exposed to a particularly high risk of transmission. Theoretical and practical training is therefore offered continuously both in the use of the personal protective equipment and of all technical measures and skills that reduce the risk of infection. Quality standards are developed to ensure that consistent minimum requirements on technical equipment and staff training apply in all centres. www.rki.de/stakob-en

Competence centres in Germany

The STAKOB competence centres operate within the German Public Health Service. Their professional expertise can be supplemented by that of the public health officer and a range of different institutions (e.g. representatives of the associated treatment centre, the federal state healthcare authorities, agencies responsible for hygiene and ambulance services, German Federal Armed Forces).

The competence centres provide advice by telephone and on-site support for health authorities, doctors and hospitals on diagnostics, anti-epidemic measures, logistical organization of ambulance services, etc. They obtain and forward up-to-date epidemiological information and support press and public relations work.

Stakob issues statements which are published on the website www.stakob.de



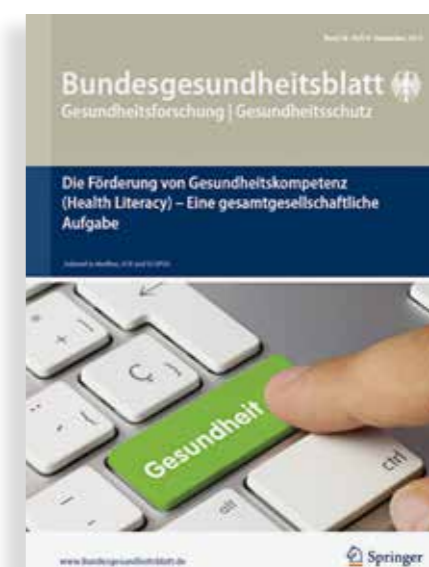
Editorial Board of the Bundesgesundheitsblatt

The public health journal “Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz” is published monthly by the federal institutes within the portfolio of the Federal Ministry of Health (BMG). The journal addresses medical and scientific questions, which are relevant for the public health system and governmental health policies. The aim is to provide up-to-date information on significant developments and on specific measures for health protection, prevention concepts, risk prevention and health promotion. It covers a broad spectrum of topics, ranging from infection prevention, epidemiology of communicable and non-communicable diseases, environmental health protection, public health, health economics, care research and health telematics to questions regarding medical ethics and legal issues. Furthermore, relevant recommendations and notices from federal institutes operating in the health sector are published in this journal.

The “Bundesgesundheitsblatt” is published in collaboration with an interdisciplinary editorial board with 18 members. All of them are experts in different fields of public health and are being elected every four years. In this process, present members can be reelected or new members can be appointed.

The members of the editorial board meet with the editors twice a year to discuss key topics for the following journal issues. The editorial office of the “Bundesgesundheitsblatt” is located at the Robert Koch Institute. The responsible editor in chief is Dr. Heidemarie Rohdewohld, who is temporarily replaced by Sara Preisetanz.

At present, the journal is ranked first place in Google Scholar’s category “Top publications – German”. Moreover, it is indexed in Medline, Science Citation Index Expanded and Scopus. In 2009, the journal received its first impact factor. Article abstracts are available in German and in English on the journal’s website. Full texts in German are accessible for subscribers. The “Bundesgesundheitsblatt” can be purchased from the “Springer Verlag” in Heidelberg. www.rki.de/eb-bgb



TREATMENT CENTRES (ISOLATION UNITS) – Charité University Hospital Berlin – Düsseldorf University Hospital
University Hospital Frankfurt – University Medical Centre Hamburg-Eppendorf – St. Georg Hospital Leipzig – Municipal Hospital Schwabing, Munich
Robert Bosch Hospital Stuttgart

COMPETENCE CENTRES (PUBLIC HEALTH AUTHORITIES) – Berlin (State Public Health Authority) – Frankfurt (Centre of Competence for Highly Pathogenic Agents) – Hamburg (Institute for Hygiene and Environment) – Leipzig (Public Health Authority) – München (Bavarian Health and Food Safety Authority, Munich Public Health Authority) – Münster (NRW Centre for Health) – Stuttgart (Baden Wuerttemberg State Health Office)

TRAINING CENTRES – Charité University Hospital Berlin – University Medical Centre Hamburg-Eppendorf – St. Georg Hospital Leipzig
Würzburg Medical Mission Hospital, Department of Tropical Medicine

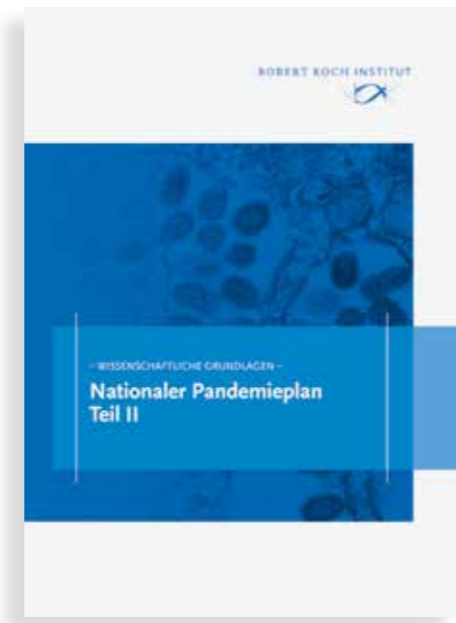
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Dr. Joseph Kuhn – Prof. Dr. Iris Pigeot – Dr. Ingrid Schubert – Dr. Wolfgang Straff – Prof. Dr. Stefan Uhlig – Prof. Dr. Rüdiger von Kries

Expert Advisory Board on Influenza

The RKI Expert Advisory Board on Influenza was founded in November 2012. It advises the RKI prior to and during an influenza pandemic with regard to scientific questions concerning influenza, including the update of the scientific part of the German Influenza Pandemic Preparedness Plan (Part II). The scientific part describes the current scientific knowledge on pandemic influenza preparedness planning and response to pandemic influenza. The experiences from the 2009 pandemic have been incorporated, such as preparing a flexible response to different pandemic scenarios and performing national risk assessments as a basis for measures to be taken. Thus, it serves as a technical basis for decisions on measures to prepare for the event of a pandemic, as well as measures in the event of a pandemic. These measures aim to protect the health of the German population in a future pandemic and to mitigate the overall effects of a pandemic. The executive secretariat of the RKI Expert Advisory Board on Influenza is part of unit 36.

www.rki.de/eab-influenza



The scientific part of the National Pandemic Preparedness Plan is also published on the RKI website www.rki.de/pandemieplanung

National Advisory Committee Blood

The National Advisory Committee Blood (AK Blut) advises the federal authorities and the authorities of the Federal States (Länder) on the most appropriate ways to ensure the safety of blood, blood products and cells for transfusion as laid down in the Transfusion Act. This includes advice on microbiological safety, emerging pathogens, donor selection, and standards for training in transfusion medicine. The committee takes into account the need to maintain adequate supplies of blood and blood products of appropriate quality. It evaluates the efficacy of transfusion interventions, including the introduction of new safety measures or their reduction. AK Blut identifies where research is most urgently required. Finally, the potential impact of its advice on both donors and recipients is considered.

AK Blut was established in 1993. Its 34 unpaid members are appointed by the German Federal Ministry of Health for a three-year period. They include representatives of blood establishments, medical universities, the German Federal Chamber of Physicians, the Federal Ministry of Defence, the relevant scientific societies, the pharmaceutical industries, authorities of the Länder and patient representatives. In addition, the Federal Ministry of Health, the Federal Institute for Drugs and Medical Devices, the Paul Ehrlich-Institute and the Robert Koch Institute are permanent guests without voting rights.

AK Blut holds 2 to 4 closed meetings every year. It publishes votes and statements in the journal "Bundesgesundheitsblatt". These include for instance statements on scientific evidence for the change of donor deferral criteria or recommendations on new challenges in transfusion medicine like the use of convalescent plasma. Furthermore, AK Blut compiles elaborate statements on transfusion relevant pathogens which are regularly published in English in "Transfusion Medicine and Hemotherapy". The minutes of the meetings are available on the RKI website.

The executive secretariat of the AK Blut is a staff unit of the RKI-president's office. The main task of the secretariat is the preparation and the documentation of form and content of the meetings. The work includes the compilation of scientific evidence for the topics and resolutions of the committee. Members of the secretariat also provide their personal expertise in subgroups which prepare the recommendations. The secretariat drafts and supports the votes and recommendations and is responsible for their publication. Additionally, they respond to all requests from the public, scientific experts and the media. Together with the chairperson, they present the work of AK Blut at scientific meetings. The secretariat is also responsible for the adherence to the terms of reference of AK Blut and provides interpretation in case of doubt.

www.rki.de/nac-blood



"Safe blood for patients in Germany."

Dr. Ruth Offergeld

Publications:

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2. Pauli G, Aepfelbacher M, Bauerfeind U et al. (2015) Hepatitis E Virus Transfus Med Hemother 42(4): 247–265.
3. Arbeitskreis Blut (2015) Bewertung von Apherese- und Pool-Thrombozytenkonzentraten. Bundesgesundheitsbl 58: 1126–1128.
4. Arbeitskreis Blut (2015) Hygienebedingungen bei Spendeprozessen und deren mikrobiologische Überwachung. Bundesgesundheitsbl 58: 1346–1348.
5. Arbeitskreis Blut (2015) Stellungnahme zur Gewinnung und Nutzung von Rekonvaleszentenplasma (RKP) als Therapieoption bei Ausbrüchen schwerer Infektionen. Bundesgesundheitsbl 58: 1371–1377.

"We can't predict when the next influenza pandemic will happen but we are planning our response based on sound scientific evidence."

Prof. Dr. Lothar H. Wieler



MEMBERS ~ Prof. Dr. Lothar H. Wieler (*Head*) ~ Dr. Bernhard Bornhofen ~ PD Dr. Roswitha Bruns ~ Prof. Dr. Petra Gastmeier ~ Prof. Dr. Timm Harder ~ Prof. Dr. Ulrich Hartenauer ~ Prof. Dr. Eberhard Hildt ~ Prof. Dr. Hanna Kaduszkiewicz ~ Peter Lang ~ Regine Lehnert ~ Prof. Dr. Thomas Mertens ~ Prof. Dr. Georg Peters ~ Prof. Dr. Mathias Pletz ~ Prof. Dr. Tom Schaberg ~ Prof. Dr. Horst Schrotten ~ Prof. Dr. Peter Stäheli

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National Certification Committee for Poliomyelitis Eradication in Germany

Poliomyelitis (polio) was once a disease feared worldwide, striking suddenly and paralyzing mainly children. Since 1988, the Global Polio Eradication Initiative has worked towards the millennium goal to eradicate polio globally and has reduced polio case numbers by more than 99.9%. There are just two countries which have never stopped transmission (Afghanistan and Pakistan) from which polio can spread to infect people in other countries with inadequate vaccination levels.

The certification process for polio eradication is overseen by the Global Certification Commission of the World Health Organization (WHO) and is conducted on a regional basis. Each WHO region can consider certification only when all countries in the area meet specified criteria: 1) absence of indigenous wild poliovirus (WPV) transmission for at least three consecutive years monitored by a sensitive, certification-standard surveillance such as Acute Flaccid Paralysis (AFP) surveillance, environmental surveillance or enterovirus (EV) surveillance; 2) ensure highest possible immunity levels; 3) capacity to detect, report, and rapidly respond to any imported WPV; and 4) implementation of containment measures according to the global action plan for laboratory containment of WPV. The WHO European Region was certified polio-free in 2002. The member states have committed themselves to take all required measures to survey and preserve this status until the global eradication will be achieved. Each country has an independent National Certification Committee (NCC) to collect, verify and submit country documentation related to polio eradication activities to WHO.

In Germany, the Robert Koch Institute (RKI) is responsible for these activities and hosts the office of the NCC. Assurance of polio-free status is based on EV surveillance which offers EV testing to all hospitals for patients with viral meningitis/encephalitis or AFP independent of age. For implementation of EV surveillance a Laboratory Network for Enterovirus Diagnostics (LaNED) was established, which is supervised by the National Reference Laboratory at RKI.

The German NCC was founded in 1997 and comprises ten experts representing all relevant fields such as public health, virology and clinical medicine. The members are appointed by the Ministry of Health for four years. The NCC meets at least once a year. It is their duty to support and advise RKI on all activities to maintain polio-free status, to evaluate the effect of measures taken, and to review and certify polio-free status until the circulation of WPV has been interrupted globally. The office of the NCC is run by Dr. Katrin Neubauer.

www.rki.de/poliocommittee



“Based on several indicators and outbreak reports we must conclude that measles is still a public health problem in Germany. Activities should be enhanced by all stakeholders to attain the goal of elimination.”

