

Review Article

The Epidemiology and Diagnosis of Measles

Special Aspects Relating to Low Incidence

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Summary

Background: Measles is a highly contagious viral disease (contagion index near 100%) with a complication rate of up to 30%. The worldwide incidence for 2022 was calculated as 29 cases per million people. Measles can be eliminated if 95% of the population is either vaccinated or immune and measures are taken to limit its spread as soon as an initial suspected case is encountered. However, the worldwide immunization rate has fallen since 2020 (from 86% in 2019 to 81% in 2021).

Methods: To assess the epidemiological situation and describe the state of scientific knowledge regarding laboratory tests for measles, we analyzed recent epidemiological data from the Robert-Koch Institute (RKI) and reviewed pertinent publications retrieved by a selective literature search.

Results: Repeated importations of measles virus have led to a new rise in case numbers in Germany since last year. 79 cases of measles were reported to the RKI in 2023, and 475 in the first eight months of 2024. The latter figure corresponds to the pre-pandemic level. There are still immunization gaps in the population: for instance, by the age of 24 months, 93.7% of children have received their first immunization, and only 80.5% have received the second.

Every suspected case must be confirmed by laboratory testing so that targeted measures can be initiated. Serology is no longer considered sufficiently reliable; a reliable diagnosis now requires a polymerase chain reaction (PCR) test. The specimen can be a throat swab or a urine sample. PCR also enables the differentiation of measles virus variants and the tracing of transmission chains.

Conclusion: Reliable laboratory testing makes it possible to detect measles cases rapidly, initiate measures to slow the spread of the disease, trace infection chains, and assess the risk exposure for measles in Germany.

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Measles is a highly contagious viral disease (contagion index near 100%) that is transmitted primarily via the airborne route. For infection to occur, it is sufficient for a person to stay in a room in which an infected individual has been 2 h previously (1–3). Measles has a high complication rate (up to 30%) (4, 5). Particularly in immunosuppressed individuals, the disease may be severe and result in death. In the case of infection in early childhood (under the age of 5 years), the risk of subacute sclerosing panencephalitis (SSPE) as a fatal long-term sequela is particularly high (approximately 1:1300 to 1:3300) (6–8). Measles causes a long-

term weakening of the immune system since memory B and T cells that have already been formed against various other pathogens are destroyed, thus reducing antibody diversity (referred to as immune amnesia) (9). Patients in one study lost between 11% and 73% of their antibody repertoire (10). This results in increased susceptibility to other pathogens over a prolonged period of time (11).

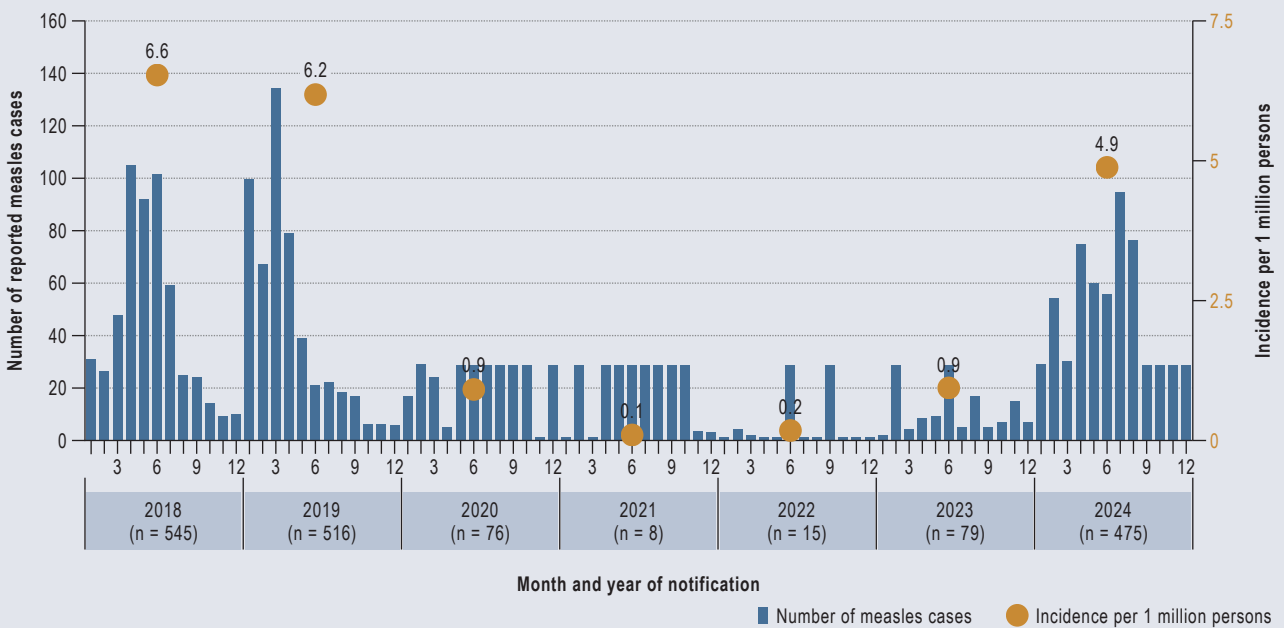
Measles infection begins with fever, conjunctivitis, runny nose, and cough. From the 2nd/3rd day, the fever rises and an enanthem appears on the buccal mucous membrane (small, white Koplik spots) (12). This is followed by the characteristic maculopapular confluent exanthem, which begins on the face and behind the ears and lasts for 4–7 days. On the 5–7th day of illness, the fever declines. In vaccinated individuals, the symptoms may be less pronounced or occur individually.

