Review Article

Measles is back

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Abstract

Measles is one of the most deadly vaccine preventable diseases. The incidence of measles, and resultant mortality, had dropped drastically following the introduction of widespread measles immunisation since the 1960s. However, there is currently a worldwide surge in measles cases, with a marked increase over the past 3 years. Measles outbreaks and endemic transmission have been re-established in countries which had previously achieved measles elimination. The rise in measles cases has been mainly attributed to a drop in the recommended two dose vaccination schedule below the 95% uptake threshold necessary for interruption of transmission and sustainment of herd protection. This resurgence of measles is largely a result of the damage done by Andrew Wakefield, who in 1998 incorrectly and maliciously suggested a possible link between the measles, mumps and rubella (MMR) vaccine and autism. Such a possible association has subsequently been disproven by several scientifically robust studies. Still, most cases of measles have occurred in unimmunised individuals, mainly teenagers, who had missed out on vaccination in early childhood, and in infants under one year of age, who are too young to be vaccinated. Measles is highly contagious, with up to 18 people being potentially infected from a single case, so containment measures are important to prevent spread. These include isolation and immediate notification of suspected or confirmed cases, as well as wearing appropriate personal protective equipment when in contact with these patients. Health care professionals have a crucial role in promoting measles immunisation, which is the only rational way of preventing measles.

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Measles is one of the most deadly vaccine-preventable diseases[1] and is included in the top overall causes of death in children under 5 years of age worldwide.[2]

Prior to the introduction of widespread measles vaccination in 1963, measles accounted for about 2.6 million deaths annually.[3] In fact, one of the aims of the Global Vaccine Action Plan 2011 – 2020[4] was the elimination of measles in 4 out of 5 World Health Organization (WHO) regions by 2015, but this aim has not been achieved.[5] Measles elimination is defined as the absence of endemic measles virus transmission in a region or other defined geographic area for ≥12 months, in the presence of a high quality surveillance system that meets targets of key performance indicators.[6]

In theory, eradication of measles is possible because humans are the only reservoirs,[7] measles is only infectious during the acute phase,[7] specific and rapid diagnostic tests are available,[8] the measles virus is monotypic[8] and a monovalent vaccine is effective against all known virus isolates.[8]

The measles virus is aerosol-borne and is easily spread by coughing and sneezing, close personal contact or direct contact with infected nasal or throat secretions.[3] Measles is highly contagious, starting from four days prior onset of the rash until four days following rash appearance.[1] Over 90% of contacts develop the disease.[9] The basic reproduction number (R_0) for measles lies between 12 and 18,[10] meaning that a single patient with measles may infect up to 18 susceptible people.[9] In comparison, R_0 for influenza is estimated between 2 and 4[11] while R_0 for varicella ranges between 3.7 and 5.[12]

The clinical description for measles by the Centers for Disease Control and Prevention (CDC) states that measles is an acute illness characterised by a generalised maculopapular rash that is present for at least 3 days, an oral temperature of at least 101℉ (38.3℃) and the presence of cough, coryza, and conjunctivitis.[13] The pathognomonic Koplik spots on the buccal mucosa, which are not always present, are not a diagnostic criterion.[7] The incubation period for measles is 10 days for onset of fever; the rash usually appears 4 days later.[7] Laboratory diagnosis, which is a requisite for case confirmation, may be performed by detecting measles IgM in serum or saliva.[14] Of note, 30% may be negative in the initial 3 days and the tests should not be performed later than 4 weeks from onset of the rash.[15] False positives may occur especially with rubella and parvovirus B19 infections.[16] PCR testing on respiratory secretions, nasopharyngeal swab, blood or urine may be needed for genetic characterisation of the virus, which can help identify the source of infection.[17] There is no specific treatment for measles.

Measles complications can occur in up to 40% of patients and are more common in high-risk patients.[7] Pneumonia occurs in up to 1 in 16 patients[18] and is the leading cause of measles-associated death.[1] Other complications include otitis media (in about 1 in 12 measles cases)[18], diarrhoea (in about 1 in 12 measles cases),[18] ocular complications and central nervous system manifestations, such as encephalitis (in about 1 in every 1000 - 2000 measles cases)[18] or subacute sclerosing panencephalitis (in about 4 - 11 per 100,000 measles cases).[1] Measles also causes long-lasting memory B and T cell impairment.[19] High-risk patients include immunosuppressed patients (in whom typical signs and symptoms may be absent), patients with Vitamin A deficiency, malnourished patients and travellers.[7] Young infants also have a higher risk of mortality and complications,[7] especially if born to mothers with vaccine-derived immunity or who are infected with HIV.[20] Passive immunity lasts longer in mothers with natural immunity to measles but by 6 months of age less than 5% of all infants retain maternal antibodies.[21]

A proportion of individuals with measles will need hospital admission. Unfortunately, hospital admission is associated with measles transmission,[22] including outbreaks amongst healthcare workers.[23] The cost of delay in diagnosis and the resultant potential exposure is prohibitive, in view of the high infectivity of measles.[24] Patients suspected of having measles should be isolated immediately and measures should be in place to prevent further spread during outbreaks. The virus remains infective for two hours on solid surfaces, which should be borne in mind when decontaminating a room.[25] Infection control measures should be implemented as per local recommendations and respiratory protection by means of N95 or FFP3 (filtering facepiece class 3) mask should be worn when attending to a patient with suspected or confirmed measles,[26] irrespective of the immunity of the healthcare worker to measles. A normal surgical mask should be worn if a FFP is not available – this will still provide a reasonable level of protection.[27]

