



Article

# The Study of the Resurgence of Measles, a Vaccine-Preventable Illness, and How Present Concerns Differ from Earlier Expectations of Measles Eradication

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**Abstract:** This article demonstrates how measles, a vaccine-preventable viral illness, moved from being eradicated to resurgent in less than 40 years. Several factors have contributed to a "perfect storm" of increasing measles infections, fatalities, and hospitalizations throughout the world at this time, particularly in wealthier nations like Europe. The present rise in measles infections in 2024 is connected to decades of erroneous assertions about vaccinations' detrimental effects, such as vaccine hesitancy and complacency, decreased childhood vaccination rates in the aftermath of the COVID-19 epidemic, and a bogus link to autism. It is critical that all countries quickly adopt public health and primary care initiatives, as well as take efforts to promote awareness about the dangers of measles and the significance of following vaccine regimens.

**Keywords:** Vaccination Hesitancy, Measles, MMR Vaccine, Review

## 1. Introduction

Measles is an infectious respiratory illness. Severe instances are prevalent in young children and those with compromised immune systems. It also gets worse during pregnancy, increasing the risk of an early delivery, stillbirth, or miscarriage [1]. The most effective strategy to reduce measles is to increase vaccination rates with two doses of the triple vaccine (measles, mumps, and rubella). Sustained high vaccination coverage is required to eliminate endemic measles, which the World Health Organization defines as the absence of endemic measles in a country with an adequate monitoring system for at least a year [2]. The German trivalent vaccination, introduced in England between 2021 and 2022, falls short of the WHO objective of  $\geq 95\%$ . Less than 90% of children received the first dose at age 2 and 86% received the second dose at age 5. Public Health England (PHE) research has found that the level of community immunity in the UK is significantly lower than what is required to prevent measles transmission in a number of birth cohorts [3]. Those born between 1998 and 2004 (19-25 years estimated to 2023) are the most vulnerable, as are teenagers who have not yet got the vaccination. The self-immunity objectives for primary and secondary school children have not been met, making London the region most at risk of rising incidence [3]. Measles is particularly prevalent in areas whose children are not fully vaccinated, such as the Travelers community, Orthodox Jewish community, Steiner group (anthroposophists), and new immigrants [4,5]. Furthermore, vaccination rates vary by area, ethnicity, and deprivation.

**Citation:** Al-Kheroo, Z., Al-abase, A., Altobje, M. The Study of the Resurgence of Measles, a Vaccine-Preventable Illness, and How Present Concerns Differ from Earlier Expectations of Measles Eradication. Central Asian Journal of Medical and Natural Science 2025, 6(3), 1169-1176.

Received: 30<sup>th</sup> Apr 2025

Revised: 15<sup>th</sup> May 2025

Accepted: 23<sup>rd</sup> May 2025

Published: 31<sup>st</sup> May 2025



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Measles transmission restarted in 2018 amid extensive outbreaks throughout Europe, despite the UK's brief success in eradicating endemic measles in 2016 and 2017. Measles activity sharply declined during the COVID-19 pandemic due to extensive travel and social restrictions. As a result of this disruption in transmission, measles eradication status has theoretically been reclaimed in the UK in 2023 (based on surveillance data from 2022). However, in 2023, the incidence rose in England once more, as it has done throughout the world. Significant outbreaks are already occurring in a number of South Asian and African nations, so this is unlikely to continue.

Continuous measles monitoring is required to identify symptomatic cases and classify them as endemic, imported, or perhaps import-related, based on extensive epidemiology and viral sequencing data, in order to continue the measles reduction or eradication strategy. In order to eradicate the measles, the WHO requires that a sizable portion of probable cases be eliminated [2]. This is an essential indicator of the sensitivity of the monitoring system as well. Determining the epidemiological and virological links between confirmed cases is also crucial to detecting outbreaks. Targeted vaccination efforts are informed by outbreaks, which identify vulnerable communities with low immunization rates. Several similar epidemics have happened in recent years, especially among Charedi Orthodox

This publication offers comprehensive public health guidelines for managing contacts of suspected measles cases, assessing their risk, and describing the laboratory testing services that can be used to support these efforts. This is placed against the backdrop of the UK Measles and Rubella Elimination Strategy, which calls for the establishment of a national monitoring system to assist and track progress toward WHO elimination targets.