Prof. Dr. Oliver Razum

National Verification Committee for Measles and Rubella elimination in Germany

Since 1984 the World Health Organization (WHO) European Region pursues the goal to eliminate measles. In 2005, it was decided to stop also endemic transmission of rubella-virus, thereby eliminating congenital rubella syndrome. Both infections should have been eliminated by 2015. The German Action Plan for the Elimination of Measles and Rubella 2015–2020, which was released by the federal states and the German Federal Ministry of Health (BMG) in 2015, stipulates targets to be met by 2020 to attain the elimination goal. WHO Euro requested from their member states the establishment of national verification committees (NVCs) to assess the progress towards elimination in a standardized way, to prepare and submit an annual report to WHO as a documentation of the elimination status and related activities in the country, and to verify the elimination of measles and rubella at country-level once achieved.

In December 2012, BMG established the German NVC for measles and rubella elimination. The committee consists of honorary, independent experts from the fields of applied infectious disease epidemiology and health sciences, public health services, paediatrics and occupational health as well as virology and behavioural sciences. Additionally, representatives of BMG, the Robert Koch Institute, the Federal Centre for Health Education and a deputy of the supreme state health authorities participate regularly as permanent guests at the meetings. The executive secretariat of the NVC is hosted by the Immunization unit of the Robert Koch Institute. The secretariat is responsible for organizational matters and the scientific prearrangement of the meetings as well as for the maintenance of a database with relevant indicators and the preparation of a draft annual report to be submitted to WHO.

The committee meets at least twice a year to compile and analyse information concerning the epidemiology of measles

and rubella in Germany and data on vaccination coverage and the immunity of the German population against measles and rubella in order to assess the progress achieved with regard to elimination goals. Furthermore, the committee evaluates if the available data are sufficient or contain inconsistencies, assesses the quality of surveillance, evaluates the success of implemented key strategies, and advises on activities related to the verification of the elimination process in the country. Annual scientific reports on the committee's findings have been submitted to the WHO regional office as well as to BMG for 2010 until 2014 and are available on the official website of the committee (see references). www.rki.de/navko-en

Publications

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2. NAVKO 2015: Annual Update on Measles and Rubella Elimination Status for 2014. Online available at: http://www.rki.de/DE/Content/Kommissionen/NAVKO/Berichte/Bericht_2014_en.pdf?__blob=publicationFile. Accessed on 11.01.2015.
3. NAVKO 2014: Annual Update on Measles and Rubella Elimination Status for 2013. Online available at: http://www.rki.de/DE/Content/Kommissionen/NAVKO/Berichte/Bericht_2013_en.pdf?__blob=publicationFile. Accessed on 11.01.2015.
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“It is a privilege as well as an obligation for all of us to be an active partner on the way to a world without polio!”

Dr. Fabian Feil

Scientific Advisory Board for Public Health Microbiology

For effective control of infectious diseases in Germany, it is necessary to coordinate the different activities on infectious disease epidemiology and to strengthen these by developing or expanding networks. The Robert Koch Institute continuously surveys, analyses and evaluates all relevant information necessary to fight infectious diseases. Furthermore, it identifies and prioritizes new diagnostics and information needs.

To support this role the Scientific Advisory Board for Public Health Microbiology advises the RKI by preparing official statements and reports on current issues in the field of public health microbiology. Furthermore, the advisory board advises RKI on recommendations concerning the national reference centres (NRCs) and consultant laboratories (CLs), taking into account European and international reference structures, particularly with regard to demand for certain diagnostic areas, nominating possible candidate laboratories and conducting regular evaluations.

In making its recommendations the Scientific Advisory Board for Public Health Microbiology has an advisory function in relation to the RKI. All duties and responsibilities of the later and the technical and administrative supervision of the Federal Ministry of Health remain unaffected.

The advisory board consists of up to 14 experts, appointed by the RKI for periods of three years. The members of this advisory board are renowned experts in the fields of micro-

biology, virology, hygiene, epidemiology and public health. Occasionally, further national and international professional societies and experts are consulted to achieve a solid appraisal of the candidate laboratories.

The scientific office of the advisory board is located in the Department of Infectious Disease Epidemiology at the RKI. It assists and coordinates all activities of the advisory board. The scientific office – Dr. Osamah Hamouda, Dr. Markus Kirchner and Dr. Sandra Beermann – also technically supervises the NRCs and CLs and handles calls for tender, nominations, evaluations and coordination of annual reports.

www.rki.de/sabphm

Publications

1. Beermann S, Allerberger F, Wirtz A, Burger R, Hamouda H: Public health microbiology in Germany: 20 years of national reference centres and consultant laboratories. *Int J Med Microbiol* 2015; 305 (7): 595–600.
2. Vogel U, Beermann S, Gerlich W, et al.: Twenty years of National Reference and Consultant laboratories for infectious diseases in Germany. *Int J Med Microbiol*. 2015; 305 (7): 591–594.
3. Laude G, Kist M, Krause G: Referenznetzwerke aus Nationalen Referenzzentren mit assoziierten Konsiliarlaboratorien in Deutschland. *Bundesgesundheitsbl* 2012; 55: 223–230.



“A systematic and evidence-based approach is needed when developing vaccination recommendations. It not only improves the quality of the recommendations, but it also contributes to transparency and the acceptance of the recommendation in the professional community and the public.”

Dr. Jan Leidel

Standing Committee on Vaccination

The German Standing Committee on Vaccination (STIKO) is an independent advisory group which is responsible for the development of national vaccination recommendations. The committee consists of 12 to 18 unpaid members, who are appointed by the German Federal Ministry of Health for a 3-year period. The committee members are experts in various disciplines which are important in the field of vaccinology, such as paediatrics, family medicine, occupational medicine, microbiology, virology, immunology, epidemiology, public health, and evidence-based medicine.

STIKO holds at least two closed meetings every year. As permanent guests, representatives of the RKI, the Federal Ministry of Health, the Federal States, the national regulatory authority (Paul-Ehrlich-Institute), the Federal Centre for Health Education (BZgA), the Federal Joint Committee (G-BA), the Federal Foreign Office, and the Federal Armed Forces participate in the meetings without voting rights.

The executive secretariat of STIKO is located at RKI's Immunization unit. The secretariat performs systematic reviews and meta-analyses of the scientific evidence, and drafts background papers for new STIKO recommendations in close collaboration with STIKO's thematic working groups. The secretariat prepares the meetings in cooperation with the STIKO chairperson, and responds to requests from the medical community and media related to STIKO recommendations.

Since 2012, the STIKO follows a standard operating procedure (SOP) for the systematic development of vaccination recommendations [1]. The mainstay in the development of a vaccination recommendation by STIKO is a risk-benefit assessment. Besides individual risks and benefits, STIKO considers also epidemiological effects, for example herd protection

effects, the possibility of eliminating a disease if high vaccination coverage is achieved, potential pathogen replacement phenomena, or likely shifts in the age distribution of cases acquiring the target disease if a vaccination program is implemented. In addition, STIKO may integrate the results of economic evaluations in its decision-making process if the studies are applicable to the German healthcare setting [1, 2].

STIKO updates and publishes its recommendations once per year (usually in August, see latest version: [3]). Recommendations of STIKO form the basis for the federal states' vaccination guidance and G-BA's vaccination directive [4]. The latter stipulates which vaccinations are covered by the health insurance plans.

www.stiko.de/en

Publications

1. Standard Operating Procedure of the German Standing Committee on Vaccinations (STIKO) for the systematic development of vaccination recommendations. Version 2.0. February 6, 2014. Online available at: www.stiko.de/en.
2. Pfeleiderer M, Wichmann O (2015) From the licensure of vaccines to the recommendation of the Standing Committee on Vaccination in Germany: Criteria for the assessment of benefits and risks. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz*, 58: 263–273.
3. STIKO (2015) Mitteilung der Ständigen Impfkommission am Robert Koch-Institut (RKI). Empfehlungen der Ständigen Impfkommission (STIKO) am Robert Koch-Institut/Stand: August 2015. *Epidemiologisches Bulletin* 34. Online available at: www.stiko.de/en.
4. Schaade L, Widders U, Stange G, Höhl N (2009) Vaccination recommendations of the Standing Committee on Vaccination at the Robert Koch Institute. Legal basis and significance. *Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz* 52: 1006–1010.



“Working to improve the efficiency and collaboration of public health expert labs.”

Dr. Franz Allerberger

MEMBERS – Prof. Dr. Franz Allerberger (Head) – Dr. Angela Wirtz (Deputy) – Prof. Dr. Barbara Gärtner – Prof. Dr. Petra Gastmeier
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Prof. Dr. Thomas Weinke – Prof. Dr. Sabine Wicker – Prof. Dr. Fred Zepp

Central Services

The significance of the unglamorous

When you think of the Robert Koch Institute (RKI), its service units are certainly not among the first that come to mind. However, without the unremitting work of more than 150 employees in the central administration performing unglamorous tasks, the Robert Koch Institute would simply not be functional: concluding employment contracts, calculating salaries, placing orders, paying bills, securing third-party funding, maintaining buildings, water and power supplies, planning and building new laboratories, providing everyday hard- and software for everyone as well as highly specialized applications for laboratories and other number-crunching units, messaging, receiving and distributing laboratory samples, cleaning, carpool service, sterilizing laboratory equipment, or processing telephone calls. These are only some of the numerous tasks of our Central Services Department.

In general, public administration is all about putting laws in action to better serve the public. For the Central Service Department at the Robert Koch Institute, this means providing the best possible environment and the best service available for our scientific departments while strictly observing and sometimes implementing rules and regulations.

125 years of central administration: from authority to service

The rich history of the Robert Koch Institute is also reflected in its central administration department. The administration's understanding of its function has changed significantly from authoritarian Wilhelminian time to more participatory approaches and a closer proximity to citizens. In recent years, we have arrived at a modern, service-oriented self-conception, which is characterised by flat hierarchies and team-orientation and which we are eager to constantly develop further.

Nevertheless, tensions between our obligation to comply with laws, rules, regulations and budgetary restraints, and the ever-evolving demands of a spirited, dynamic research institute are inevitable and provide new challenges. We do what we think we have learned best: to manage between the two poles as best as we can, to anticipate new demands to the best of our ability, and to still maintain our good spirits. The following will give a brief overview of how we are trying to achieve this in everyday practice – from the perspective of the head of department and each of our five units – human resources; budget & procurement; construction, physical plant & technology; information technology (IT) and organization, and internal services – in the following chapters.

Smooth running: the Central Services Department today

Our five units manage and maintain the assets, financial and personnel resources of the RKI and provide the necessary services and infrastructure for the four scientific departments, project groups, junior research groups and – last but not least – the management staff.

Our main goal is to ensure the smooth running of the scientific departments according to the specifications of the president in compliance with legal and financial rules and limitations.

The Central Service Department represents the interface between the general framework of the federal administration and the specific conditions, demands and challenges of a federal departmental, but nevertheless progressive and dynamic research institute.

All rules and regulations of a higher federal authority apply directly to the Robert Koch Institute. They are the foundation of all our actions, and it is our task to communicate these to our researchers and executives in order to ensure legal conformity.

On the other hand, we do our best to meet the expectations of our specialised departments, who wish to recruit new personnel, procure consumables, place orders, raise and use external funding, be provided with a good IT-equipment and who wish to utilise state-of-the-art, smoothly running laboratories and laboratory services as effectively and, of course, as soon as possible.

It is our duty to strictly observe public services and collective bargaining laws, the federal budget code, procurement laws, laws and regulations, occupational health and safety as well as technical regulations. However, the demands of our scientific colleagues often ask for a high degree of flexibility. Although it is not always easy for us to bridge this gap, it is our policy to utilise all the available room to manoeuvre we can take responsibility for. We might even say at times that we welcome these challenges, because they enhance our own knowledge and performance.

The Central Services Department recruits and attends to the personnel of the entire institute and provides the financial budgets for the scientific departments according to the specifications of the president. We procure goods, supplies and services, provide infrastructure and logistics, and maintain the premises. An important task is to ensure the operability of laboratory equipment and building technology. We also make modern and safe communication technology available, as well as special IT required for laboratory equipment. The internal organisation must be structured effectively by systematic, transparent and lean business processes.

Our department prepares information, bases for decisions and tools for the president regarding the allocation of human resources, budgets and the use of buildings. The necessity of an effective resource management and long-term planning becomes ever more crucial under the double conditions of limited financial resources and dynamic scientific research. At the same time, we have to maintain the leeway for the president to act and make decisions to the best of our ability.



Mission statement

Based on the RKI-leitmotif “protecting health, assessing risks”, we have developed our own complementary mission statement that guides our daily actions and sets the standards for our management and our executives: we act efficiently and shape the change.