CME plus⁺

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Figure



Number of measles cases reported to the Robert Koch Institute (RKI) in the period 2018–2024 (as of: 31.08.2024); modified from (17)

Measles is easily mistaken for other febrile exanthematous diseases, such as rubella, fifth disease, Epstein–Barr virus (EBV) infection, scarlet fever, and roseola.

Humans are the only natural hosts of the measles virus (MV). A safe and reliable measles vaccine has been available for decades. A recent Cochrane review reports vaccine effectiveness of 96% after two doses (13). An investigation of a measles outbreak in Duisburg, Germany, found vaccine effectiveness of 99% (14). Under these conditions, it is theoretically possible to eradicate measles. All WHO regions have declared the elimination of this disease as their goal (15).

This article summarizes the current epidemiological data on measles and describes the optimal testing methods required to reliably identify acute cases and rapidly contain outbreaks in this pre-elimination phase.

Methods

In line with the German Infection Protection Act (*Infektionsschutzgesetz*, IfSG), all suspected/acute cases of measles as well as all cases of death due to measles must be notified to the relevant health authority, the same applies to laboratory confirmation of diagnosis. The data are reported to the Robert Koch Institute (RKI) via the federal state health authorities, in accordance with the IfSG. The RKI analyzes the notification data and publishes the results on a regular basis. The current epidemiology of measles is described in this article on the basis of these notification data as well as other international data retrieved in a selective literature search. Data on immunization rates are provided by the vaccination monitoring program of the German Associations of Statutory Health Insurance Physicians (ASHIP) (*Kassenärztliche Vereini-*

gung, KV) at the RKI, the methodology of which is published in a separate article (16). The recommendations on laboratory tests are also based on a selective literature search.

Epidemiology of measles

Since the introduction of mandatory reporting in 2001, the number of measles cases reported to the RKI in line with the IfSG has been declining due to rising immunization rates. Nevertheless, extensive measles outbreaks occurred up until 2019, in addition to sporadic cases and small outbreaks of between two and five cases. The highest age-specific incidence is seen in infants in the first 2 years of life (17). The younger the child, the greater the risk for disease complications. The risk rises again in adults aged over 20 years (18). Meningoencephalitis is described in one of 1000 cases and pneumonia in 11 of 1000 patients. SSPE has been a notifiable disease since 2020; to date, three cases have been notified to the RKI.

The COVID-19 pandemic and associated containment measures led to a sharp decline in the numbers of cases of virtually all vaccine-preventable diseases. In 2020, only 76 cases of measles were reported to the RKI in line with the IfSG—in 2021 and 2022, there were only eight and 15 cases, respectively. These are the lowest case numbers since the introduction of mandatory reporting. However, underreporting, particularly in low-incidence years, of approximately 1:3, is possible (19). In 2023, the number of reported measles cases rose again to 79, while in 2024, a total of 475 cases had been reported to the RKI by 31.08.2024 (*Figure*). In the current year (2024), the German federal states of North Rhine-Westphalia, Berlin, and

Bavaria are those particularly affected by higher numbers of measles cases. In 83 cases, it was reported that measles exposure had possibly occurred abroad. High incidences are currently being observed in the European WHO region in, for example, Great Britain, Austria, and the eastern countries (20).

Vaccine protection and recommendations

The vast majority of measles cases were not (sufficiently) vaccinated against measles. The percentage of unvaccinated cases in the last 10 years was 83% (RKI data). Of vaccinated patients with information on their vaccination status, 68% had only been vaccinated once—and thus insufficiently—at the time of measles infection.

The German Standing Commission on Vaccination (*Ständige Impfkommission*, STIKO) recommends that children receive their first MMR vaccination (MMR: measles, mumps, rubella) at the age of 11 months and the second at the age of 15 months. Younger infants can be protected by vaccinations in their immediate environment (cocooning strategy). All adults aged 18 and over who were born after 1970 should receive a one-dose MMR vaccination if they are unvaccinated, were vaccinated only once in childhood, or their vaccination status is unknown. Furthermore, it is recommended that individuals born after 1970 receive two doses of measles vaccine if they work in, for example, the health sector, care homes, or community facilities.

It is still assumed that vaccine-induced immunity to measles is lifelong (18, 21). Severe side effects to MMR vaccines are rare. For febrile seizures, a vaccine-induced attributable risk of between one case per 1150 and one case per 1700 doses was calculated. For idiopathic thrombocytopenic purpura, this was estimated to be approximately one case per 40 000 administered MMR doses (13).

Data from ASHIP vaccination monitoring at the RKI show that measles vaccination is often not given as early as recommended by the STIKO. For example, only 89.1% of 15-month-old infants born in 2019 had received their first dose of an MMR vaccine, although the vaccination schedule should have been completed, with two doses, by the age of 15 months. At 24 months, 93.7% of children born that year had received their first MMR dose and only 80.5% their second dose (22).

