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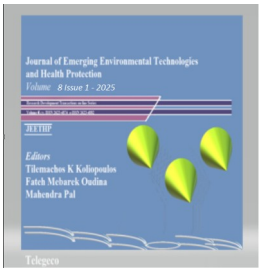

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Resurgence of Measles: A Persistent Global Threat to Public Health

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Abstract

The article presents a review about viral zoonoses, including both emerging and re-emerging infections, exert a profound influence on global public health and socioeconomic stability. Several key drivers such as rapid industrialization, population expansion, and climate variability contribute to the emergence and re-emergence of these diseases. Among them, measles remains one of the most severe viral illnesses reported across both developing and developed regions. The disease develops sporadically or as large-scale epidemics, as it accounted for an estimated 107,500 deaths among unvaccinated children worldwide in 2023. The measles virus exhibits a higher transmissibility compared to influenza, and primarily affects children, with outbreaks most frequently recorded during late winter and early spring. Transmission occurs predominantly through the airborne route, and rapid spread is facilitated when herd immunity falls below protective thresholds. Humans are recognized as the exclusive natural reservoir, although experimental transmission to non-human primates has been documented. Typical clinical manifestations include fever, cough, coryza (nasal inflammation), conjunctivitis and a characteristic cutaneous rash. In certain patients, common complications such as pneumonia may develop as a life-threatening outcome. Laboratory-based confirmation relies on techniques such as immunofluorescence, virus isolation, and diverse immunological or molecular assays. Due to absence of effective antiviral therapy, vaccination strategies combined with strengthened surveillance systems remain the cornerstone for preventing and controlling outbreaks of this highly contagious viral reverse zoonosis.

Keywords: Children, Measles, Outbreaks, Public health, Surveillance, Vaccination, Viral reverse zoonosis

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1. INTRODUCTION

In the last two decades, many viral zoonotic diseases including monkey pox, avian influenza, Nipah virus, Rift Valley fever, swine flu, COVID-19, Hendra virus, yellow fever, Hantavirus, chikungunya fever, rabies, Marburg disease, Lassa fever, Japanese encephalitis, Ebola virus, dengue fever, severe acute respiratory syndrome (SARS), rotaviral gastroenteritis, and Middle East respiratory syndrome (MERS), have emerged from different regions of the world posing serious threats to global human and animal health [1, 2, 3,4, 5, 6]. These zoonotic diseases can manifest sporadically, or escalate into epidemic and even pandemic forms, with considerable impact on illness and death rates among people of all ages. Transmission occurs through multiple pathways, including ingestion, inhalation, direct physical contact, and via animal or invertebrate vectors [7, 8].

Measles also referred to as hard measles, Morbili, red measles, Rubeola, is an important highly contagious viral disease of global public health concern, and is caused by a single- stranded, enveloped RNA virus with serotype 1 that belongs to the genus Morbillivirus and family Paramyxoviridae [1, 9]. The viral etiology of measles was first confirmed in 1911 when Goldberger and Anderson successfully transmitted the infection by inoculation of nasopharyngeal secretions and blood samples from infected patients in monkeys [10]. The measles virus is susceptible to inactivation by ultraviolet radiation, heat, and formaldehyde, and can be cultured in monkey kidney cells and human amniotic cells. It also shares antigenic relationships with bovine rinderpest virus and canine distemper virus [10]. Phylogenetic evidence suggests that the measles virus originated from rinderpest, a lethal disease of cattle that has now been eradicated worldwide [11]. The respiratory tract and conjunctiva serve as the primary entry points for the virus into the host's body, following which the virus disseminates through the bloodstream to the reticuloendothelial system [10]. The development of rash is suggestive of immune reaction between the T lymphocytes and virus-infected cells [10]. Measles is primarily a human disease and remains endemic in many regions, including India [1, 12, 13]. However, infections have also been reported in langurs, marmosets, and monkeys, while antibodies have been detected in chimpanzees, gibbons, and orang-utans. In this context, Wily and co-investigators [14] reported an outbreak of measles among Old World non-human primates in the USA. Current evidence suggests that monkeys acquire the infection from humans, and therefore, measles is considered as a reverse zoonosis (zooanthroponosis) [1]. The present review delineates the public health significance of measles, a highly infectious life-threatening viral zoonosis.