This mission statement is based on an identity consisting of seven guiding principles:

- ▶ We meet demands; work flexible and result-oriented, always complying with regulatory frameworks and budgetary conditions.
- ▶ We maintain a high level of expertise; we work on schedule, anticipatory, and we communicate efficiently.
- ▶ We are a socially competent team and set high value on friendly and courteous demeanour.
- ▶ We act transparently on the basis of structured business processes, well-grounded decisions and all necessary information.
- ▶ We act efficiently and cost-effectively.
- ▶ We provide the technical and organisational infrastructure.
- ▶ We improve ourselves constantly and optimise our quality of service.

www.rki.de/zv-en

HEAD OF DEPARTMENT ~ Dr. Anke Engelbert

ADMINISTRATIVE STAFF ~ Bettina Raabe ~ Uwe Schäfer

HEADS OF UNITS ~ Silvia Schuckert ~ Marina Pioch ~ Detlef Reichenbacher ~ Dr. Michael Goltz (Deputy Head of Department)
Ines Abramowitsch

ZV 1: Human Resources

The Human Resources Unit takes care of all aspects relating to employment, from recruitment to retirement. It offers competent and comprehensive advice and information about legal, financial and other terms of employment. Human resources are dedicated to appreciate all employees and to provide them with an attractive work environment that promotes initiative, creativity and transparency. Personal development is a key component of this effort and promoted by a number of interesting offers for employees.

Flexible work hours

Human Resources development continues to further the advancement of flexible employment models. Contracts providing flexitime and part-time work, including telecommuting and mobile computing, creating a corresponding framework for meeting the needs of individual employees.

Education and training

Education and training of employees is a central component of our Human Resources development programme. Human Resources personnel and institute employees work on and plan educational, training and qualification measures. Training needs assessment is carried out annually. The results provide the basis for RKI's annual internal education and training programmes. Employees are also encouraged to take part in external qualification programmes.

Operational health management

Improvement of working conditions, prevention and health

maintenance, and bettering the well-being of employees are central aspects of operational health management. Operational health is promoted by supporting regular physical activity in cooperation with the staff council, equal opportunities and safety representatives, and the representative of the disabled. Beyond that, programmes for reintegrating employees after an illness have also been established at the institute.

Demographic change and intergenerational human resources' policy

The Robert Koch Institute is actively addressing the challenges posed by demographic developments. Evolving generational structures are taken into account by the Human Resources Unit and its policies. A central element of intergenerational human resources policy is creating an environment that values every age group, shapes fair employment relations between generations, and creates age- and family-appropriate workplaces and working conditions, including furthering inclusion of all age groups in education, training and operational health management. This also encompasses motivating employees to engage in life-long learning and takes into consideration that varied experiences mean every generation learns in its own way. As a result, user-oriented and self-directed education and training are supported. In short, the institute and our employees are oriented towards demographic change through a range of measures, projects and events.

Compatibility of life and career

Promoting and supporting the compatibility of life and career is considered throughout all activities undertaken within the framework of human resources development. It is an integral part of human resources development. www.rki.de/zv1-en



MEMBERS – Silvia Schuckert (*Head*) – Christine Steinicke (*Deputy*) – Marianne Ehlert – Maureen Fechner – Anna-Rebecca Friedrich – Jürgen Grunzke – Heike Henkel – Björn Kersten – Kerstin Kunke – Sabine Liedtke – Katrin Löffler – Melanie Loppaschewski – Carsten Maurer – Rosika Moll – Katrin Otter – Christiane Plath – David Rohde – Susanne Schaller – Juliane Schmelzer – Susanne Schönrock – Christina Sorge – Ralf Tischendorf – Gesa Woschkeit – Sylvia Wustmann

TRAINEES (RKI) – Sina Ackermann – Leyla Al-Sabbagh – Julia Almonat – Duygu Demirel – Esra Firat – Sarah Friedländer – Pauline Gau – Kevin Große – Jennifer Gubi – Danilo Günzel – David Haney – Maxi Heinrich – Julian Heinze – Salina Heyduk – Edin Hrstic – Kevin Jacobi – Hannes Jarmuth – Marcella Jung – Sarah Kallweit – Kim-Laureen Kämmer – Asena Kiani – Michelle Kilz – Florian Klocke – Andre Kötschau – Henning Krüger – Nikita Kuzjaev – Ulrike Mathis – Julia Mitschke – Conny Müller – Daniel Muth – Phuong Nguyen – Janina Pautsch – Louisa Pfefferkorn – Maximilian Prohl – Helen Reibstirn – Petr Rotkang – Katja Schulze – Juliette Schuster – Franz Stephan – Viktoria Streib – Sabrina Tanz – Antje Thiel – Jennifer Torge – Robert Trojaner – Beatrice Ueberholz – Felix Walper – Florian Welteroth



ZV 2: Budget and Procurement

Budget/Procurement

The Budget and Procurement Unit's main tasks are budgetary planning, budget implementation, accounting and the procurement of goods. In addition to budgetary resources, the unit also administers third-party funds that have been received by scientists for their research work. Depending on third-party funding volumes, the unit manages budgetary resources that annually amount to more than EUR 80 million. Three teams – Accounting, Third-Party Funding Administration and Procurement/Materials Administration – make up the department.

Accounting

Each year the Accounting team processes thousands of incoming invoices from suppliers in Germany and abroad. It also audits these bills and promptly releases payment. The team also files a large number of outgoing invoices each year and monitors incoming payments. Accounting operations are rounded off by periodic balancing of accounts.

Third-Party Funding Administration

The Third-Party Funding Administration team supports scientists in managing and accounting for research funds that have been received from third parties. The team helps to prepare a large number of financial plans and requests for amendments and prolongations of project periods. It also provides actual cost reports documenting how third-party funding is used. It also documents the conclusion of projects. Third-Party Funding Administration processes incoming invoices for goods and services that are procured with third-party funds. It also files outgoing invoices and accounts for third-party funding income.

Procurement/Materials Administration

The Procurement/Materials Administration team processes around 9,000 orders annually. In addition to conventional price enquires, the team prepares national or EU-wide invitations to tender. The affiliated materials administrations are made up of the central receiving areas for all incoming goods at each institute location. Their stocks ensure that supplies are continually available to both the institute's offices and laboratories. www.rki.de/zv2-en

MEMBERS – Marina Pioch (*Head*) – Gabriela Merzdorf (*Deputy*) – Hüzzam Atay – Franziska Bading – Sven Bärwald – Dennis Behs – Marco Breninek – Sabine Busch – Gülsüm Deliorman – Ann-Christin Fritzsche – Marion Gotthardt – Theresa Hille – Martina Jaensch – Birgit Klitzke – Floronce Lindner – Danica Mende – Andreas Merzdorf – Martina Montag – Petra Neitzel – Katja Neumüller – Kristin Ochmann – Marcus Piotrowski – Jessyca Pötter – Christian Retzlaff – Joanna Schultze – Christian Schumacher – Fabian Strohecker – Hans-Peter Strohecker – Axenia Treichel – Dana Zenke – Elisabeth Zielinski

ZV 3: Construction, Physical Plant and Technology

The unit's main task is to oversee the technical and technological operations and to maintain the physical plant to guarantee the technical and functional reliability of the Institute. Through maintenance, servicing, warranty tracking and renovation, the unit makes a significant contribution to sustaining scientific research operations. Professionally trained personnel carry out work primarily in the following areas:

- ▶ Heating, sanitation, ventilation and air conditioning, and electro-technical facilities
- ▶ Technical safety systems, such as access control systems, burglar alarms, electroacoustic warning systems, fire alarms, video surveillance and building control systems
- ▶ central emergency generating units
- ▶ special laboratory devices
- ▶ large general use devices
- ▶ structured wiring
- ▶ building maintenance
- ▶ minor repairs
- ▶ computer-aided facility and area management systems

Furthermore, the unit handles the contractual and technical support of the cafeteria and its leaseholders. It also is responsible for the coordination and processing of property management and occasionally works in cooperation with Germany's Federal Real Estate Authority, the Bundesanstalt für Immobilienaufgaben (BImA). Printing is another special service, as is carrying out the administrative processing of applications in accordance with Germany's genetic technology laws (Gentechnikgesetz (GenTG)) and biological materials regulations (Biostoffverordnung (BioStV)). Among other services offered are:

- ▶ preparing and guaranteeing the proper functioning of technical facilities
- ▶ informing and advising users
- ▶ support in planning, procurement and restructuring
- ▶ contract administration for services provided under VOB (German building contract terms)
- ▶ building maintenance
- ▶ administration of space, areas and facilities
- ▶ plan administration
- ▶ occupancy records and administration
- ▶ space allocation
- ▶ key administration
- ▶ operation of an administration and ticketing system for internal facility management (FM)
- ▶ technical support, carrying out FM commissions
- ▶ issuing identification cards
- ▶ technical support for auditorium events in coordination with the unit for Information Technology
- ▶ administration of genetic engineering facilities

www.rki.de/zv3-en



ZV 4: Information Technology, Organisation and Controlling

Information Technology (IT)

The unit for Information Technology (IT) takes care of the essential information and communication technology (ICT) infrastructure required to process tasks relevant for the institute's work. Continually furthering the development of this infrastructure within the scope of the institute's changing demands, keeping pace with technological innovations and operating the systems are vital tasks. The ongoing development of the ICT infrastructure is also subject to stipulations by Germany's Federal Ministry of Health (Bundesministerium für Gesundheit (BMG)) with the aim of harmonising and consolidating ICT. The IT unit must also comply with Germany's federal administration guidelines.

Among the constant challenges faced by the unit is guaranteeing IT security while simultaneously fulfilling the scientific need to transfer data and information within Germany and abroad.

The unit also equips workstations with stationary and mobile PC systems, supplies software for them all and manages them centrally. Among the available software are the classic office applications as well as special applications, e.g. for laboratory research, bioinformatics or statistics. Many laboratory devices are also controlled by their own PC systems. Employees

at the institute can get technical assistance at a central user help desk, which is run on a ticket system. Modern architectures and technologies are used for networks, servers and storage systems. The focus here is on flexibility, scalability, economical operation and meeting high demands on availability. Various virtualisation technologies are also being applied.

All the RKI's locations are linked together via the institute's central IT system network. For both data and voice communication, the institute's network is connected to the Federal Government's network. There are additional connections to the German National Research and Education Network (Verein zur Förderung eines Deutschen Forschungsnetzes (DFN)).

The unit's administrative responsibilities also include managing contracts and licenses, economic assessment and project management in the area of ICT.

Organisation and Controlling

Organisation and Controlling develops proposals to optimise processes and the structural organisation. Among its regular tasks is the customisation of agendas and other codes of practices for special business processes. Other projects are furthering the development of records management to document management (electronic files), the development of appropriate project management tools and systems of reporting. Structural extension of the intranet as well as the development of knowledge management systems are further projects in this area.

www.rki.de/zv4-en

MEMBERS – Detlef Reichenbacher (*Head*) – Karl-Heinz Rothe (*Deputy*) – Madeleine Antoniak – André Aulich – Karsten Bergtich – Julia Braune – Wolfgang Brüchert – Sven Eggert – Mario Exner – Arne Fix – Mario Fritsche – Wolfgang Gajewski – René Gürtler – Ulrich Haskamp – Salina Heyduk – Philippe Jardin – Hannes Kamin – Sascha Klatt – Karola Klein-Mehling – Olaf Köppe – Florian Loncle – Detlef Neumann – Wolfgang Niehof – Harald Niemietz – Olaf Rogge – Uwe Sack – Marko Schmidt – Thomas Schramm – Andrea Schuckert – Udo Schulze – Gerd Tielke – Tom Wandslebe – Tobias Witing – Alexander Wolff

MEMBERS – Dr. Michael Goltz (*Head*) – Wolfgang Weigelt (*Deputy*) – Christian Baars – Dr. Karen Bade – Anja Bartelt – Cornelia Bartz – Sven Bergholz – Stefan Biere – Olaf Bindszus – Robert Denker – Wolfgang Erlemeyer – Matthias Fiedler – Saskia Fuhrmann – Gunter Gebhardi – Anke Giesemann – Detlef Groth – Benjamin Häringer – Matthias Heyn – Thomas Jänicke – Florian Kientz – Ralf Kirsch – Reinhard Klingenberg – Vivi Lieu – Matthias Loose – Andrea Meister – Doreen Michaelis – Christian Nitsche – Ada Nitze – Roabi Saman – Christiane Saynisch – Martin Schwark – Marco Sieslack – Petros Stathakis – Pascal Steinberg – Tobias Strunz – Tim Vargas – Dr. Michael Voigt – Robert Vonderwolke – Dr. Thomas Wiebach

ZV 5: Internal Services

Internal Services administers the institute's real estate in Berlin and Wernigerode. Its responsibilities include, among other things: maintenance of exteriors and gardens by building superintendents and groundskeepers, management of moving and waste removal, records, postal and messenger services, entrances, the telephone exchange, the car pool, and the issuing of access permits. The department also manages the contracting of services like snow removal, cleaning, and window washing.

In addition, Internal Services manages five guest apartments and ensures the security of infrastructure on all properties.

Another service provided is central laboratory supply, including cleaning laboratory areas and providing lab assistance.