However, missing vaccinations are caught-up with by the time children start school: At school entry medical check-ups in 2020, 97.5% (range at federal-state level: 95.0–98.9%) of all children examined had received their first and 93.2% (range at federal-state level: 87.1–97.1%) their second vaccine dose. In all federal states investigated, over 95% of children had been vaccinated against measles at least once by the time of school entry. A second-dose immunization rate of 95% was achieved in Brandenburg, Hesse, North Rhine-Westphalia, and Mecklenburg-Western Pomerania (22).

Individuals born after 1970 who do not have adequate protection against measles or whose immune status is unknown were asked as part of a 2021 population survey why they had not yet sought immunization against measles. Of those surveyed, 59% reported that no one had hitherto made them aware of the recommendation regarding

vaccination (23). There is clearly room for improvement in medical practices in this regard.

Global WHO target to eliminate measles and rubella

All WHO regions pursue the target of eliminating measles. The European WHO region additionally aims to eliminate rubella. Elimination can be verified independent of the number of reported cases if chains of infection triggered by imported MV are stopped within less than 12 months, which is the definition of interrupting endemic transmission. Elimination status is granted when the interruption of endemic transmission can be demonstrated for a period of 3 years. Genomic surveillance plays an important role when estimating the length of transmission chains (24).

In order to sustainably interrupt endemic transmission and build community protection, more than 95% of the population needs to be protected against measles (15, 25–30). The WHO has set an immunization rate of 95% as a key strategy for achieving its elimination goal (31, 32).

The estimated worldwide immunization rate for the first-dose measles-containing vaccine against measles (MCV1) rose between 2000 and 2019 from 72% to 86%. As a result, the global incidence of measles fell from 145 cases/1 million people in 2000 to 21 cases/1 million people in 2020. According to WHO extrapolations, approximately 57 million deaths were averted between 2000 and 2022. However, the rate of immunization then fell worldwide to 83% by 2020 and further to 81% by 2021 (33, 34). In 2022, around 22 million children worldwide did not receive MCV1 as part of their routine vaccinations. The incidence of measles rose in 2022 compared to 2021 from 17 to 29 cases/1 million people (34). Compared to 2022, the number of cases of measles worldwide almost doubled in 2023 from approximately 171 000 to around 323 000 cases (WHO data) (35). The global decline in immunization is attributed to the COVID-19 pandemic and global conflicts, which have restricted access to and uptake of vaccinations (36). Furthermore, misinformation about the measles vaccination affects the trust put in the vaccine by parents and as yet unvaccinated individuals.

The status of measles and rubella elimination in Germany

In Germany, the National Verification Commission for Measles/Rubella (*Nationale Verifizierungskommission Masern/Röteln*, NAVKO) was set up at the RKI by the Federal Ministry of Health (*Bundesministerium für Gesundheit*, BMG) to report to the BMG and the WHO's Regional Verification Commission (RVC) on the status of elimination based on all available data. The NAVKO has already concluded that the endemic transmission of measles and rubella in Germany was interrupted in the 2019–2022 period (37). The RVC concurred with the NAVKO's assessment for 2022 and granted Germany the status of interrupted measles transmission for 12 months. No assessment is available as yet for 2023. With regard to rubella, the RVC certified Germany's rubella elimination status in 2020, retroactive from 2017.

Table

Laboratory tests for suspected acute measles

Laboratory test		Specimen	Transportation	Time period in which a positive result can be expected	Comments
PCR detection of viral RNA		Throat swab (recommended), nasal swab	Moist swab in viral transport medium	Symptom onset to 7 days after exanthem onset, in vaccinated individuals , up to 5 days after exanthem onset	<ul style="list-style-type: none"> • Serum is not a suitable specimen for PCR. • Testing negative in RNA detection does not reliably rule out acute measles.
PCR detection of viral RNA		Urine	Urine Monovette	3–10 days after exanthem onset, in vaccinated individuals , up to 3–7 days after exanthem onset	<ul style="list-style-type: none"> • ≥ 2 mL
Genotyping		Specimens obtained for PCR analysis			<ul style="list-style-type: none"> • Only possible if RNA detection is positive and viral load is high
Antibody detection	Measles anti-IgM	Blood/serum	Serum (gel) tube	3 days after exanthem onset and up to 4–6 weeks thereafter	<ul style="list-style-type: none"> • Only recommended if the timeframe for PCR has been exceeded and/or vaccine failure is suspected! • Low positive predictive value • Often only detectable from day 3 after exanthem onset • If the result is negative by day 3, taking a further specimen is recommended
	Measles anti-IgG	Blood/serum	Serum (gel) tube	5–7 days after exanthem onset, permanent residual titer	

Modified from (e12); PCR, polymerase chain reaction

Diagnosis

Laboratory testing for measles

Although the number of cases is on the rise again, measles is now comparatively rare in Germany. When incidence rates are low, it becomes challenging to reliably diagnose acute measles (38, 39).

Due to the very high risk of infection, a diagnostic investigation should be immediately initiated upon the appearance of the first suspected case of measles, in order that protective measures such as post-exposure vaccinations or post-exposure administration of immunoglobulins can be promptly initiated to contain the spread. This requires a rapid and unequivocal diagnosis, ideally starting with the first known case (index case) (24). All cases of suspected measles must be reported to the relevant health authority, in line with the IfSG. It is also important to report clinically suspected cases even in the absence of laboratory confirmation.