2. CLINICAL SPECTRUM

This section analyses the clinical spectrum for the investigated study.

- Humans:

The incubation period of measles is typically 7–10 days [15]. The onset of illness is marked by a sudden rise in body temperature accompanied by coryza, conjunctivitis, cough, hoarseness, laryngitis, pharyngitis, bronchitis, and stomatitis. The key diagnostic feature is the development of Koplik's spots on the buccal mucosa [1, 16], which are occasionally observed on the conjunctiva and intestinal mucosa (Figure 1) [10].

A reddish-brown maculopapular rash initially appears on the face and later spreads across the body (Figure 2). In some cases, complications, such as encephalitis, otitis media and pneumonia may develop. Additionally, subacute sclerosing panencephalitis (SSPE), a rare but fatal neurological condition, can occur in children [10].

The disease tends to be more severe in undernourished children, where mortality often results from secondary pneumonia. Measles generally affects children and unexposed adults who lack prior immunity [9, 16]. Koplik's spot is considered as a pathognomonic sign of measles virus infection [9, 17, 18], are usually detected before rash onset in approximately 50–70% of patients [19]. In pregnant women, infection due to measles virus has been associated with adverse outcomes, such as premature birth [20]. Also a child could be affected with measles with rashes on the face [9].

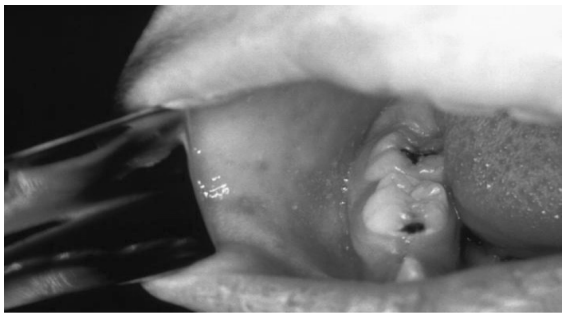

Figure 1. Patient presented with "Koplik spots" indicative of the beginning onset of measles [Source: 20]

- Animals:
Animals may remain asymptomatic or may exhibit clinical signs such as rhinitis, dry cough, pneumonia, conjunctivitis, maculopapular eruptions, and desquamation [1].

3. EPIDEMIOLOGY

Outbreaks of measles have been reported from multiple countries, including Austria, France, Germany, India, Israel, the Netherlands, United States, Indonesia, Philippines, China, Romania, Madagascar and the Democratic Republic of Congo, among others [1, 12, 15, 16, 21, 22]. During the COVID-19 pandemic, routine immunization services were severely disrupted, leaving approximately three million children in India without measles vaccination [23]. The highest incidence of measles is reported among children aged 1–5 years [10], and is typically observed during late winter and early spring [10]. Infants, children, immunocompromised individuals, and pregnant women are at particularly high risk of infection [20]. Measles is transmitted directly from human to human, affecting both sexes equally [24]. A single infection usually confers lifelong immunity, and repeat infections are extremely rare [24]. Severe disease and high mortality are most frequently reported in children with compromised immune systems [1,19]. Among these, pneumonia is the leading cause of death, whereas congenital measles is associated with serious complications such as encephalitis and mortality [9, 24].
According to the World Health Organization, vaccination efforts prevented more than 600 million deaths between 2000 and 2023 [16]. Majority of deaths have been reported in Africa, the Middle East, and Asia, where immunization rates are suboptimal [WHO]. Nonetheless, recent resurgences of measles cases have been documented, including outbreaks in Maharashtra, India [13]. Rosen and co-investigators [12] reported an outbreak in New York, USA, even among individuals with prior evidence of immunity. Similarly, Hahne and co-investigators [25] described an outbreak in the Netherlands among previously vaccinated healthcare workers, while Bernandou and co-workers [26] reported a measles outbreak in the Nouvelle-Aquitaine region of France that was linked to inadequate vaccine coverage. To effectively prevent outbreaks and maintain measles elimination, a minimum of 95% population coverage with two doses of a measles-containing vaccine is required. However, in 2023, global coverage with the first dose reached only 83%, falling short of the target [27]. Measles has been verified as eliminated from USA, while the remaining five WHO regions have adopted elimination goals, and the global distribution of measles incidence per million population across regions with verified elimination, varying incidence levels and unreported data is shown in Figure 2 [28].