#### **Diagnosis, differential diagnoses, and clinical presentation**

The measles virus can incubate for six to twenty-one days, during which time it can spread widely [6]. The measles virus causes viremia when it infects the respiratory system or conjunctivae and travels to the lymph nodes. Measles can spread up to 4 days after the rash goes away and up to 5 days before a skin rash shows [10]. Koplik's spots are small, white, red, or gray lesions, about a millimeter in size, that appear on the oral mucosa. They were first reported in 1896 [7]. In 50–70% of measles patients, Koplik spots are a common sign of the prodromal phase of the illness and frequently appear before the skin rash [6,7]. During the incubation period, patients infected with the measles virus are asymptomatic. A second incidence of the virus generally appears in the blood a few days after the first, including the development of symptoms [6]. Children with defective or weak immune systems are more likely to become infected and die from the virus because humoral and cellular immunity triggered by infection is required to eradicate it and achieve long-term immunity [6]. Although the measles virus undergoes changes that alter its harmful character, measles infection is mild in those who have protection from vaccination or prior infections. Infection with the virus generally results in lifetime immunity [8]. The secondary infection linked to measles is frequently caused by reactivation of infections with TB, parainfluenza virus, adenovirus, pneumococcal, *Haemophilus influenzae*, *Staphylococcus aureus*, and *Streptococcus pyogenes* [9, 10]. Moreover, immunological failure linked to measles may endure for up to three years after contracting the virus [8].

The diagnosis of measles virus infection requires the presence of positive serum measles IgM, significantly elevated IgG titers between acute and convalescent titers, measles virus isolation in culture, and additional criteria. Measles virus RNA can also be detected by reverse transcriptase polymerase chain reaction (RT-PCR) testing [9, 10]. Particularly in the years after the COVID-19 pandemic, differential diagnosis guarantees discrimination between several viruses, making laboratory confirmation of measles virus infection by DNA detection essential [6]. As of right now, there are no approved particular antiviral medicines for measles; instead, supportive care is the mainstay of treatment.

## Clinical and epidemiological features of measles, and definitions

To ensure efficient measles monitoring and timely public health treatment, physicians and public health specialists must detect measles using a combination of clinical and epidemiological criteria. It is crucial for doctors to be able to identify measles patients clinically and to use the most up-to-date techniques in laboratories to identify suspected cases. Prior to the release of test results. However, risk assessment should be the foundation for managing suspected cases and contacts. This necessitates considering several factors, such as the age of the individual, history of vaccinations, clinical presentation, and epidemiological traits such as proximity to outbreaks or an epidemiological link to a confirmed case. Developing an understanding of plausible epidemiological linkages would enhance the precision of risk evaluations and progress our understanding of the measles outbreak in the general public.

Primary transmission of measles It should be advised for a patient with probable measles to be alone, especially from immunocompromised individuals and other vulnerable populations (pregnant women and young children). Even while the majority of suspected cases prove not to be measles, it's still crucial to protect contacts against other infectious causes of illness that manifest as a rash. Those who have contracted the main measles are infectious for around four days prior to the rash's appearance and for four full days following Secondary transmission is typically more common in tight relationships, such as between household members and non-household individuals who have had extended interaction, like pupils in the same classroom [11, 12]. A greater infectious dosage of the virus may also result from close, extended interpersonal contact, such as that which occurs in homes, which raises the risk of both transmission and the development of more serious illness [13].

To prevent extended exposure to probable measles cases in waiting areas, appropriate triage and isolation protocols in healthcare settings are crucial. Five out of the seven secondary cases in a recent series of cases linked to transmission in healthcare settings spent 2.5 to 4 hours in the same room as the index case [14].

Even while face-to-face and/or extended contact are necessary for the majority of transmission events, transmission through less formal contact has also been reported [15, 16]. Because of this, it might be suitable to start a mass communication when a big number of people exposed but the degree of interaction cannot be determined on a people basis. For example, utilizing methods like email, posters or text messages to "warn and inform" those who could have been exposed. In addition to ensuring that any pertinent instances are promptly identified and diagnosed, this method aims to reassure those who may already be protected and improve the speed at which persons who may be at risk are identified.