If measles is clinically suspected, a laboratory investigation that directly detects the pathogen should always be performed (38). It confirms the diagnosis rapidly, and in addition makes it possible to characterize circulating viruses, thereby shedding light on the links between cases of infection and making it possible to estimate the length of transmission chains (24, 40). Direct detection of MV should be performed primarily by polymerase chain reaction (PCR) on throat swabs and urine. This method offers significantly greater diagnostic certainty (sensitivity and specificity) than does serological testing. Moreover,

the collection of noninvasive samples with this method makes it more suitable for the testing of children.

Measles-specific IgM serology alone is no longer recommended for the laboratory confirmation of measles, since measles IgM is detectable in around only 70% of cases within the first 3 days of the disease (e1, e2). Thus, taking a blood sample too early can lead to false-negative results. An even greater problem is the low predictive value (PPV) of measles IgM detection has in times of low measles incidence (e3). The PPV indicates how many of the individuals who test positive actually have the disease or are infected. In a Canadian study, this value was only 17% for measles (e4): less than one fifth of IgM-positive individuals actually had measles. This distortion may be explained by a recent measles vaccination or polyclonal stimulation following EBV or parvovirus B19 infection, among other things. These findings may also arise from, for example, immunity determinations that unnecessarily include the determination of IgM antibodies. IgM determination should only be performed if there are specific reasons for suspecting disease.

MV can be detected in throat swabs approximately 7 days after the onset of symptoms and in urine from day 3 to around day 10 (Table). The German National Reference Centre for Measles, Mumps, Rubella (*Nationale Referenzzentrum Masern, Mumps, Röteln*, NRZ MMR) at the RKI offers PCR testing free of charge. Specimen collection kits and the specimen submission form, which must to be filled out and included with the specimen, can be

Box

Conclusions for clinical practice

- All patients born after 1970 should be checked to establish whether they have been vaccinated according to the vaccination recommendations of the German Standing Committee on Vaccination (STIKO). Missing vaccinations with an MMR vaccine (MMR: measles, mumps, rubella) can be caught-up at any time, even if there is already immunity to one or two of the three components.
- From a differential diagnostic perspective, one should consider measles if an individual has corresponding symptoms (even if mild in vaccinated individuals) and:
 - They could have been in contact with someone who has measles
 - The epidemiological situation makes measles infection seem likely
 - They could have been exposed to measles abroad or in another German federal state with known cases of measles during the incubation period (7–21 days, 10–14 days on average).
- Every suspected case of acute measles, irrespective of vaccination status and the results of further laboratory tests, is subject to mandatory notification. The relevant health authority must receive notification within 24 h.
 - Relevant health authorities can be notified via the electronic DEMIS reporting system.
- If acute measles is suspected, laboratory testing should be ordered as soon as possible (*Table*).
 - All clinically suspected cases should be confirmed by polymerase chain reaction (PCR). The viral genome can be reliably detected in a throat swab or urine within the first 7 days after exanthem onset.
 - IgM serology should only be performed if the timeframe for successful PCR testing has been exceeded or as an additional test in the case of suspected vaccine failure.
 - A pre-stamped sample collection kit can be ordered free of charge from the National Reference Centre for Measles, Mumps and Rubella (NRZ MMR) to be held in stock (more information is available at www.rki.de/DE/Content/Infekt/NRZ/MMR/Masernentnahme.pdf?__blob=publicationFile).

requested from the NRZ MMR website (www.rki.de/DE/Content/Infekt/NRZ/MMR/Entnahmesets/Entnahmesets_node.html).

Molecular fine typing makes it possible to determine not only the MV genotype but also its sequence variant. One can draw conclusions from this regarding the individual transmission chains to which the viruses belong. MV are divided according to WHO nomenclature into 24 genotypes based on the nucleotide sequence of a defined genome segment (450 nucleotides of the N-gene). However, in 2018, only the genotypes B3, D4, and D8 were still in worldwide circulation. Fine typing is essential for surveillance (33, e5). Genotyping is performed free of charge at the NRZ MMR.

As part of integrated genomic surveillance, the molecular data on the detected MV are linked to the case-related epidemiological data in order to determine transmission pathways and assess the duration of transmission. Analyses of the available data show that endemic transmission of MV in Germany has been unlikely for some years. However, if there was a greater number of analyzed specimens, it would be possible to more precisely assess transmission chains of variants.

Diagnosing measles in vaccinated individuals

Immunity against measles is built up through immunization or after having contracted the disease. Vaccinated individuals with secondary vaccine failure show attenuated typical symptoms and experience only rarely complications (e6–e10).

Measles infection in vaccinated individuals can only be reliably confirmed by means of virus detection using PCR.

Since the viral load is usually lower in vaccinated individuals, throat swabs should be taken as soon as possible, but no later than the fifth day, and urine samples no later than the seventh day.