Housing assistance is a speciality of the unit. It administers housing applications in cooperation with Germany's Federal Real Estate Authority the (Bundesanstalt für Immobilienaufgaben (BImA)).

www.rki.de/zv5-en

Other services provided are:

- ▶ administration and assignment of conference rooms
- ▶ furnishing and equipping conference rooms
- ▶ procuring and managing art works and the related record-keeping
- ▶ supporting events, remodelling spaces and supporting the catering service
- ▶ signs and room-numbering
- ▶ management of parking spaces
- ▶ administration of service bicycles
- ▶ administration of official seals



MEMBERS ~ Ines Abramowitsch (*Head*) ~ Daniel Robertson (*Deputy*) ~ Valentina Aleksic ~ Angelika Altmann-Hannig ~ Karoline Aydin ~ Petra Baer ~ Holger Bindig ~ Ulrich Brandt ~ Monika Bulik ~ Günter Chruszcz ~ Jasmine Dietrich ~ Irfan Djemali ~ Sabine Eifßrich ~ Habibe Ersöz ~ Burgitta Ewert ~ Gerhard Fuchs ~ Jovana Gabisch ~ Kornelia Gericke ~ Gabriela Gewert ~ Andreas Golisch ~ Helmut Görtz ~ Lutz Grünheid ~ André Guttzeit ~ Birgit Guttzeit ~ Steffen Helmecke ~ Klaus Hoffmann ~ Dagmar Hornig ~ Eveline Hosse ~ Andrea Jensen ~ Nurcan Kalayli-Kanat ~ Jolanta Kandziora ~ Sabrina Kemp ~ Claudia Kieselhorst ~ Andreas Klinke ~ Janine Kohlschmidt ~ Mandy Kreienbring ~ Sabine Kretzschmar ~ Kristof Kronberg ~ Christina Kropp ~ Claudia Krüger ~ Martina Kuhr ~ Nicolas Lehmann ~ Petra Leist ~ Andreas Lorenz ~ Manuela Lübcke ~ Phun Lullies ~ Ronny Maciejewski ~ Jutta Masopust ~ Josef Matuschek ~ Ulrike McLernon ~ Uwe Meinhardt ~ Renate Melisch-Gierok ~ Christina Metzdorf ~ Marion Mielke ~ Katrin Naschitzki ~ Michael Niecke ~ Annette Niessen ~ Figen Onur ~ Hardy Pietsch-Pofahl ~ Norbert Pitscheck ~ Melina Rathjen ~ Sabina Reichert ~ Gudrun Riemenschneider ~ Alexander Riess ~ Annett Ruch ~ Gerold Ruf ~ Stefanie Schadow ~ Sönke Schipmann ~ Iris Schlegel ~ Nadja Schlegel ~ Christian Schmidt ~ Heike Schulze ~ Antje Schwappach ~ Ruth Stölzer ~ Emine Temür ~ Nathalie Tollard ~ Marija Vukadin ~ Ute Weiss ~ Marina Wildner ~ Monika Wolf ~ Andrea Woolard ~ Simone Zumkowski



Administrative office of the Commission on Genetic Testing, one of the Staff Units

Staff Units

Management Staff

The Management Staff provides advice and support for the Institute's leaders through the drafting of documents, the coordination of institute-wide tasks and the processing of tasks of general significance. Further tasks are the legal counselling of the various commissions located at RKI and the representation of RKI in external committees in the public health field. Three units are assigned to the Management Staff: Fundamental and Legal Issues (see page 137), Genetic Engineering (see page 138) and Stem Cell Research Authorisation (see page 139), the latter two are in charge of special tasks in the field of health policy. Close relationships exist with the office of the Central Ethics Committee for Stem Cell Research and the office of the Commission on Genetic Testing (see below).

Research Coordination/International Affairs

The unit supports the scientific management of the institute by taking care of a variety of tasks related to research, be it enquiries from the Federal Ministry of Health or other institutions or the implementation of quality control of the scientific work. The unit is also the contact point for international collaborations and serves as an interface between the institutions abroad and the internal scientific coordinators. For further information see page 134.

Press, Public Relations, Library

One focus of this unit is media relations. The unit also coordinates the institute's internet activities and publications. The editorial offices of two journals are also embedded in this unit. The library collects and organises the supply of literature according to the institute's core competences and deals with all questions concerning research data management. The RKI has a small museum displaying memorabilia from Robert Koch's life and work and the mausoleum containing Robert Koch's ashes. For further information see page 136.

Strengthening Global Health and Biosecurity

In order to fulfil political commitments the German government decided to assign several international projects to the RKI. RKI established Global Health and Biosecurity (GGBS)

to implement related projects. GGBS is, inter alia, coordinating projects funded by the Federal Foreign Office within the framework of the German Partnership Programme for Excellence in Biological and Health Security. For further information see page 135.

Executive Secretariat of the National Advisory Committee Blood

The Executive Secretariat of the National Advisory Committee Blood is a staff unit of the RKI president's office. The main task of the secretariat is the organisation and the rework in form and content of the meeting. The work includes the compilation of scientific evidence for the topics and resolutions of the committee. Members of the secretariat also provide their personal expertise in subgroups which prepare the recommendations. For further information see the chapter on scientific committees (page 121).

Administrative Office of the Commission on Genetic Testing

The Administrative Office supports members and deputy members in the outline, finalization and publication process of guidelines and written opinions based on the Act on Genetic Testing (Gendiagnostikgesetz, GenDG). The Administrative Office organizes the Commission's general and working group meetings, prepares meeting protocols and tri-annual reports describing the past activities of the commission. These reports also include the evaluation of current and prospective developments in genetic diagnostics. For further information see the chapter on scientific committees (page 115).

Executive Secretariat of the ZES

The Executive Secretariat of the Central Ethics Committee for Stem Cell Research (ZES) is located at the RKI as a staff unit of the president's office. The staff unit organises and supports the meetings of the ZES, assists and supports the members and deputy members of the committee in the assessment of applications according to the Stem Cell Act and coordinates the collaboration between the ZES and the RKI, the competent authority. For further information see chapter on scientific committees (page 112).

Research Coordination/ International Affairs

The unit Research Coordination/International Affairs is directly assigned to the president of the Robert Koch Institute. Primarily, the unit supports the management of the institute by taking care of a number of tasks related to research, be it inquiries from the Federal Ministry of Health or other institutions or the implementation of quality control of the scientific work.

Research Coordination takes care that the schedule of responsibilities and the organizational chart of the RKI are up-to-date. It organizes symposia, expert meetings and other scientific events or supports other members of the RKI in this area and manages the institute's budget for these events. The organization of the regular internal seminar for instance is one of the duties of the unit.

The unit also serves as the scientific secretariat for the external Scientific Advisory Committee and the internal Research Board. The formulation of the research agenda is a major task attributed to Research Board, assisted by Research Coordination.

Applications for internal funding of new research projects can be submitted by RKI's scientific groups to the Research Coordination which will then organize the review and approval process. After successful evaluation by the internal Research Board, Research Coordination administers the grants and

supervises the projects. The yearly granting of positions for PhD students is also conducted by the unit.

Regular evaluations of the scientific departments, the project groups and the junior research groups are organized by Research Coordination in order to maintain high scientific quality standards. Pivotal to these evaluations is a strong engagement of all members of the Scientific Advisory Committee, additionally supported by external experts.

The support of the scientific working groups in the acquisition of external funding is another important task of the unit. This includes detailed advice on the application conditions, arranging the legal review of contracts, as well as examining and approving the budgets of the research projects. Close cooperation within a cross-functional support team for the acquisition of third-party funds facilitates the application process. The support team is composed by the unit Legal and Fundamental Affairs, the Budget and Procurement unit and the unit Research Coordination.

After approval all international third-funded projects are financially administered and logistically supported by the unit. This comprises particularly the supervision of the financial resources of the research projects, the preparation of financial reports and the conduct of internal and external audits.

Besides the above-mentioned activities the unit is the contact point for international collaborations and serves as an interface between institutions abroad and the internal scientific coordinators. www.rki.de/fo-en



“From global politics to local action.”

Dr. Walter Biederbick

Strengthening Global Health and Biosecurity

The governments of the G 8 countries agreed on their summit in Deauville (2011) to bundle their activities in the Global Partnership against the Spread of Weapons and Materials of Mass Destruction. At the summit in Elmau (2015), the countries committed themselves to offer their assistance to countries implementing the International Health Regulations. In order to fulfill those political commitments the German government decided to assign several international projects to the RKI. RKI established Global Health and Biosecurity (GGBS) to implement related projects.

GGBS is coordinating projects funded by the Foreign Office within the framework of the German Partnership Program for Excellence in Biological and Health Security. The overarching aim of the programme is to enhance health-security and stability in partner countries. Another objective is to prevent inappropriate use of biological agents that could pose a potential threat.

The portfolio of GGBS projects in partner countries builds on diversity: It ranges from support in guideline development for risk assessment and control of materials with a dual-use potential to assistance in awareness building and training for applied biosecurity.

At the same time, GGBS is continuously represented at the German Federal Foreign Office's branch for WMD disarmament and non-proliferation: Besides running the program office, GGBS staff is representing the programme towards partner-countries and external stakeholders but also providing scientific advice to the Federal Foreign Office.



An example for GGBS's joint activities was the organization of a ten-day full-scale simulation exercise in 2014 together with ZBS 2: The exercise involved multiple countries and institutions within the UN Secretary-General's Mechanism for investigation of alleged use of biological and chemical weapons framework.

For the future RKI is aiming to go beyond the preparedness dimension in its country support: Currently, a rapidly deployable response force is being established to assist in the management of international large scale public health emergencies. The teams will be able to mobilize the capabilities urgently needed on a modular approach – adapted to specific situations. Within this concept, GGBS is assigned to coordinate the contributions from inside RKI.

GGBS contributes to the transformation of decisions from highest political levels to local action. www.rki.de/gbs-en

“We are proud that we can help our colleagues to conduct research work on the highest possible level.”

Dr. Heinrich Maidhof



Press, Public Relations, Library

One focus of this unit is media relations. Effective media communication is a key responsibility of public health professionals. “Communicate well and one can reach more people with a clear and credible public health message”, as the World Health Organization puts it. The press office provides information about public health emergencies, scientific findings, important publications and recommendations; it publishes press releases, posts tweets and holds press conferences. Its staff also coordinates requests by national and international media. In terms of public relations, the unit is in charge of visiting groups and organising events.

Internet and Journals

For many years, the Robert Koch Institute has been providing information about its tasks, projects and research to the scientific and general public on the internet. The press office coordinates the institute’s internet activities and edits the German and English websites. The information is updated continuously and used frequently: on average, there are between 3 million and 5 million page views per month on the institute’s website, with peaks of more than 17 million views in times of unusual outbreaks.

The unit supervises and coordinates publications and information brochures and takes care of the institute’s corporate design. The Robert Koch Institute (RKI) publishes two journals on a regular basis whose editorial offices are

embedded in this unit: the monthly “Bundesgesundheitsblatt”, a journal for public health, health research and health protection, and the weekly “Epidemiologisches Bulletin” which ensures a rapid information exchange between different stakeholders such as doctors in surgeries, clinics, laboratories, counselling centres and facilities of public health service as well as medical societies, national reference centres and sites of teaching and research. By this, it helps to optimise infection prevention and public health.

Library

The library collects and organises the supply of literature according to the institute’s core competences and deals with all questions concerning research data management. It operates the institutional repository and supports scientists during the publication process. Around 100,000 stock units are available to the RKI staff – books, periodical volumes as well as a large number of electronic magazines. The library is also open to visitors (prior registration by phone required). The historical stock from Robert Koch’s time is unique.

Museum and Mausoleum

The Robert Koch Institute possesses parts of Robert Koch’s historical heritage. It has a small museum displaying memorabilia from Robert Koch’s life and work. Visitors can have a look, for example, at his desk, at some of his microscopes, biological preparations and photomicrographs as well as at a collection of certificates and photographs. They can also visit the mausoleum containing Robert Koch’s ashes. www.rki.de/press



Fundamental and Legal Issues

To give legal advice is an important task with regard to the institute’s public health activities. The unit provides information on the legal framework of specific measures, for example on the Protection against Infection Act. It supervises the procedures stipulated by the law, for example the various commission activities within the RKI. The unit assists in giving scientific political advice by structuring complex questions from the political field (for example the draft of a legal act) for scientific treatment and by coordinating contributions from the scientific departments.

Legal advice is also often required for carrying out research activities in the public health field. Since these research activities are often related to sensitive personal data, issues belonging to the complex legal field of data protection become crucial for the design of many projects.

Networking between scientific projects, working groups and scientific institutions at the national, European and global level and integration into more and more complex funding structures has been becoming increasingly important for the RKI in recent years and decades. This reflects to some extent a general trend in the scientific field but even more the development of the RKI into a central scientific institution in the field of biomedicine in Germany. The networking and funding structures are organised in legal form. Hence, contract negotiations in this field has become one of the most important tasks of the Legal and Fundamental Affairs unit.