### Surveillance of measles

Measles is a dangerous illness that requires notification and follow-up of suspected cases, according to the Health Protection Regulations (UK) 2010. Health protection teams are in charge of encouraging early measles detection and notifying medical experts of new cases in collaboration with local partners. The doctor no longer has an obligation to send patients to the proper local authority case officer after notifying the local health protection team. Additionally, physicians handling new instances had to notify the health protection team.

Since November 1994, diagnostic laboratories such as the Virus Reference Department (VRD) in Colindale have been conducting extended monitoring, which includes oral fluid testing of all reported or suspected cases.

When a suspected case is identified and/or reported to the local Health Protection Team (HPT), a measles kit should be sent directly to the individual (or their parent/guardian) or through their general practitioner (GP). As soon as measles is

suspected, samples should be collected and sent by mail or courier back to the UKHSA Colindale's Virus Reference Department. There, they are tested for measles RNA, measles IgG, and/or anti-measles IgM. The results are subsequently shared with the patient's primary practitioner and the local HPT. The relevant oral fluid kit documentation may be accessed online.

Accurate national data is essential to understand chains of transmission and identify sensitive populations where the vaccination schedule may need to be adjusted (17).

### Laboratory investigation

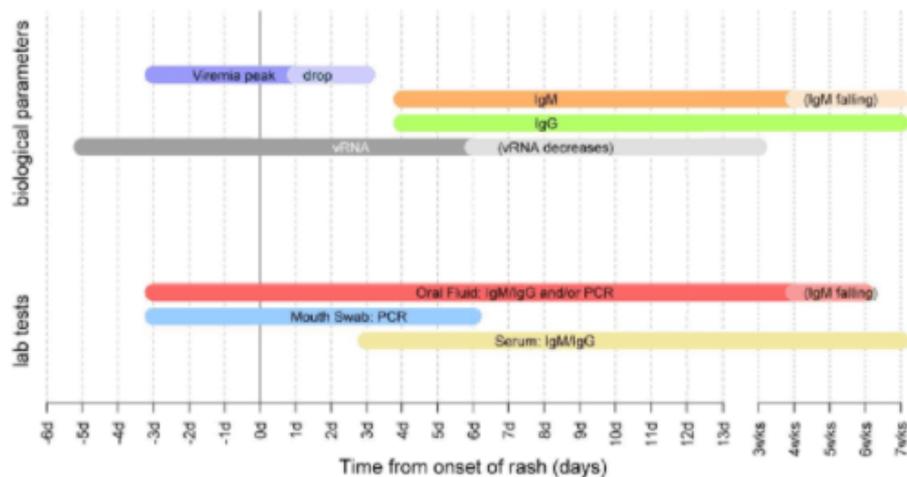
Measles virus belongs to the family Paramyxoviridae and is classified as a single-stranded 15RNA virus. There are 24 genotypes known to exist, several of which have been eradicated as part of the international effort to contain the measles. Less than three genotypes are known to exist worldwide as of 2021, and their distribution varies throughout geographical regions. To rule out measles for WHO purposes, a measles antibody test is necessary. A crucial component of laboratory surveillance for measles is genotyping verified samples in order to track the disease's progress toward eradication and identify imported cases. Oral fluid (OF) is the best sample for measles surveillance in the United Kingdom. These samples are a preferable alternative for validating cases in infants and babies since they are less invasive than serum.

Crucially, it is possible to screen for measles RNA, IgM, and IgG, and can therefore:

1. Both confirm and reliably rule out a measles diagnosis.
2. State if this is a case of breakthrough measles or primary measles (reinfection).
3. Cases with proven genotypes If there isn't a mouth swab or oral fluid sample, serum should be submitted to VRD instead

An outline of the biological factors and laboratory test scheduling for measles diagnosis is shown in Figure 1.

It is crucial to remember that serum should be used in place of oral fluid samples for evaluating the immunological state of susceptible contacts (18).



**Figure 1.** Dynamics of biological/viral indicators and timings of laboratory test during primary measles infection

### Complications of Measles

There are worries that the general public and medical experts may not be aware of the seriousness of a measles infection [17]. All age groups are susceptible to complications from measles, but certain groups are more vulnerable than others: children under five, adults over twenty, pregnant women, immunocompromised individuals (such as

HIV/AIDS patients), and patients with long-term co-infections (like tuberculosis). One in five unvaccinated cases of measles in the US will necessitate hospitalization. After the initial acute sickness, 10% of cases have mild sequelae such as ear infections, 10% have skin rashes, and 10% have diarrhea. There is a chance of serious side effects such as encephalitis and pneumonia (5%) [17]. After measles, pneumonia is the leading cause of mortality among children [19].