If measles is suspected in a vaccinated individual, serology is helpful in identifying the cause of possible vaccine failure. Primary vaccine failure is caused by, for example, improper storage or administration of the vaccine. In such cases, the vaccine fails to trigger a primary immune response and infection follows the same course as in unvaccinated individuals, also in terms of laboratory tests. Cases such as this are characterized by a positive PCR, high IgM, and rising IgG levels with low antibody avidity (binding strength to the antigen). Secondary vaccine failure is the consequence of a slow decline in the IgG titer induced by immunization (e11). Following renewed contact with MV, the rise in the IgM titer may be weak or completely absent; (highly) positive IgG with high avidity due to antibody maturation is typical.

In 3–5% of vaccinated individuals, the live vaccine causes what is referred to as vaccine-induced measles, a vaccine reaction associated with fever and exanthem. Using a special PCR technique carried out at the NRZ MMR, it is possible to distinguish between a vaccine reaction and true measles. Vaccine-induced measles is not contagious and does not require any further measures. Rapid testing can help to avoid unnecessary isolation measures.

Summary

The findings of this article have been summarized in the *Box* as conclusions for clinical practice. This article

describes which laboratory tests are required in order to rapidly identify acute cases, take measures, and trace transmission chains, thereby enabling a valid assessment to be made of the potential risk for measles and the status of elimination in Germany.

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Conflict of interest statement

DMK is head of the office of the National Verification Commission for Measles/Rubella at the Robert Koch Institute.

HH is Vice President of the Austrian Society for Vaccinology (*Österreichische Gesellschaft für Vakzinologie*) as well as a member of the Scientific Advisory Board and Organization Committee of the Austrian Vaccination Day (*Österreichischer Impftag*).

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References

1. Bloch AB, Orenstein WA, Ewing WM, et al.: Measles outbreak in a pediatric practice: airborne transmission in an office setting. *Pediatrics* 1985; 75: 676–83.
2. Remington PL, Hall WN, Davis IH, Herald AL, Gunn RA: Airborne transmission of measles in a physician's office. *JAMA* 1985; 253: 1574–7.
3. de Jong JD: The survival of measles virus in air. *Antonie Van Leeuwenhoek* 2005; 29: 327–8.
4. Holzmann H: Masern. *Osterr Arzteztg* 2015; 1/2: 20–30.
5. Perry RT, Halsey NA: The clinical significance of measles: a review. *J Infect Dis* 2004; 189 (Suppl 1): S4–16.
6. Schönberger K, Ludwig MS, Wildner M, Weissbrich B: Epidemiology of subacute sclerosing panencephalitis (SSPE) in Germany from 2003 to 2009: a risk estimation. *PLoS One* 2013; 8: e68909.
7. Wendorf KA, Winter K, Zipprich J, et al.: Subacute sclerosing panencephalitis: the devastating measles complication that might be more common than previously estimated. *Clin Infect Dis* 2017; 65: 226–32.
8. Garg RK, Mahadevan A, Malhotra HS, Rizvi I, Kumar N, Uniyal R: Subacute sclerosing panencephalitis. *Rev Med Virol* 2019; 29: e2058.
9. Petrova VN, Sawatsky B, Han AX, et al.: Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles. *Sci Immunol* 2019; 4: eaay6125.
10. Mina MJ, Kula T, Leng Y, et al.: Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. *Science* 2019; 366: 599–606.
11. Gadroen K, Dodd CN, Masclee GMC, et al.: Impact and longevity of measles-associated immune suppression: a matched cohort study using data from the THIN general practice database in the UK. *BMJ open* 2018; 8: e021465.
12. Kimura H, Shirabe K, Takeda M, et al.: The association between documentation of koplik spots and laboratory diagnosis of measles and other rash diseases in a National Measles Surveillance Program in Japan. *Front Microbiol* 2019; 10: 269.