Increasing attention to scientific affairs also threw a light on their economic importance. As a result the unit has been taking a key role in the management in RKI’s patent management.

Classical judicial affairs as asserting and defending of legal claims or carrying out of legal actions form a smaller part of the unit’s workload. The unit also takes care of administrative procedures e. g. in the field of freedom of information and proceedings of internal legal appeal.

The unit is assigned to the Management Staff which provides advice and support for the institute’s leaders through the drafting of documents, the coordination of institute-wide tasks and the processing of tasks of general significance.

www.rki.de/l1-en



MEMBERS – Susanne Glasmacher (Head) – Günther Dettweiler (Deputy) – Marieke Degen – Jens Erling – Sarah Friedländer – Heidrun Golisch Katharina Heldt – Regina Klinke – Kathrin Meyer – Claudia Paape – Judith Petschelt – Sara Preisetanz (Dr. Heidi Rohdewohld) – Jessica Riedel Alexander Roy – Petra Schön – Dr. Jamela Seedat – Henriette Senst – Francesca Smolinski – Heide Trölmich – Dieter Umlauf – Nadin Watzke

MEMBERS – Claudia Lerch (Head) – Dr. Helmut Fouquet – Bettina Hanke – Sabine Hofmann – Dr. Antonia Mehlitz

Genetic Engineering

The unit Genetic Engineering is concerned with tasks related to the Genetic Engineering Act of Germany and ordinances of the European Union in this field. The Robert Koch Institute (RKI) is one of the federal authorities in Germany involved in the safety assessment of genetically modified organisms (GMO) with respect to experimental release of GMO into the environment and placing on the market of GMO for food, feed and industrial purposes as well as for import, processing and cultivation.

The implementation of Regulation (EC) No 1829/2003 on genetically modified food and feed ensures an adequate level of protection for man and animal. Authorization should include food and feed products, because a complete separation of both uses cannot be guaranteed during transport, use and processing.

The main focus of safety assessment by RKI relates to aspects of human and animal health. Genetically modified food and feed should be as safe as the comparable conventional food and feed. Therefore, the applicant has to provide sufficient information, among others on characteristics of the donor and recipient organism, genetic modification and its functional consequences, compositional characteristics of genetically modified plants and derived food and feed, potential toxicity and allergenicity of gene products (proteins, metabolites) and the whole genetically modified food and feed. Studies have to be performed according to internationally accepted guidelines. The main task of risk assessors is to evaluate completeness, validity and reliability of the data focusing on a case-by-case and step-by-step approach. As a result, RKI

forwards a scientific opinion to the Federal Office of Consumer Protection and Food Safety (BVL) which is the competent authority in the field of genetic engineering in Germany.

Furthermore, the unit Genetic Engineering provides advice to the German Federal Ministry of Health in the area of protection of human health on natural science aspects with respect to a broad spectrum of biotechnological subjects. The unit cooperates with national federal authorities such as the Federal Biological Research Centre for Agriculture and Forestry (JKI), the Federal Agency for Nature Protection (BfN) and Federal Institute for Risk Assessment (BfR) and is participating in international discussions regarding the safety assessment of GMO. In the RKI's internal organization the unit is assigned to Management Staff. www.rki.de/l2-en

“All our efforts for ensuring a high level of protection of human and animal health in relation to genetically modified food and feed.”

Dr. Simone Jung



Regulatory Authority for the Import and Use of Human Embryonic Stem Cells

The ability of human embryonic stem cells (hESCs) to reproduce almost limitlessly and to differentiate into many, if not all, cell types of the human body has generated an enormous amount of scientific interest. These unique capabilities provide a means to explore many promising lines of research, which are likely to reveal a deeper understanding of human cellular biology and which may lead to potential cures for many diseases. Currently, 16 clinical trials based on hESCs are being performed worldwide. Since hESCs are derived from early human embryos (which are generated in the course of an in vitro fertilization procedure but are not longer needed to establish a pregnancy), research into these cells is ethically controversial. The German Stem Cell Act that came into force in July 2002 was the result of an intensive public and parliamentary debate on the pros and cons of using hESCs for research. It defines the conditions under which hESCs can be imported to Germany and used for research. RKI is the competent authority for the implementation of the Stem Cell Act.

The central task of the authorization office is the organization of the authorization procedure for research involving hESCs. This predominantly includes a scientific review of the respective proposals, the decision on whether a research project and the hESC lines to be imported and used meet the requirements of the Stem Cell Act and the granting of the corresponding authorizations. The authorization office is also in charge of the national registry on hESC research, presenting information on approved research projects and on essential reasons for the approval to the public. This registry provides a globally unique degree of transparency on hESC research. The authorization office closely cooperates with the RKI department of fundamental and legal issues and with the office of the Central Ethics Committee for Stem Cell Research.

Additional tasks of the authorization office include the advising of applicants, the monitoring of the scientific literature for novel developments in stem cell research, eventually participation in task-specific national and international committees as well as the preparation of the stem cell reports which have to be provided regularly by the Federal Government to the Bundestag. As a result of the continuous survey of the scientific literature in the stem cell field several large databases were generated that contain a magnitude of data on globally available hESC lines and scientific papers published in the stem cell field. These data pools gave rise to several comprehensive analyses on the development in the stem cell field that were published in international scientific journals.

The authorization office is assigned to RKI Management Staff. www.rki.de/l3-en

Publications

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2. Schuldt BM, Guhr A, Lenz M, Kobold S, MacArthur BD, Schuppert A, Löser P, Müller FJ (2013) Power-laws and the use of pluripotent stem cell lines. *PLoS One* 8: e52068.
3. Löser P, Kobold S, Guhr A, Müller FJ, Kurtz A (2012) Scope and impact of international research in human pluripotent stem cells. *Stem Cell Rev* 8: 1048–1055.
4. Wobus AM, Löser P (2011) Present state and future perspectives of using pluripotent stem cells in toxicology research (2011). *Arch Toxicol* 85:79–117.
5. Löser P, Schirm J, Guhr A, Wobus AM, Kurtz A (2010) Human embryonic stem cell lines and their use in international research. *Stem Cells* 28: 240–246.



Bodies

A complex research institute with a diversity of tasks requires the support of a number of advisory panels and service units. These bodies support scientific achievements and ensure that the research results will be of the quality expected from the Robert Koch Institute.

The areas where these bodies are active cover a wide variety of expertise. There are two committees to directly ensure the scientific quality of the institute. Firstly, the Scientific Advisory Board composed of external experts from different scientific fields gives advice to the Institute on the general objectives of the scientific work. It also makes recommendations concerning the structure of the institute and how to generally improve research.

Secondly, the internal Research Council is more specific concerned with the organization of the research work and decides on funds and additional support for successful research groups. The quality management of the laboratory diagnostics is supported by a specialized unit.

A number of bodies act as service units for the needs of the employees of RKI. In this context several bodies have to be named: the Staff Council, the Equal Opportunities Commissioner, the Occupational Health and Safety unit, the Social Consulting unit, The Youth and Trainee Representative Council and the Severely Handicapped Employee Representative. They cooperate in many ways to support the staff and to find solutions for personal problems and any problem related to work. Particular attention is drawn to the compatibility of work and family obligations.

The following bodies are going to be introduced subsequently:

- ▶ Scientific Advisory Board
- ▶ Research Council
- ▶ Data Protection Officer
- ▶ Equal Opportunity Commissioner
- ▶ Occupational Safety
- ▶ Social Consulting
- ▶ Quality Management
- ▶ Staff Council
- ▶ Youth and Trainee Representative Council
- ▶ Severely Handicapped Employee Representative

Scientific Advisory Board

The Scientific Advisory Board (“Wissenschaftlicher Beirat”) of the Robert Koch Institute (RKI) was established in 1998 following a recommendation in the course of the first evaluation of the RKI by the German Council of Science and Humanities (“Wissenschaftsrat”). The 12 to 16 members are appointed to a four years term (ending 2017) by the president of RKI after consultation with the German Federal Ministry of Health.

These members are outstanding scientists covering the relevant disciplines of infectious diseases, public health research and epidemiology of communicable and non-transmittable diseases. Additionally, representatives of affiliated federal health institutes, selected research institutions and the Federal Ministry of Health participate as permanent guests. The chairman is elected by members during the constituting session. The current chairperson is Prof. Georg Peters (see picture), Institute of Medical Microbiology of University of Münster, deputy-chairperson is Prof. emeritus Angelika Vallbracht, Institute of Virology, University of Bremen.

The Scientific Advisory Board shall give guidance and advice for RKI to conduct its scientific activities on an international and highly competitive level. Accordingly, the main tasks of the Council comprises the continuous appraisal of RKI’s technical and scientific performance, to give recommendations concerning the mid- and long-term goals and strategies, and to foster cooperation with the federal health authorities, scientific institutions and professional associations.

The Scientific Advisory Board convenes at least biannually to discuss both current scientific operations and health political assignments of the RKI. The meetings’ minutes reflect opinions and recommendations by the Council, and are well appreciated and considered by the president of RKI. Furthermore, the Council takes the lead in the frequent evaluations of entire departments and project and junior research groups of RKI, respectively. Those evaluations are carried out with the aid of highly competent external consultants in order to render an expert opinion. The office of the Scientific Advisory Board is run by Dr. Nils Holger Kirsch.



“The RKI has developed substantially over the last decades towards the science-based national Public Health Institute.”

Prof. Dr. Georg Peters

Research Council

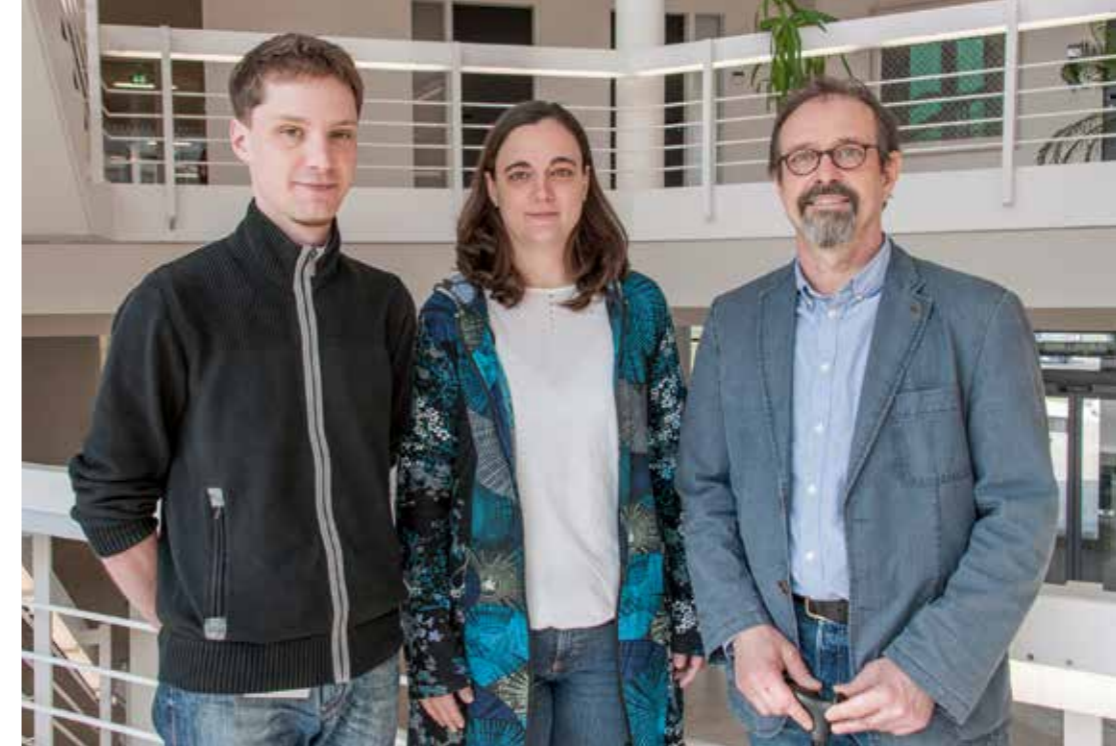
The primary task of the internal Research Council is to take care of the quality assurance of the scientific work performed at the RKI. This includes scientific advice to the president of RKI, long- and medium-term planning of research as well as priority-setting of research topics. Furthermore, the Research Council evaluates the research areas at the RKI. It recommends changes and new research projects if it identifies the necessity regarding the general tasks of RKI.

In collaboration with the ombudsman, it is also the responsibility of the Research Council to safeguard good scientific practice. In case of suspicion of scientific misconduct the Research Council investigates the incident in an unprejudiced manner and gives advice on how to proceed further.

All research groups can apply annually for special funding. The applications are evaluated by a team of internal reviewers with respect to the relevance of the proposal for RKI's duties and the scientific quality of the proposal. The Research Council finally recommends the best applications for funding.

The same procedure is applied for the approval of 3-year-term doctoral grants. Four grants are awarded every year after thorough discussion within the Research Council.