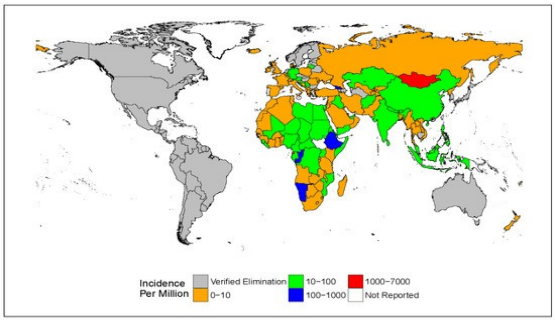

Figure 2. Current incidence of measles and countries with verified elimination [Source: 28]

Humans are regarded as the sole natural host of the measles virus [10]. However, the disease has also been reported in monkeys, which are believed to acquire the infection from humans, supporting its classification as a reverse zoonosis [1,10]. Hitherto, there is no evidence of naturally occurring measles in other species of animals, such as dog, cat, goat, buffalo, cattle, sheep, pig, donkey, horse, camel etc. [1].

4. DIAGNOSIS

The clinical diagnosis is supported with confirmatory laboratory tests. A complete blood count may show leukopenia, particularly lymphopenia, and thrombocytopenia. Electrolyte

abnormalities may occur in children with poor intake or diarrhoea. The isolation of virus from clinical specimens, such as pharyngeal washings, blood, conjunctival swabs, and nasal secretions, and urine can be attempted by using primary human kidney cell cultures or Vero (monkey kidney) cell lines [1]. Smear prepared from the nasal swab may be examined to detect virus antigen by immunofluorescence technique [10]. Immunological techniques, such as complement fixation and hemagglutination inhibition, along with molecular methods like polymerase chain reaction (PCR), reverse transcriptase- polymerase chain reaction (RT-PCR) are valuable tools for the diagnosis of measles [1, 10, 29, 30].

However, reverse transcriptase-polymerase chain reaction (RT-PCR) may detect the viral RNA in throat, nasal, nasopharyngeal secretions, peripheral blood mononuclear cells, and urine samples up to 10 days after rash appearance, but is most sensitive in the first 3 days [31]. RT-PCR is the most commonly used laboratory method to diagnose measles [32]. It is recommended that when a physician observes facial rash (particularly on the forehead) in combination with white oral lesions (Koplik's spots), measles should be strongly suspected and clinical specimens should be submitted for laboratory confirmation. Viral isolation from respiratory secretions, tears, and blood is most successful during the prodromal stage, which typically lasts 2–4 days [10]. However, virus recovery from urine is possible up to four days after the appearance of rash [10]. Serological testing also plays a crucial role in determining potential causes of vaccine failure [29], and laboratory confirmation is strongly advised whenever acute measles infection is clinically suspected [29]. Measles should be differentiated from other diseases including rubella, roseola, scarlet fever, and Epstein- Barr virus (EBV) by employing standard laboratory techniques [29].