The only rational way of preventing measles in a population is through vaccination. The MMR (measles, mumps, rubella) vaccine has 99% effectiveness against measles following 2 doses,[28] is well tolerated, safe,[29] and offers long-lasting protection.[30] In fact, measles vaccination is estimated to have prevented 20.4 million deaths between 2000 – 2016.[31] However, in view of the high R_0 for measles, a high uptake of at least 95% for both doses is needed in order to eliminate measles from a population and to attain herd protection.[32-33]

In Malta, the first dose of MMR vaccine is administered at 13 months of age, with the second dose being given at 3 to 4 years of age.[34] This is in line with the WHO recommendations that two doses of measles-containing vaccine, such as the MMR vaccine, for countries with low risk of measles should be given at around 12 months of age for the first dose and that the second dose of MMR vaccine should be given at the age when maximum coverage at national level is anticipated.[35] A supplementary dose of measles vaccine is recommended from 6 months of age onwards during measles outbreaks[35]. Any dose of measles vaccine given before 12 months of age should not be counted as part of the series and these children should be revaccinated with 2 doses of the MMR vaccine after 12 months of age.[36]

Unfortunately, measles immunisation rates have dropped globally. During 2017, 85% of children received one dose of measles vaccine by their second birthday, with only 67% receiving the second dose as part of routine immunisation.[37] In Europe, immunisation rates for 2017 were 95% for the first dose and 90% for the second dose.[38] The single most influential factor for the drop in measles vaccine uptake was an article by Dr Andrew Wakefield in The Lancet in 1998,[39] which suggested a potential link between the MMR vaccine and developmental regression and autism, among other conditions. This paper received disproportionate media coverage and caused the biggest public health scare in UK history.[40] Flaws in research methods were immediately pointed out, including that it was a case series of 12 children without controls and that data collection relied on parent's personal beliefs and recalls.[41] Large epidemiological studies over the years,[42-46] as well as a WHO extensive review[47] and a Cochrane systematic review,[48] have since disproved any links between the MMR vaccine and autism. The UK General Medical Council found that Dr Wakefield had falsified his data and had breached ethical standards in this publication[49] and consequently he was struck off the register because of his serious professional misconduct.[50] The paper was also withdrawn by The Lancet in 2010.[51] However, it is still widely quoted by anti-vaccine campaigners and parents, some of whom remain unsure whom to believe, despite all the robust scientific evidence proving that the MMR vaccine is not associated with autism.[52]

Endemic transmission of measles can be re-established once vaccination rates fall below the elimination threshold.[53] In fact, measles has again become endemic in all five WHO regions during 2018, with the rate of measles being the highest in a decade[54] and continuing to rise by a further 300% during the first quarter of 2019.[55] Over 82,000 people in the WHO European region contracted measles during 2018, with up to 61% needing hospitalisation and 72 deaths in children and adults.[38] This is more than three times as many as in 2017, 15 times as many as in 2016[18] and even surpassed the number of measles cases in the WHO African region in 2018, which totalled 33,879.[56] This figure includes national outbreaks in countries having previously achieved measles elimination, such as The Netherlands[57] and Greece,[58] and also the re-establishment of endemic transmission in countries where measles had been eliminated, as happened in the United Kingdom.[59]

Malta has maintained the status of measles elimination in 2018, because there have not been any cases of measles due to sustained transmission.[60] However, there is an increasing trend in locally acquired measles, rising from 6 cases in 2018[60] to 15 confirmed cases so by April 2019 - 23 cases in adults and 2 cases in children.[61] During 2018, 95.5% of children in Malta received the first dose of MMR and 95% received the second dose of MMR vaccine.[62] This is in contrast to previous years, when immunisation rates in Malta had dropped below the 95% uptake rate (for both doses) needed to prevent disease transmission. In fact, only 91% of children received the first dose of MMR vaccine and 83% received the second dose during 2017[63], although this could be a result of inadequate notification. This is the ideal scenario for breakthrough cases of measles and, in the absence of herd protection, the potential for outbreaks, as has happened in other countries.

Indeed, the surge in measles in Europe has been mainly attributed to a drop in two-dose measles vaccine coverage below 95% and a drop in prevalence of individuals with vaccine-induced protection of measles to less than 94.4%.[64] Out of the 14,400 reported cases of measles in Europe in 2017[65] with known vaccination status, 87% were unimmunised, 8% had received one dose of measles-containing vaccine, 3% had received two or more doses of vaccine and 2% were vaccinated with an unknown number of doses.[66] Immunisation status was unknown for 6%.[66] Thirty seven percent of measles occurred in children under 5 years of age, with the highest disease burden occurring in children below the age of 1 year, while 45% occurred in patients older that fifteen years.[66] Therefore, nearly half of the measles cases in Europe occurred in unimmunised adolescents aged 15 years or older, highlighting the need to identify and catch-up those who missed out on routine vaccination in childhood.

The resurgence of measles at a global level is being driven by multiple factors, including conflict, poor health education, lack of access to health care, complacency, increasing vaccine hesitancy and low support amongst medical personnel.[67] In addition, vaccine coverage may be suboptimal in at-risk groups, including Roma, Irish travellers, orthodox religious communities[67] and adolescent and adult migrants, who might be excluded from the immunisation catch-up initiatives provided to younger children.[68] Failure to address vaccination shortfalls in vulnerable populations will create immunisation gaps and lead to subnational coverage.

Measles is a vaccine-preventable disease which carries a high morbidity and mortality. Elimination of measles is dependent on sustaining herd protection and in limiting transmission during outbreaks. Our role as health care professionals is to actively encourage MMR vaccine uptake, including opportunistic vaccination for those who were not immunised at the appropriate times, address public concerns, expedite the diagnosis of measles, notify immediately any suspected or confirmed cases and help in containing outbreaks.

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