Usually the Research Council meets four to six times a year. The unit Research Coordination acts as the committee's office and takes care of the preparation of the meetings, the elaboration of meeting documents and the implementation of the decisions of the Research Council.



MEMBERS – Prof. Lothar H. Wieler (*President of RKI, Head*) – PD Dr. Lars Schaade (*Vicepresident and Head of ZBS*) – Prof. Dr. Martin Mielke (*Head of Department 1 Infectious Diseases*) – Dr. Bärbel Maria Kurth (*Head of Department 2 Epidemiology and Health Monitoring*) – Dr. Osamah Hamouda (*Head of Department Infectious Disease Epidemiology*) – Dr. Heinrich Maidhof (*Head of Research Coordination*) – Dr. Anke Engelbert (*Head of Administration*) – PD. Dr. Michael Beekes (*Ombudsman for Good Scientific Practice*) – Torsten Semmler (*Speaker of Junior Research Groups*) – Prof. Dr. Dirk Brockmann (*Speaker of Project Groups*) – Dr. Heinzfried Ellerbrok (*elected representative of laboratory scientists*) – Dr. Viviane Bremer (*elected representative of epidemiologists*) – Sabrina Neumann (*elected representative of technical staff*)
Permanent guests: Claudia Lerch (*Head of Management Staff*)

Data Protection Officer

Data protection

Protection of personal data is a fundamental right in Germany and Europe. The Robert Koch Institute is collecting, processing and using personal data to benefit individuals and the society with respect to public health. In medicinal diagnostics and epidemiology we have to deal with special categories of personal data (health information), for which higher protection measures have to be implemented. Following the German Federal Data

“Data protection and information security are tasks for all.”

Dr. Jörg Lekschas

Protection Act (Bundesdatenschutzgesetz) and the Directive 95/46/EC the processing of personal data should be designed to serve data subjects (individuals). The Data Protection Officer examines every new automated processing operation prior to its use at Robert Koch Institute. He has to provide the public procedure register to everyone. In addition the Data Protection Officer is responsible to familiarize the persons employed in the processing of personal data with the provisions of the Federal Data Protection Act.

Information security

Information processing plays a key role in the fulfilment of the duties of the Robert Koch Institute. All key strategic and operational functions and tasks are significantly underpinned

by information technology (IT). Information is an important asset and must therefore be protected appropriately. Information security is defined on the basis of the central protection objectives arising from compliance with laws and regulations as well as the requirements arising from the work and fields of activity of the Robert Koch Institute with regard to the institute's data and IT systems. An Information Security Management System has been established on basis of BSI standard 100-2 (“IT-Grundschutz”). It is implemented by the Information Security Management.

The top management level at the RKI is generally responsible for ensuring that all business areas act in a systematic and proper way and therefore that IT security is guaranteed both internally and externally. Although the management bears responsibility for the achievement of security objectives, all employees of the RKI are also responsible for ensuring and shaping the process of security itself. Coordination of the information security process is delegated to the Chief Information Security Officer and his information security management team.

The following central security objectives are defined for the Robert Koch Institute:

- ▶ Reliability of action
- ▶ Ensuring the good reputation of the institute in the public arena
- ▶ Preservation of assets
- ▶ Securing the quality of information
- ▶ Ensuring compliance with the legal requirements
- ▶ Reduction of costs incurred as a result of damage
- ▶ Correlation with topic-specific objectives of the RKI

The Chief Information Security Officer and his information security management team act in strong cooperation with the Information Technology Unit. They are involved in all IT projects and advise scientists, project leaders and all interested persons in secure implementation of information technology. In addition they are responsible for the sensitization of the employees.

MEMBERS – Dr. Jörg Lekschas (*Data Protection Officer, Chief Information Security Officer*), right – Mandy Herbst – Sebastian Kärsten

Equal Opportunity Commissioner

The main task of the Equal Opportunity Commissioner is to promote and monitor the implementation of Federal and State Equal Opportunities Acts, federal bodies' occupation law and General Equal Treatment Law at Robert Koch Institute.

“Closing the gender gap – act now.”

OECD, 2012

The duties of the Equal Opportunity Commissioner include in particular:

- ▶ support the institute to achieve and implement the aim of the laws
- ▶ increasing the proportion of women in management positions, decision-making bodies and committees
- ▶ to ensure the equal treatment of women and men and the prevention of discrimination regarding employment, training, education
- ▶ to ensure an adequate work-life balance

Involvement and participation in:

- ▶ the institution's internal bodies
- ▶ monitoring the implementation and updating of the Equal Opportunities Plan
- ▶ initiation of seminars, lectures and information sessions on topics of professional qualification, human resources development and gender aspects

Counselling interviews:

- ▶ support in organizational, social and gender-related matters
- ▶ assistance in sexual harassment, bullying and other forms of violence at work
- ▶ advice on personal problems, individual working time arrangements and workplace design
- ▶ support for reintegration into work (corporate integration management)

Occupational Safety

Occupational health and safety standards are the means to keep employees safe and healthy at the workplace. In Germany the implementation of industrial health and safety standards is based primarily on the Factories Act (ArbSchG), the Industrial Safety Act (ASiG) as well as the seventh book of the Code of Social Law (SGB VII). The realization of the support and care of the technical safety department is regulated by the Industrial Safety Act (ASiG) and is substantiated in the DGUV regulation 2 (DGUV Vorschrift 2).

Therefore, at the Robert Koch Institute, a separate unit was established more than 20 years ago. The unit for occupational health and safety now consists of 3 employees.

We have the task to advise and support the employer in all questions of safety and health of the employees and we observe the implementation of occupational safety and accident prevention. Furthermore, we have the duty to inform and counsel the Staff Council.

Our duties comprise advice and support especially regarding the following tasks:

- ▶ Identifying and evaluating workloads, occupational accidents and health hazards and possible factors for health promotion. This particularly requires identifying, analyzing, evaluating and documenting the risks posed by physical, chemical and biological hazards and stress factors as well as by emotional and psychosocial strains for the employees. We chair the health and safety committee meetings (ASA), which are conducted regularly at the Robert Koch Institute.
- ▶ Preparing and shaping of processes that are safe, healthy, suitable, and humane. This particularly requires the determination of goals and requirements (under target conditions), which are based on the ranking of the necessary measures, concurrent with the assessed risks. On this basis, concepts for occupational health and safety standards have to be developed and appropriate advice needs to be given when:
 - designing work places, work flows, the work environment; and in other questions of ergonomics
 - planning, execution and maintaining of industrial, social and sanitary installations
 - choosing and using machines, equipment, and facilities as well as working substances
 - selecting and testing of materials and items of personal protective equipment
 - arranging work organization and work tasks as well as configuring staff and social conditions
 - evaluating the working conditions.
- ▶ Maintaining principles of operation that are humane and conducive to health and safety of the employees,
- ▶ Integrating occupational safety and the protection of health into managing and conducting processes; embedding it into the structure and process flow of operations and into the regular assessment of the current state and the development and verification of a continuous improvement of the existing safety and health standards. From this follows that support must be given with regard to a suitable organisation (structure and process flow of operations), so that safety and the protection of health are taken into account regarding all activities and are tied into the operational management structures.
- ▶ To ensure that conditions are always safe, the principles of operation must be re-examined attentively, and facilities as well as work areas must be supervised time and time again. In connection therewith we
 - visit the workplaces at regular intervals and notify the employer or another person responsible for occupational safety and accident prevention of any deficiencies; propose measures to remedy these shortcomings and work towards their implementation
 - pay attention to the use of personal protective equipment
 - investigate the causes for occupational accidents, capture and evaluate the findings, and recommend to the employer appropriate measures to prevent these accidents
 - organize first-aid courses and training for employees
 - obtain the necessary first-aid materials and equipment of the first-aid rooms
 - keep the occupational medical file of the employees and organize the occupational healthcare in close cooperation with the company physician.
- ▶ Furthermore we advise on the operational management of hazardous substances as well as waste prevention and waste disposal (notably hazardous wastes), organize the disposal of toxic waste and have the duty of supervising the storage of dangerous materials at three different locations.
- ▶ We work towards all employees behaving in accordance with the requirements of occupational safety and accident prevention, in particular teach them about accident and health risks to which they are exposed at work, as well as the facilities and measures to avert these dangers, and assist in the training of security officers.



To reach these goals, we support the employer and employees with all our know-how and energy, striving for a symbiosis between legal requirements and the ability to work, focusing on a steady improvement of safety and protection of health of our employees.



Social Consulting

The Social Consulting is a service for employees and executives at the Robert Koch Institute and other Berlin federal authorities, like ministries and scientific institutes. We, Astrid Weber and Yvonne Janczak, are long-time experienced coaches and trainers with special knowledge about the organization and needs of modern scientific authorities and their employees.

Our central theme is occupational health, based on a comprehensive physical, mental and social wellbeing. Our defined goals are to encourage personal health and performance of the workforce and keep their productivity high.

There are many situations or problems that can affect ones efficiency, motivation or creativity at work. For the various issues and problems we offer a very broad range of support for employees and executives: Coaching, counselling, mediation and training, for teams and individuals respectively, tailored to the different demands.

It is important to us, if employees are experiencing problems at work or at home, that they obtain easy access to our assistance. People in immediate crisis are seen preferably at the same day of their call. We offer brief, solution-focused counseling to help employees immediately.

Sometimes employees are supported with a particular health-coaching program to develop a better ability of awareness, resilience and relaxation.

Managers are coached by Social Consulting to all questions of personnel guidance, provided with strategies for addressing employee problems, along with optional onsite training and consultation for lab working groups or teams who need assistance as well.

“Our defined goals are to encourage personal health and performance of the workforce and keep their productivity high.”

Astrid Weber and Yvonne Janczak

RKI with its diverse employee structure of international origin and different cultural backgrounds requires a professional approach of the counsellors. The diversity of employees and their integration and equal treatment is an important success factor for achieving the public health goals of the institute.

Over the past two decades the interest in our counselling has increased. Our customers of the Federal authorities value our confidential cooperation and the high qualified service as an important resource for employees, to work healthy and have happier and more productive lives by reducing stress and frustration, solving work place conflicts and finding meaningful solutions for arising problems.



MEMBERS – Astrid Weber, left – Yvonne Janczak



Quality Management

Nowadays, public health institutions increasingly establish quality management systems based on international standards.

These efforts demonstrate the emphasis of public health institutions to provide their service on a quality secured level in line with improved transparency and efficacy of tasks and activities. Since 2008, the Robert Koch Institute pursues the objective to implement an approved international quality management system (QMS) on the basis of ISO 9001 and – for the laboratory units – according to DIN EN ISO 15189 and DIN EN ISO 17025.

The first accreditation round of laboratories took place in 2010. The increased awareness that data produced in our labs are of key importance for the public set quality assurance on top of our agenda.

A central issue of quality assurance at the Robert Koch Institute is the detection of pathogens. This includes the validation of the examination procedures and continuous performance of verification and documentation of all quality influencing procedural characteristics as well as continuous participation in internal and external quality control activities and trainings.

In 2010, Katharina Holschbach-Bussian has been nominated as Quality Management Officer. She coordinates the activities of the quality management division and supervises the standard conformity of all activities within the quality

management section. Subordinated to the management, she promoted the development of the quality management system. Quality policy, approved by the management, fosters the constantly improving quality management system. In close cooperation with authorized quality management agents of the laboratory units, specified and well documented objectives are planned and continuously implemented to guarantee the conformity of all laboratory activities to the standards as well as the transparency of professional practice in the laboratories. Since 2011, André Schier assists the quality management division. He is responsible for all administrative activities in the Quality Management unit.

In 2015, a re-accreditation round of all medical diagnostic laboratories at RKI has been performed by the national accreditation body of Germany (DakkS). Thirteen laboratories including five national reference centres, five consultant laboratories, one central laboratory of epidemiology, one service laboratory and one integrated service unit successfully defended their accreditation.

MEMBERS – Katharina Holschbach-Bussian (Head) – André Schier

Staff Council

The legal basis of the work is the Federal Personnel Representation Law -BPersVG.

The staff representation rights apply not only to the working conditions of employees and workers, but also covers working conditions of public officials. Each group is basically represented, according to their share of the total number of employees. The participation and co-determination rights of the Staff Council, negotiations of the service agreements and the involvement of the conciliation committee are governed by the Council laws.

Assignment of the Staff Council, inter alia,

- ▶ to apply measures aimed at intra-service, social or personal issues of employees
- ▶ to ensure that the rules in favour of workers laws, regulations, collective agreements, service agreements and administrative regulations are carried out
- ▶ suggestions and complaints from employees and if they are entitled to take action through negotiations with the Head of Service on their execution
- ▶ to cooperate with the severely handicapped employee representatives, the Youth Council, the Equal Opportunities Commissioner and the representation of foreign workers

Furthermore the staff council has codetermination, participation and consultation rights in numerous measures of the service. Some are listed here:

- ▶ Employment and classification.
- ▶ Not only temporary transfer of an activity corresponding to the activity features of a higher or lower price or wage group.
- ▶ relocations, transpositions, terminations.
- ▶ refusal or withdrawal of secondary employments.
- ▶ continued employment above the age limit.
- ▶ working time arrangements.