13. Di Pietrantonj C, Rivetti A, Marchione P, Debalini M, Demicheli V: Vaccines for measles, mumps, rubella, and varicella in children. *Cochrane Database Syst Rev* 2020; 4: CD004407.
14. Wichmann O, Hellenbrand W, Sagebiel D, et al.: Large measles outbreak at a German public school, 2006. *Pediatr Infect Dis J* 2007; 26: 782–6.
15. Anderson RM, May RM: Directly transmitted infectious diseases: control by vaccination. *Science* 1982; 215: 1053–60.
16. Rieck T, Feig M, Eckmanns T, Benzler J, Siedler A, Wichmann O: Vaccination coverage among children in Germany estimated by analysis of health insurance claims data. *Hum Vaccin Immunother* 2014; 10: 476–84.
17. Robert Koch-Institut: Infektionsepidemiologisches Jahrbuch meldepflichtiger Krankheiten für 2019. www.rki.de/DE/Content/Infekt/Jahrbuch/Jahrbuch_2019.pdf?__blob=publicationFile (last accessed on 31 October 2024).
18. Walter AO, Paul AO, Kathryn ME, Stanley AP: Plotkin's vaccines. Philadelphia, PA: Elsevier 2024.
19. Takla A, Wichmann O, Rieck T, Matysiak-Klose D: Measles incidence and reporting trends in Germany, 2007–2011. *Bull World Health Organ* 2014; 92: 742–9.
20. World Health Organization: EpiData measles and rubella. World Health Organization 2024. www.who.int/andorra/publications/m/item/epidata-8-2024 (last accessed on 31 October 2024).
21. Markowitz LE, Preblud SR, Fine PE, Orenstein WA: Duration of live measles vaccine-induced immunity. *Pediatr Infect Dis J* 1990; 9: 101–10.
22. Rieck T, Feig M, Siedler A: Impfquoten von Kinderschutzimpfungen in Deutschland – aktuelle Ergebnisse aus der RKI-Impfsurveillance. *Epid Bull* 2022; 48: 3–25.
23. Seefeld L, Horstkötter N, Müller U, et al.: Einstellungen, Wissen und Verhalten von Erwachsenen und Eltern gegenüber Impfungen – Ergebnisse der Repräsentativbefragung 2021 zum Infektionsschutz. BZgA-Forschungsbericht. Köln: Bundeszentrale für gesundheitliche Aufklärung, 2022.
24. World Health Organization: Eliminating measles and rubella in the WHO European region; Integrated guidance for surveillance, outbreak response and verification of elimination. Copenhagen: WHO Regional Office for Europe 2024.
25. Funk S, Knapp JK, Lebo E, et al.: Combining serological and contact data to derive target immunity levels for achieving and maintaining measles elimination. *BMC medicine* 2019; 17: 180.
26. Hayman DTS: Measles vaccination in an increasingly immunized and developed world. *Hum Vaccin Immunother* 2019; 15: 28–33.
27. Gay NJ, Hesketh LM, Morgan-Capner P, Miller E: Interpretation of serological surveillance data for measles using mathematical models: implications for vaccine strategy. *Epidemiol Infect* 1995; 115: 139–56.
28. Wallinga J, Heijne JC, Kretzschmar M: A measles epidemic threshold in a highly vaccinated population. *PLoS medicine* 2005; 2: e316.
29. Gay NJ: The theory of measles elimination: implications for the design of elimination strategies. *J Infect Dis* 2004; 189 (Suppl 1): S27–S35.
30. van Boven M, Kretzschmar M, Wallinga J, O'Neill PD, Wichmann O, Hahné S: Estimation of measles vaccine efficacy and critical vaccination coverage in a highly vaccinated population. *J R Soc Interface* 2010; 7: 1537–44.
31. World Health Organization: Eliminating measles and rubella. Framework for the verification process in the WHO European region 2014. World Health Organization, Regional Office for Europe 2014.
32. World Health Organization: Measles vaccines: WHO position paper, April 2017—recommendations. *Vaccine* 2019; 37: 219–22.
33. Dixon MG, Ferrari M, Antoni S, et al.: Progress toward regional measles elimination—worldwide, 2000–2020. *MMWR Morb Mortal Wkly Rep* 2021; 70: 1563–9.
34. Minta AA, Ferrari M, Antoni S, et al.: Progress toward measles elimination—worldwide, 2000–2022. *MMWR Morb Mortal Wkly Rep* 2023; 72: 1262–8.
35. World Health Organization: Global measles and rubella monthly. Update. World Health 2024. <https://immunizationdata.who.int/global?topic=Provisional-measles-and-rubella-data&location=> (last accessed on 31 October 2024).

36. Maltezou HC, Medic S, Cassimos DC, Effraimidou E, Poland GA: Decreasing routine vaccination rates in children in the COVID-19 era. *Vaccine* 2022; 40: 2525–7.
37. Nationale Verifizierungskommission Masern/Röteln: Berichte der Nationalen Verifizierungskommission Masern/Röteln beim Robert Koch-Institut. www.rki.de/DE/Content/Kommissionen/NAVKO/Berichte/Berichte_node.html (last accessed on 31 October 2024).
38. Filardo TD, Crooke SN, Bankamp B, et al.: Measles and rubella diagnostic and classification challenges in near- and post-elimination countries. *Vaccines* 2024; 12: 697.
39. Hübschen JM, Bork SM, Brown KE, et al.: Challenges of measles and rubella laboratory diagnostic in the era of elimination. *Clin Microbiol Infect* 2017; 23: 511–5.
40. Williams D, Penedos A, Bankamp B, et al.: Update: circulation of active genotypes of measles virus and recommendations for use of sequence analysis to monitor viral transmission. *Wkly Epidemiol Rec* 2022; 39: 485–92.

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Supplementary material
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CLINICAL SNAPSHOT



Loss of Head Voice Function in Long-Standing Hashimoto's Thyroiditis

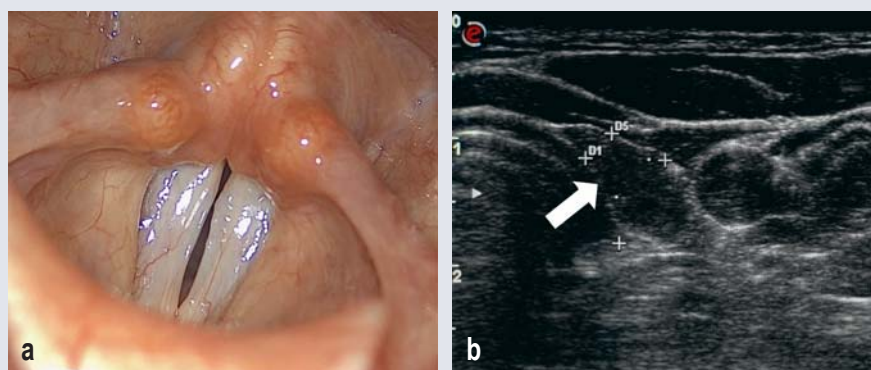


Figure:
 a) laryngeal videostroboscopy image showing incomplete glottic closure in the chest voice register and unsuccessful vocal fold elongation during attempted phonation in the head voice in bilateral paralysis of the external branch of the superior laryngeal nerve (EBSLN).
 b) ultrasound overview image of the left lobe of the thyroid in the transverse plane with evidence of atrophic, hypoechoic and inhomogeneous parenchyma (arrow) in chronic Hashimoto's thyroiditis.