### **Subacute Sclerosing Panencephalitis (SSPE)**

Subacute sclerosing panencephalitis (SSPE), a potentially lethal measles consequence, affects one kid out of every 1,000 [18]. One to three measles-infected youngsters out of every 1,000 will pass away from pneumonia or neurological problems. Even though SSPE is an extremely uncommon CNS consequence, it can be fatal and is typically the outcome of early childhood measles infection, especially in infants under the age of two. SSPE can appear seven to ten years after the first infection, provided the patient recovers from the initial sickness [17]. There have been very few occurrences of SSPE documented in the US since the measles was eradicated in 2000 [17]. Nonetheless, there is a good chance that the current rise in measles infections will contribute to a rise in SSPE cases in the future [1,19]. Since Dawson identified SSPE as spherical spheres implanted in the brains of afflicted children in the early 1930s, the name "Dawson body encephalitis" was used to describe the condition [18]. In the late 1960s, electron microscopy revealed that paramyxovirus was present in the CNS [18]. Complete loss of cognitive function (vegetative state), chorioretinitis, blindness, cognitive deterioration, and altered gait are clinical indicators of SSPE. Electroencephalography (EEG) reveals classic drug discharges, whereas neuroimaging reveals cerebral atrophy caused by periventricular white matter loss [19]. The presence of high levels of antibodies in the cerebrospinal fluid (CSF) as a result of measles infection is required for a definite diagnosis of SSPE, which is caused by the mutant measles virus [21].

Numerous demographic studies have revealed that SSPE might be more common than previously believed or might have different origins than childhood encephalitis. For instance, population research from California that examined cases that were reported from 1998 to 2015 was published in 2017 by Wendorf and colleagues in an effort to determine the incidence and risk variables for SPPE [20]. By analyzing state death certificates, medical data, and the presence of measles antibodies in CSF, this study was able to identify cases of SSPE based on diagnostic symptoms [20]. Despite its limitations, this study demonstrated that unvaccinated children in California had a higher incidence of SSPE cases, primarily from measles infections during infancy [20]. At the time of the first measles infection, the prevalence of SSPE was 1: 1,367 for children under the age of five and 1: 609 for children under the age of twelve [22]. Children with a latency duration of 9.5 years (which is ranged between 2.5–34 years) and a median age of 12 years (range, 3–35 years) were diagnosed with SSPE [21]. The authors recommended that early immunization between the ages of 6 and 11 months before to travel or avoiding travel to endemic areas be used as precautions for unvaccinated infants [20]. These findings are consistent with the present global environment of widespread vaccination reluctance and significant rates of population mobility as a result of economic need and climatic change [1,24].

### **Presumptive Measles Virus Immunity**

People born before 1957 are deemed immune to measles, rubella, and mumps. During that time, people were virtually exclusively affected with infectious illnesses as children. Health care professionals born before 1957, whose immunity level had not been measured, were required to take two doses of the MMR vaccination [25] since they are more likely to spread the disease. Despite widespread immunity to measles, health studies reveal that imported measles can spread among health care personnel. As a result, newly employed professionals or those who interact with their community and patients should be regarded at higher risk and require MMR vaccine more than others [26].

## Protective Immune Responses from Infection and Vaccination

Measles virus targets alveolar macrophages in the lungs via the signaling molecule stromal lymphocyte activation molecule (SLAM), which fuses with respiratory cells receptor-dependently. Macrophages can spread measles virus to adjacent lymph nodes, exposing memory T and B cells to viral antigens. Measles virus infection decreases T and B cells, which has immunosuppressive consequences. [15, 16]. As a result, by avoiding immunological memory loss linked to measles, vaccination against the disease may have long-term advantages. Programs for population immunization produce polymicrobial herd immunity in addition to herd protection against the measles [15, 16].