The Staff Council is legitimized by the election of employees to attend to their interests and concerns at the collective level in relation to the RKI's management. The Staff Council is the representative of all employees. It follows the task to realize participation of employees in the scheme of service and remuneration and working conditions and to represent the interests of employees.

The Staff Council and the agency management files undergo strict requirements for cooperation with the agency management by the commandment of "trusting cooperation" in accordance with § 2 para. 1 BPersVG. Dialogue as a concept of internal conflict resolution is a deduction from this cooperation maxim. Each Staff Council regulates the performance of its duties independently and autonomously, without being subject to legal supervision or instructions of agency management.



Youth and Trainee Representative Council

In agencies with staff committees, which usually employ at least five workers who have not attained the age of 18 (young workers) or who are in vocational training and have not yet completed 25 years of age, youth and trainee representatives (JAV) are installed. This is done on the basis of § 57 Federal Personnel Representation Act (BPersVG).

A JAV represents those young employees and trainees by whom it is elected. It advises on all matters relating to vocational training and monitors the compliance with the applicable laws, regulations, accident prevention regulations, collective agreements, service agreements and administrative arrangements in its field. It cooperates with the Staff Council and together with this tries to resolve all legitimate concerns of young people and trainees.

At the Robert Koch Institute, more than 50 apprentices are trained in ten different professions in 2016.

The current JAV is strongly committed to close cooperation with the training manager and the Staff Council. The goal is to strengthen the apprentices in their training and to identify new areas for training. The units of RKI which have functioned as training sites have accumulated good experiences with trainees from all years of apprenticeship. Due to the diversity of occupations it is suitable for almost any area of the institute to train apprentices. Therefore, trainees are deployed everywhere in the institute: in the mail room of the institute, the secretariat of the president, the laboratory services, the various laboratory areas, the maintenance of technical systems, the electron microscopy department and in many other places.

For the future, it is important to keep on training and promoting dedicated young talents.



MEMBERS – Michael Seibold (Head) – Uwe Schäfer (Deputy) – Kerstin Schönerstedt-Zastrau (Deputy) – Birgit Arnold – Andreas Bergholz – Hans Butschalowsky – Arne Fix – Stefanie Herfort – Dr. Nils-Holger Kirsch – Ute Obst – Dr. Julia Sasse – Christina Sorge – Marco Sieslack

MEMBERS – Lousia Pfefferkorn (Head) – Edin Hrstic (Deputy), left – Florian Weltheroth (Deputy), right

Severely Handicapped Employee Representative

The disabled staff representative is the main contact for severely disabled employees in the institute. The representative represents the interests of all severely disabled and equivalent employees towards the employer. Core task is to promote the participation of severely disabled persons in working life, as well as to assist them and help them with advice. The confidant provides opportunities to talk, gather their knowledge and experiences and will call in to manage difficulties. The SBV representative is working under professional discretion, so all the problems and conflicts that are entrusted to the representative and her colleagues are confidential. She represents the interests of severely disabled people and associates them with measures envisaged by the establishment or agency. For this, it is necessary that she knows the severely disabled people very well and their jobs accurately. She keeps them in mind to detect problems in time.

Additionally, she needs a good overview of the workplace at the departments and the possibilities for people with disabilities. Disability occurs when a health damage leads to functional limitations.

In other words: Each health damage and any physical, mental or emotional change that is not temporary and leads to health problems, constitutes disability. It is irrelevant whether a disability is due to illness or accident, or innate. It depends solely on the type of disability.

A severely disabled person is someone who's degree of disability is more than 50%.

Unfortunately, an equivalent physical or mental functional impairment often differs in the degree of disability. For example, a lawyer who has only one arm is as good in his job as someone without an impairment. Therefore you can see that someone who is severely disabled, even with a degree of disability of 100%, is able to perform as expected in his/her profession, if he/she is working in a professional carrier in which he/she is not affected by the disability. So it depends on the type of impairment in connection with the profession.

Furthermore with a variety of different tools and improvements of the working place someone severely disabled is able to provide the same performance as someone without disabilities.

The representative supports and advises accordingly in all cases related to a health problem and a consequent disability. We assist the severely disabled employees, act in their interests and also support others with advice and help (e.g. as application) who have health problems but do not qualify as "severely disabled".

In 2008, the Robert Koch Institute has been awarded the Integration Prize of the State of Berlin, for the exemplary employment of severely disabled people.



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Bibliography on the Institute's History

The 125th anniversary of the foundation of the Robert Koch Institute (RKI) provides an appropriate opportunity to document how the history of the institute has been reflected in the scientific literature over the decades.

The "Bibliography of papers from Robert Koch Institute", published on the occasion of the 75th anniversary of the institute, covered all scientific papers from RKI until then, including papers about the institute itself. Today, this completeness is no longer feasible due to the wealth of publications. We refer to the relevant databases and the website of the Robert Koch Institute as far as details are concerned.

This bibliography contains exclusively literature about the institute and individuals who worked at the institute. The biographies of Robert Koch were included in the selection, since the foundation of the institute was inextricably linked to his scientific career. The announcement of structural changes at the institute (such as the setting up of a new commission) was taken into account in the same way as the description of novel methods which were applied at the institute and lead to fundamental changes in the scientific work (e.g. the introduction of SurvStat). Regular recommendations by commissions at the RKI, scientific meetings, advanced trainings as well as information from the press were not taken into account.

Apart from the "Bibliography of papers from the Robert Koch Institute", we reviewed all volumes of the "Bundesgesundheitsblatt" (a journal for public health, health research and health protection, see page 119) since the beginning of its publication in 1952 as well as the literature lists of fundamental works on the history of the institute. The most important ones in this regard are the publication by Annette Hinz-Wessels "Das RKI im Nationalsozialismus" (RKI during National Socialism), Christoph Gradmann's book "Krankheit im Labor" (Disease in the Laboratory) as well as the biography of Robert Koch by Thomas Brock. We once more looked through and reviewed the literature lists of these publications on the history of the institute.

The bibliography is not categorised by topics or periods, but alphabetically by authors. It does not claim to be complete.

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Compiled by Lisa Marx, Sarah Friedländer and Henriette Senst

Publications

For many years, the RKI has been providing information about its tasks, projects and research to the scientific and general public on the internet. The information is updated regularly and frequently used: On average, there are between 3 million and 5 million page views per month on the German website www.rki.de and its English version www.rki.de/EN.

The Robert Koch Institute publishes two magazines on a regular basis, the monthly “Bundesgesundheitsblatt” and the weekly “Epidemiologisches Bulletin”, and various other publications and information brochures. Most publications are available on the institute’s website and on a special document server (<http://edoc.rki.de/>). RKI scientists also publish numerous articles and reviews in scientific journals. Furthermore RKI offers research and surveillance data on the internet too, e.g. on antimicrobial resistances (<http://ars.rki.de/>), notifiable diseases and other public use files (see below).

Internet Databases

Cases of notifiable diseases / SurvStat

The Robert Koch Institute maintains a database of cases of notifiable diseases and confirmation of pathogens, reported under the German Protection against Infection Act (Infektionsschutzgesetz, IfSG). SurvStat@RKI 2.0 is an application that allows retrieval of aggregated data from a limited version of the German notification system database. Queries can be created individually or customized from pre-defined queries to generate tables, charts, and maps according to the user’s needs. The accessible data is updated weekly.

<http://survstat.rki.de>

Cancer Registry Data

The German Centre for Cancer Registry Data (ZfKD) is located at the Robert Koch Institute in Berlin. It is responsible for pooling and quality-checking the data it receives from the population-based cancer registries in each German federal state. After pooling and quality-checking, the ZfKD analyses and evaluates the data and publishes its findings on a regular basis. In an online database one can find current cancer statistics available through an interactive query. The pooled data set of the German Epidemiological Cancer Registries is available to scientists on application. An important publication is “Cancer in Germany”, which is released every two years (see below).

www.krebsdaten.de

Information System of the Federal Health Monitoring

RKI’s publications are complemented by the Information System of the Federal Health Monitoring (Informationssystem der GBE, IS-GBE). It is an online database which provides information on all GBE topics and is maintained by the Federal Statistical Office. The database systematically pools information from over 100 different data sources, including official statistics, administrative and registry data, and surveys.

www.gbe-bund.de

Public Use Files

The data from surveys conducted by the Robert Koch Institute are available to use by the scientific community on application as



Public Use Files. Each Public Use File comprises the respective data record along with documentation and a description of the study, sample survey documents, a code plan and user instructions (in German only). The data records can be requested upon application from the Epidemiological Data Centre (Robert Koch Institute, unit 21). Additional data may be made available within the framework of cooperation agreements and are jointly analysed where appropriate.

www.rki.de/publicusefiles

Periodicals

Epidemiological Bulletin

The weekly Epidemiological Bulletin (“Epidemiologisches Bulletin”) ensures a rapid information exchange between different stakeholders such as doctors in surgeries, clinics, laboratories, counselling centres and facilities of public health service as well as medical societies, national reference centres and sites of teaching and research.

www.rki.de/epidbull

Bundesgesundheitsblatt – Journal for Public Health, Health Research and Health Protection

The journal for public health, health research and health protection (“Bundesgesundheitsblatt – Gesundheitsforschung – Gesundheitsschutz”) is published monthly by the federal institutes within the portfolio of the Federal Ministry of Health. The journal addresses medical and scientific questions, which

are relevant for the public health system and the governmental healthcare policies. The aim is to provide up-to-date information on significant developments and on specific measures for health protection, prevention concepts, risk prevention and health promotion. Article abstracts are available in German and in English on the journal’s website.

www.bundesgesundheitsblatt.de

Journal of Health Monitoring

The Journal of Health Monitoring, established in 2016, provides scientific information about health in Germany. It is published by Federal Health Reporting Service (Gesundheitsberichterstattung des Bundes, GBE) at Robert Koch Institute. In each issue, recent epidemiological research about one health topic is presented and illustrated by current data. Topics are for example, how many people in Germany suffer from diabetes mellitus or how population ageing develops and what implications this has for healthcare. The articles are written by scientists of the Robert Koch Institute. This journal targets a broad audience and is published once a quarter. It is only available as PDF document.

www.rki.de/EN

UMID: Environment and Human Health – Information Service

The “UMID: Environment and Human Health – Information Service” (German: “UMID: Umwelt und Mensch – Informationsdienst”) is published annually in two issues under the Action Programme Environment and Health (APUG) and is available free of charge. It provides information to public authorities and institutions working in the areas of environment and health, as well as for environmental health professionals and interested members of the public. The abstracts are available in English.

www.rki.de/umid

Epidemiological Yearbook of Notifiable Infectious Diseases

In accordance with the German Protection against Infection Act (Infektionsschutzgesetz, IfSG), the RKI records and analyses data on the occurrence of numerous infectious diseases in Germany. Each year, the results are published in the Epidemiological Yearbook of Notifiable Infectious Diseases. The executive summaries of the yearbook are also provided in English; more detailed information can be obtained online from the SurvStat Database of Notifiable Diseases.

www.rki.de/jahrbuch

Fact sheets for physicians

The publication of fact sheets for physicians (RKI-Ratgeber für Ärzte) is done on the basis of § 4 Protection against Infection Act (Infektionsschutzgesetz, IfSG). They provide practical important and current information and guidance on major infectious diseases. The info sheets are worked out in collaboration with national reference centres and other experts. They are published in the Epidemiological Bulletin and on the internet and revised regularly.

www.rki.de/ratgeber

Newsletters

The Robert Koch Institute offers regular newsletters (in German) about infection protection, health monitoring and approvals for the import and use of human embryonic stem cells. The newsletters can be subscribed at the RKI Website.

www.rki.de/newsletter

Reports on Different Diseases

The Robert Koch Institute publishes regular reports on different diseases, partly within the Epidemiological Bulletin (e.g. HIV/AIDS or travel-associated diseases), partly as printed reports, and partly as GBE booklets (see below).

Report on the Epidemiology of Influenza in Germany

The Report on the Epidemiology of Influenza in Germany is published yearly. An executive summary in English provides an overview of the noteworthy developments and events in influenza epidemiology of the season before. Results of the influenza surveillance of the Robert Koch Institute are primarily based on the analysis of: (1) reports of primary care physicians about patients with acute respiratory illnesses; (2) data from laboratory tests of respiratory samples taken from patients with influenza-like illness and (3) mandatory reporting of laboratory confirmed influenza submitted by county health departments via state health departments to RKI.