A 63-year-old soprano who was incapacitated for work presented for a phoniatic consultation due to an 11-year history of gradually progressive loss of head voice. Laryngeal videostroboscopy revealed flaccid vocal folds with glottic insufficiency in the chest voice register and bilateral inability to elongate when transition to the head voice was attempted (*left Figure*). The patient's voice range profile was significantly reduced, given that notes above the central passaggio (from D#4) could no longer be formed. Ultrasound of the neck showed hypoechoic, atrophic cricothyroid muscles on both sides together with hypoechoic, inhomogeneous parenchyma of the two atrophic lobes of the thyroid in the setting of Hashimoto's thyroiditis that had been known for decades and was under L-thyroxine replacement therapy (*right Figure*). Transcutaneous laryngeal electromyography of the cricothyroid muscles confirmed the diagnosis of bilateral paralysis of the external branch of the superior laryngeal nerve (EBSLN) with classic signs of denervation. The case described here suggests that, in addition to cervical trauma, chronic inflammatory processes in this immediate anatomical vicinity may also be a cause of EBSLN lesions. Due to the lack of restorative treatment options for EBSLN paralysis, we recommend regular phoniatic monitoring for professional singers with Hashimoto's thyroiditis. Timely ("prophylactic") neuromonitoring-guided thyroidectomy for head voice preservation is open to critical discussion, taking into account the risk of intraoperative damage to the recurrent laryngeal nerve.

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Supplementary material to accompany the article

The Epidemiology and Diagnosis of Measles

Special Aspects Relating to Low Incidence

by Dorothea Matsysiak-Klose, Annette Mankertz, and Heidemarie Holzmann

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eReferences

- e1. Helfand RF, Kebede S, Gary HE Jr, Beyene H, Bellini WJ: Timing of development of measles-specific immunoglobulin M and G after primary measles vaccination. *Clin Diagn Lab Immunol* 1999; 6: 178–80.
- e2. Semmler G, Aberle SW, Griebler H, et al.: Performance of four IgM antibody assays in the diagnosis of measles virus primary infection and cases with a serological profile indicating reinfection. *J Clin Microbiol* 2021; 59: e02047–20.
- e3. Woods CR: False-positive results for immunoglobulin M serologic results: explanations and examples. *J Pediatric Infect Dis Soc* 2013; 2: 87–90.
- e4. Bolotin S, Lim G, Dang V, et al.: The utility of measles and rubella IgM serology in an elimination setting, Ontario, Canada, 2009–2014. *PLoS One* 2017; 12: e0181172.
- e5. Patel MK, Goodson JL, Alexander JP, et al.: Progress toward regional measles elimination—worldwide, 2000–2019. *MMWR Morb Mortal Wkly Rep* 2020; 69: 1700–5.
- e6. Hahné SJM, Nic Lochlainn LM, van Burgel ND, et al.: Measles outbreak among previously immunized healthcare workers, the Netherlands, 2014. *J Infect Dis* 2016; 214: 1980–6.
- e7. Bonneton M, Antona D, Danis K, Ait-Belghiti F, Levy-Bruhl D: Are vaccinated measles cases protected against severe disease? *Vaccine* 2020; 38: 4516–9.
- e8. Gibney KB, Attwood LO, Nicholson S, et al.: Emergence of attenuated measles illness among IgG-positive/IgM-negative measles cases: Victoria, Australia, 2008–2017. *Clin Infect Dis* 2020; 70: 1060–7.
- e9. Hubiche T, Brazier C, Vabret A, Reynaud S, Roudiere L, Del Giudice P: Measles transmission in a fully vaccinated closed cohort: data from a nosocomial clustered cases in a teenage psychiatric unit. *Pediatr Infect Dis J* 2019; 38: e230–2.
- e10. Iwamoto M, Hickman CJ, Colley H, et al.: Measles infection in persons with secondary vaccine failure, New York City, 2018–19. *Vaccine* 2021; 39: 5346–50.
- e11. Schenk J, Abrams S, Theeten H, Van Damme P, Beutels P, Hens N: Immunogenicity and persistence of trivalent measles, mumps, and rubella vaccines: a systematic review and meta-analysis. *Lancet Infect Dis* 2021; 21: 286–95.
- e12. Robert Koch-Institut: RKI-Ratgeber Masern. *Epid Bull* 2024; 46: 3–23. DOI 10.25646/12902.

Questions on the article in issue 26/2024:

The Epidemiology and Diagnosis of Measles

The submission deadline is 26 December 2025. Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

What is the worldwide incidence of measles reported to be for 2022?