## Measles Vaccination, Elimination, and Resurgence

The hemagglutinin on the virus envelope aids in the virus's attachment to the host cell's surface, whilst the fusion protein allows the viral DNA to penetrate the host cell. Several live attenuated measles vaccinations are currently accessible at health clinics. Previously, the immunizations were administered in single doses or in conjunction with the MMR vaccines. The 1954-isolated Edmonston strain of the measles virus is the source of several attenuated versions of the virus that are in use today [5]. The first two measles vaccinations were licensed on March 21, 1963, marking the beginning of the vaccination era in the US 60 years ago [24]. Leningrad-16, Shanghai 191, CAM-70, and TD 97 are further live attenuated vaccine strains. Cell culture or primary chick embryos are the sites of attenuated measles virus replication. The virus is isolated and clarified prior to lyophilization. Subcutaneous or intramuscular injection is the method used to administer the reconstituted lyophilized measles vaccine [5].

President John F. Kennedy signed the first law in the United States allocating government monies to support kid immunization programs in 1962. The US Congress extended the program's coverage of measles in 1965 [24]. The first two measles vaccinations were licensed on March 21, 1963, marking the beginning of the vaccination era in the US 60 years ago. The average weekly number of measles cases decreased to 200 six months into the 1967 US measles immunization program. But during the course of the following ten years, it became evident that not all populations were protected by measles vaccine. One of the most significant consequences of early measles eradication was the implementation of school vaccination requirements in the early 1970s and early 1980s [27, 28]. State vaccination legislation for polio, diphtheria, rubella, measles, pertussis, tetanus, and mumps were enforced. The National Childhood Immunization Initiative, initiated by the Carter administration in 1977, contributed to mass immunization rates reaching about 90% of children [27]. In 1981, the new trivalent measles vaccine (MMR) became the standard vaccination procedure in the United States, immunizing roughly 96% of students against measles [28].

When President Bill Clinton assumed office in 1993, his priorities were health care reform and vaccination access for children, which resulted in the introduction of the Universal Childhood Immunization Act and the vaccination Entitlement for Children (VFC) program [28, 29]. In 2000, the year before President Clinton left office, measles was officially declared eradicated and no longer endemic in the US; the few cases that remained were either imported from outside or disseminated by other imported cases [26, 27]. But starting in 2000, as more online social media platforms became available, vaccination-averse groups grew and concentrated on the measles portion of the MMR vaccine due to concerns about potential connections to immune system malfunction, childhood autism, and SIDS [27]. When autism rates increased, a report was published in the lancet journal and subsequently retracted in 2011. The rationale for the retraction was that this article offered scientific proof of a relationship between autism and the MMR vaccine, which impacted the decision not to continue administering the vaccine [31].

## Global Responses

In order to protect millions of vulnerable youngsters, both the Northern and Southern hemispheres have started to respond quickly to the measles outbreak [1]. The rise in measles infections in Europe in 2023 prompted immediate measures to encourage vaccination and inform the public and medical professionals about the risks of measles infection and the consequences of weakened immunity in communities [32, 33]. On July 26, 2023, the World Health Organization announced the Grand Recovery Strategy for Immunization. The recovery strategy attempted to restore worldwide vaccination efforts after the COVID-19 pandemic caused a decrease in vaccine distribution. The recovery strategy includes three parts: catch-up, recovery, and reinforcement. This coordinated effort was carried out in collaboration with the United Nations Children's Fund (UNICEF) through the Immunization Agenda 2030 (IA2030) [34,35]. In its most recent release, WHO observed a spike in measles infections and warned that major outbreaks of the illness might occur this year in more than half of the world's countries, emphasizing the need for a worldwide preparation response [35].

## 2. Conclusion

This research demonstrates how the vaccine-preventable viral illness measles has gone from perhaps being eliminated to maybe making a comeback in less than 40 years. Due to a "perfect storm" of different factors, measles incidence, hospital admissions, and fatalities have surged throughout this time, particularly in developed countries like Europe. The increase measles infections in 2024 are mostly due to several misleading assertions regarding the detrimental consequences of vaccines, such as the link between measles vaccine and autism. Furthermore, vaccination reluctance and satisfaction have a negative influence. Childhood vaccination rates were low during and after the COVID-19 pandemic, which hampered the implementation of immunization programs. All nations must develop public health and primary care initiatives to promote awareness of the hazards of measles other epidemic illnesses, as well as the need of adhering to vaccination schedules.

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