<https://influenza.rki.de/Saisonbericht.aspx>

Report on the Epidemiology of Tuberculosis in Germany

An executive summary in English provides an overview of the noteworthy developments and events in tuberculosis epidemiology of the year before. The summary contains case numbers and the number of deaths, analyses of demographic data, citizenship, country of birth, tuberculosis in children, site of disease, drug resistance, treatment outcome and a short conclusion.

www.rki.de/tuberkulosebericht

Cancer in Germany

The German Centre for Cancer Registry Data (ZfKD) is located within the Robert Koch Institute in Berlin. It is responsible for pooling and quality-checking the data it receives from the population-based cancer registries in each German federal state. After pooling and quality-checking, the ZfKD analyses and evaluates the data and publishes its findings on a regular basis. An important publication is “Cancer in Germany”, which is released every two years. In an online database one can find current cancer statistics available through an interactive query (see above).

www.krebsdaten.de

Recommendations by Committees

Fifteen scientific committees have their scientific office at the Robert Koch Institute, e.g. the Standing Committee on Vaccination or the National Advisory Committee Blood. Their recommendations, reports or statements are either published in the Epidemiological Bulletin, in the Journal for Public Health, Health Research and Health Protection (Bundesgesundheitsblatt) or on the RKI website.

Standing Committee on Vaccination

The national immunisation schedule is developed by the Standing Committee on Vaccination (STIKO), and an updated version is usually published once a year (usually in August) in the Epidemiological Bulletin of the Robert Koch Institute. Besides the routine immunisation schedule, STIKO also recommends vaccinations for specific indications or target groups. The current vaccination recommendations are also available in English.

www.rki.de/stiko-en

Recommendations of the Commission for Hospital Hygiene and Infectious Disease Prevention

Medical treatment is often associated with a certain risk of infection. To minimize this risk – based on up-to-date knowledge of how to avoid healthcare-associated infections (HAI) – is the intended goal of the recommendations by the Commission for Hospital Hygiene and Infection Prevention (KRINKO). This commission has been set up at the RKI according to § 23 of the German Protection against Infection Act (Infektionsschutzgesetz). By now, the KRINKO recommendations refer to several aspects of medicine such as prevention of HAI, hygiene management in special fields such as dialysis or endoscopy, reprocessing medical equipment, disinfection and sterilization and surveillance of HAI. They are recommended by mutual consensus of the commission and are published in Bundesgesundheitsblatt and on the website of RKI.

www.rki.de/krankenhaushygiene

Reports of the Central Ethics Committee for Stem Cell Research

The Central Ethics Committee for Stem Cell Research (Zentrale Ethik-Kommission für Stammzellenforschung, ZES) was established in 2002 as part of the German Stem Cell Act. The committee is an independent and interdisciplinary expert body whose activities are governed by this law, the ‘Act ensuring the protection of embryos in conjunction with the import and use of human embryonic stem cells’ (Stem Cell Act – StZG) dated 28 June 2002 and by the ‘Regulation concerning the Central Ethics Committee for Stem Cell Research and the competent authority pursuant to the Stem Cell Act’ (ZES Regulation – ZESV) dated 18 July 2002. Annual reports are submitted to the Federal Ministry of Health and can be accessed via the websites of the ministry and the RKI.

www.rki.de/zes-reports

Reports of the Commission on Genetic Testing (GEKO)

Triannual reports describe the past activities of the commission. These reports also include the evaluation of current and prospective developments in genetic diagnostics. Besides, it processes requests for general interpretation and application of the guidelines, maintains the GEKO website at www.rki.de/geko and participates in national and international fora on issues of genetic diagnostics.

www.rki.de/geko-bericht

Federal Health Reporting (GBE)

Federal Health Reporting (Gesundheitsberichterstattung des Bundes, GBE) continuously supplies data and information on the German population’s state of health and the country’s healthcare services. It covers a broad spectrum of topics, ranging from diseases, symptoms and risk factors to subjective wellbeing and health-related quality of life, utilization of preventive and healthcare services as well as the structures and costs of the healthcare system. Current figures and information on health is provided by the established GBE publications such as RKI’s booklets, GBE kompakt, Contributions on Federal Health Reporting and the reports Health in Germany. GBE’s types of publication differ with respect to breadth and depth of presentation and analysis. They also target different user groups. Even so, they relate to each other, complement each other and are further developed together. The publications are complemented by the Information System of the Federal Health Monitoring (Informationssystem der GBE, IS-GBE, see above).

Health in Germany

The report “Health in Germany” provides a profound overview of the status and development of human health in our country in 2015 in 11 chapters. It is the third comprehensive report of this kind in Federal Health Reporting. A broad database was included in order to represent the disease spectrum, the distribution of risk factors, the use of prevention and healthcare. Overall, it can be observed that there are two major developments which are essentially determining the health and care developments in Germany: demographic changes and the strong influence of the social situation on health. The impact of the demographic development on health and healthcare is analysed in detail in a separate chapter. The report provides an important information base and orientation for different players, who shape the processes and measures to improve health. It hence supports evidence-based decisions for more health in Germany. A summary of the report “Health in Germany” is available in English. The report “Health in Germany” will be published every five to seven years.

www.rki.de/health-in-germany

GBE Booklets

Booklets (Themenhefte) published by Federal Health Reporting deal with specific topics and issues that are given a high priority by health policy. They target health policy-makers, healthcare professionals and scientific experts, but also give the general public an opportunity to learn about health issues. The data and information in the booklets is presented in a scientifically well-founded, action-oriented and clear way. One can either download these booklets as PDF files (German version only) or receive a printed copy by post. Executive summaries are also available in English.

www.rki.de/health-reporting

Contributions to Federal Health Reporting

Supplementing the series of publications by Federal Health Reporting, the Robert Koch Institute releases the series “Contributions to Federal Health Reporting”. Appearing sporadically, the publications offer the reader additional and in-depth information on important aspects of health reporting, for example on the health of men. You can download the publications as PDF files (German version only). Executive summaries are also provided in English.

www.rki.de/health-reporting

GBE kompakt

GBE kompakt is a series of publications by Federal Health Reporting (Gesundheitsberichterstattung des Bundes, GBE). In each issue, one health topic is presented, illustrated by current data. Information is given for example, about how many people have a diabetes mellitus in Germany or what is population ageing and has it any implications for healthcare? GBE kompakt is written by scientists at the Robert Koch Institute. This series targets a broad audience and is published at least once a quarter. It is only available as PDF file.

www.rki.de/health-reporting

Further Scientific Publications

Technical dictionary “Infection Prevention and Infectious Disease Epidemiology”

In this technical dictionary, numerous terms relating to infection control and prevention and infectious disease epidemiology are explained. The dictionary is in German, with English translations for all terms. (“Infektionsschutz und Infektionsepidemiologie: Fachwörter – Definitionen – Interpretationen”).

www.rki.de/fachwoerterbuch

Case definitions and criteria for transmission

In accordance with the German Protection against Infection Act, RKI develops and publishes case definitions and criteria for transmission and evaluation of cases. The case definitions offer uniform criteria for the control of infectious diseases.

www.rki.de/falldefinitionen

Fact sheets on rare and imported infectious diseases

Fact sheets on rare and imported infectious diseases offer information at a glance for doctors so that they are well prepared if tourists business travellers or migrants come back ill.

www.rki.de/steckbriefe

CDC surveillance definitions of healthcare-associated infections

Within healthcare-associated infection (HAI) surveillance, infection definitions provide a uniform basis for diagnosing groups of symptoms as HAIs. They ensure the comparability of national and international surveillance data. The National Reference Centre for Surveillance of Nosocomial Infections uses the same definitions as the Centres for Disease Control and Prevention (CDC) in the USA. Together with the RKI, the National Reference Centre publishes the CDC definitions in German.

www.rki.de/cdc-definitionen

List of disinfectants

Proof of disinfectant activity is a basic condition that must be met for successful and appropriate use of disinfectants. The RKI publishes a list of approved disinfectants and disinfection procedures as tested and approved by the RKI, according to §18 of the German Protection against Infection Act (IfSG). The introduction of this list provides information on approaches in different application areas of disinfectants, e.g. medical and veterinary, and their legal regulation in the Germany. The list is being updated on a regular basis. Recent updates of the listing can be found in the appendix.

www.rki.de/desinfektion

Statement of the Virucide Working Group on the RKI

The Virucide Working Group publishes the state of the art for testing and labeling of disinfectants against viruses and defines of different virus activity spectra.

www.rki.de/virucide

Publications about the Robert Koch Institute

Brochure “Protecting Health, Assessing Risks”

The brochure “Protecting Health, Assessing Risks. Who we are, what we look back on, what we do and will do” introduces the Robert Koch Institute and addresses readers that do not necessarily have specialised medical knowledge. The first chapter describes the most important tasks of the institute: protection from infectious diseases and analysis of the health situation in Germany. The second chapter gives an overview of the institute’s history since its establishment in 1891. The remaining chapters go on to provide an introduction and overview of the various areas of activity at the institute. The brochure is also available in English.

www.rki.de/rki-brochure

Flyer “The Robert Koch Institute at a Glance”

The flyer offers facts and figures about the institute and gives an overview on the tasks and research topics of the different departments. The flyer is available in German and English.

www.rki.de/rki-at-a-glance

Flyer “The Robert Koch Institute: A Historical Retrospective”

The Robert Koch Institute was opened in 1891, with Robert Koch as its first director. The flyer informs about the life of Robert Koch and the institute. It is available in German and in English.

www.rki.de/history

Flyer “Robert Koch in Berlin”

The flyer informs about the places of life and work of Robert Koch in Berlin. It is available in German only.

www.rki.de/history

Reports from the field: RKI staff responds to the Ebola virus disease outbreak in West Africa

The Robert Koch Institute supported the international efforts to contain the Ebola epidemic 2014/15 in West Africa. All in all, RKI staff were on more than 80 deployments to the outbreak area. A brochure contains a series of reports about their work; it is also available in English.

www.rki.de/ebolaserie



Facts and Figures

| | |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1,102 | Number of employees |
| 461 | Number of scientists |
| 4 | Number of sites. The RKI has its headquarters and two additional locations in Berlin as well as a branch in Wernigerode, a university town in the Harz region |
| 48 | Number of trainees |
| 74 | Number of graduate students |
| 90 | Number of professional groups |
| 50 | Number of different types of degrees held by RKI members |
| 87,800,000 | Federal budget in euros Includes €12.9 million for infrastructure, mainly for construction of laboratories |
| 9,075 | Total area in square metres of laboratories operating under biosafety level 2 conditions |
| 13,030,000 | Amount of external project funding in euros, mostly from the European Union, federal ministries and the German Research Foundation |
| 417,695 | Cases of notifiable diseases reported to RKI for 2015 |
| 5,651 | Outbreaks of notifiable diseases reported to RKI for 2015 |
| 438 | Number of publications in peer-reviewed journals in 2015 (376 in 2014, 422 in 2013) |
| 100,000 | Number of books and journals in the RKI library |
| 3,809 | Number of online journals subscribed to by the RKI library |
| 62,204 | Number of the journals that RKI scientists have access to online |
| 14,184 | Citations of articles by RKI scientists in 2015 |
| 100,076 | Participants in the Health Monitoring studies |
| 15 | Number of scientific committees that have their scientific offices at RKI |
| 15 | Number of national reference centres and consultant laboratories at RKI |
| 18,000 | Number of documents on the RKI website www.rki.de and its sub-sites |
| 40,000,000 | Number of internet page requests in 2015 (38 million in 2014, 41 million in 2013) |
| 3,610 | Number of twitter followers in May 2016 (2.938 in 2015, 1670 in 2014, 503 in 2013) RKI has been tweeting since July 2013 |
| 1,825 | Number of press inquiries from May 21 to July 26 concerning the EHEC outbreak 2011 |
| 4,100 | Number of e-mails sent to the central RKI info mail box info@rki.de every year |
| 575 | Number of reports sent to the Federal Ministry of Health in response to official requests in 2015 (225 in 2014, 300 in 2013) |
| 130 | Number of unsolicited reports sent to the Federal Ministry of Health in 2015 (100 in 2014, 100 in 2013) |



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Text and Photos

Robert Koch Institute

Further Photos

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The Robert Koch Institute is a Federal Institute in
the Portfolio of the Federal Ministry of Health

Originally founded as the Royal Prussian Institute of Infectious Diseases on July 1st 1891 with Robert Koch as its director, the Robert Koch Institute has since experienced dramatic changes to achieve its present standing as the German National Public Health Institute. Today the institute is part of an international network for public health research and development. Its two major areas of responsibility lie in combatting infectious diseases and analysing health trends in the population but it also focuses on developing methods and drawing up scientific standards. Moreover, the RKI is very active in the field of qualifying scientists, including doctoral dissertations and trainee programmes. The RKI depends on the excellence of its scientists. Without their fundamental and measure-related research activities the institute would be unable to file recommendations for improving public health. The institute is run by the efforts of its more than 1,100 dedicated employees who, with their over ninety different professions, transform the institute's vision to protect health and explore risks into reality, an excellent basis for providing sound recommendations to political decision-makers. This booklet gives an insight into the Robert Koch Institute as it stands 125 years after its foundation.