- a) 2.9 Cases/1 million persons
- b) 29 Cases/1 million persons
- c) 290 Cases/1 million persons
- d) 2900 Cases/1 million persons
- e) 29 000 Cases/1 million persons

Question 2

What has been the trend over time in the estimated worldwide first-dose measles immunization rate?

- a) The immunization rate rose continuously between 2000 (72%) and 2023 (86%).
- b) The immunization rate fell between 2000 (86%) and 2019 (84%), then rose briefly (2021: 90%), only to drop back to 75% by 2023.
- c) Since its previous peak in 2000 (86%), the immunization rate continuously fell, reaching 75% in 2022.
- d) The immunization rate rose between 2000 (72%) and 2019 (86%) and then dropped to 81% by 2021.
- e) Since 2000 (75%), the immunization rate has continuously risen, reaching 91% in 2022.

Question 3

Which statement regarding the transmission of measles most applies?

- a) Domestic pets (such as dogs and cats) serve as intermediate hosts for the measles virus but do not usually transmit the virus to humans.
- b) Humans are the only host for measles viruses, which are transmitted primarily by the airborne route.
- c) Domestic pets (such as rabbits and cats) serve as intermediate hosts for the measles virus, which is usually excreted in their feces and can be transmitted in this way.
- d) The measles virus is transmitted from person to person and only via smear infections.
- e) Fruit bats (*Pteropodidae*) serve as a reservoir for the measles virus, which jumps from the bats to humans.

Question 4

What is the efficacy of two-dose measles immunization according to a Cochrane review and data from Duisburg, Germany?

- a) 71–75%
- b) 77–82%
- c) 84–89%
- d) 90–93%
- e) 96–99%

Question 5

At what age, according to RKI recommendations, should the first two immunizations be given as standard in childhood?

- a) At the age of 6 months and 9 months
- b) At the age of 11 months and 15 months
- c) At the age of 12 months and 24 months
- d) At the age of 18 months and 24 months
- e) At the age of 24 months and 36 months

Question 6

A 2021 population survey asked people born after 1970 who did not have adequate measles protection or whose immune status was unknown about their reasons for not being immunized. What did 59% of these people give as their reason?

- a) They were afraid of immunization side effects.
- b) They had existing contraindications to measles immunization.
- c) They were afraid of additional costs arising from measles immunization.
- d) They had doubts regarding the effectiveness of immunization to prevent the disease.
- e) They had not yet been made aware of the recommendation on immunization.

Question 7

Which diagnostic test should be performed as a priority if acute measles is clinically suspected?

- a) Histological investigation in the form of direct pathogen detection by microscopy of a throat swab and/or urine sample.
- b) A serological assay for indirect pathogen detection via the presence of measles anti-IgG in blood/serum.
- c) A serological assay for indirect pathogen detection via the presence of measles anti-IgG in saliva.
- d) A laboratory test in the form of direct pathogen detection by PCR of a throat swab and/or urine sample.
- e) A serological assay for indirect pathogen detection via the presence of measles anti-IgG in cerebrospinal fluid.

Question 8

Which statement regarding mandatory reporting most applies?

- a) Even suspected cases of acute measles must be reported to the relevant health authority within 24 h.
- b) If a case of acute measles is suspected, one should first await confirmation by PCR testing; once this is available, the disease must be immediately reported to the health authority.
- c) If a vaccination card shows that a person has been fully vaccinated, a case of acute measles does not need to be reported due to the low viral load.
- d) If a case of acute measles is suspected, an antibody test (IgM serology) on a throat swab must be carried out immediately and the result reported to the relevant health authority within 6 h.
- e) An acute case of measles is only subject to mandatory reporting when the infected person is aged between 0 and 18 years. For adults, reporting is voluntary.

Question 9

Which statement regarding vaccination with the live vaccine most applies?

- a) Vaccine-induced measles, a vaccine reaction involving fever and exanthem, is contagious and can be transmitted to immunosuppressed individuals, sometimes causing severe disease.
- b) Vaccine-induced measles, a vaccine reaction involving fever and exanthem, occurs only in adults and requires inpatient treatment in 3–5% of cases.
- c) Of vaccinated individuals, 3–5% develop a vaccine reaction referred to as vaccine-induced measles, which can be differentiated from true measles infection by means of PCR testing.
- d) Vaccine-induced measles occurs in, at most, 1% of vaccinated individuals and cannot be distinguished from true measles infection by means of PCR testing.
- e) Vaccine-induced measles, a vaccine reaction involving fever and exanthem, occurs only in children under the age of 5 years.

Question 10

Fine typing is essential to monitor the spread of measles. How many genotypes have been distinguished and how many were circulating worldwide in 2018?

- a) Five genotypes have been distinguished and two genotypes were circulating worldwide in 2018.
- b) A total of 15 genotypes have been distinguished and five genotypes were circulating worldwide in 2018.
- c) A total of 24 genotypes have been distinguished and three genotypes were circulating worldwide in 2018.
- d) A total of 86 genotypes have been distinguished and seven genotypes were circulating worldwide in 2018.
- e) A total of 128 genotypes have been distinguished and 24 genotypes were circulating worldwide in 2018.