5. TREATMENT

Presently, no specific antiviral therapy is available for measles [33]. Management is therefore largely supportive and includes adequate bed rest, administration of cough linctus and paracetamol, use of antibiotics to control secondary infections, sufficient fluid intake, and eye cleansing with boric powder solution [1]. In case of congenital measles, the administration of immunoglobulin to the neonate can diminish the risk of death [9]. The World Health Organization has suggested that two doses of Vitamin A at an interval of 24 hours can be beneficial to prevent blindness and damage to the eyes [16]. Vitamin A toxicity from excessive doses can cause dangerous neurologic and hepatic complications [34]. It is emphasized that sincere attempts should be made to develop safe, effective, and low-cost drug that can be easily affordable by the poor resource nations for the treatment of measles.

6. PREVENTION AND CONTROL

The history of vaccination is dated back to 1796, when Dr. Edward Jenner, a British physician, inoculated material from a cowpox lesion into a dairy maid as protection against smallpox, a devastating and highly contagious human disease [33]. The pioneer work of Jenner was a landmark in the history of medicine and public health, and laid the foundation of immunology [35]. Its success was ultimately demonstrated by the global eradication of smallpox. Since then, immunization has become a fundamental aspect in preventing and controlling many infectious diseases, including yellow fever, poliomyelitis, Japanese encephalitis, Newcastle disease, louping ill, Kyasanur Forest disease (KFD), goat pox, foot-and-mouth disease (FMD), dengue fever, contagious ecthyma, avian influenza, and others [1,36,37].

Measles is a highly contagious disease that can be eliminated through proper vaccination. Active immunization of children using the live attenuated measles vaccine, along with passive immunization of exposed individuals and immunocompromised patients through gamma globulin, is crucial for effective disease prevention [1]. The freeze- dried vaccine should be kept in cold chain i.e. refrigerator [18] and also the reconstituted vaccine must be used within four hours [24]. Vaccination is not advised in pregnant women, untreated tuberculosis patients, and immunocompromised subjects [10]. Measles vaccine can be administered alone or it can be given combination with rubella and mumps [16, 33]. In order to achieve immunity, it is essential to give two doses of measles vaccine to the children [16]. The policy of administration of two doses of vaccine for the prevention of measles has been implemented by the Government of India [38].

It is recommended that primates be strictly isolated in individual cages to prevent the spread of infection and caretakers must wear face masks and protective clothing. Proper sanitary

disposal of all secretions and discharges from infected individuals is also essential to limit spread [1]. Considering the highly infectious nature of measles virus, it is very essential to achieve herd immunity to prevent the spread of infection [30]. Education of physicians and public health workers on the necessity of vaccinating all susceptible infants and children [1].

7. CONCLUSION – RECOMMENDATIONS

Measles is an acute highly contagious vaccine preventable viral disease that primarily affect the children. Hitherto, no animal serves as a reservoir of measles virus. Maximum cases of measles occur in unvaccinated individuals. The disease is still reported in sporadic form and outbreaks from many countries of the Africa, Asia, and Middle East. Globally, measles causes substantial morbidity and mortality in children, with pneumonia remaining the leading cause of death among those affected. A pathognomonic clinical feature is Koplik's spots, which typically appear on the buccal mucosa. Laboratory confirmation may be established using RT-PCR or virus isolation techniques. It is recommended that all suspected cases of measles be promptly reported to local health authorities, with emphasis on immediate laboratory testing in acute presentations. Vaccination continues to be the cornerstone of measles virus infection control.

Ongoing research aimed at developing safe, affordable, and effective antiviral therapies, and more potent vaccines holds promising potential. There is a need to strengthen immunization programs in the primary health centres to vaccinate all the children with two doses of measles vaccine. Thus, measles is a preventable infection, and all healthcare professionals, should emphasize on educating the patients on the importance of vaccination.

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CONTRIBUTION OF AUTHORS

All the authors made substantial contribution during the preparation of the manuscript.

CONFLICT OF AUTHORS

There was no conflict of interest among the authors.

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