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# Snippets

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## 1. Vaccine-derived polioviruses

With concerted efforts of World Health Organisation (WHO) since 1988, poliomyelitis is on the threshold of global eradication. Wild poliovirus type 2 ($WPV_2$) was eradicated in 1999 and $WPV_3$ in 2012, and $WPV_1$ is still present but only in Pakistan and Afghanistan. Live attenuated oral polio vaccine (OPV) has been the mainstay. It provides durable humoral and intestinal immunity, is easy to administer and has a low cost.[1] However, OPV has two major risks due to genetic instability. First, it may very rarely cause sporadic case of vaccine-associated paralytic poliomyelitis (VAPP) when the given vaccine dose may revert to neurovirulence and cause paralysis in the vaccine recipient or a non-immune contact, who are otherwise immunologically competent. VAPP may also occur in persons who have primary immunodeficiency of antibody production. The second risk is the emergence of genetically divergent neurovirulent vaccine-derived polioviruses (VDPVs). These resemble WPV and can cause outbreaks in areas with low OPV coverage. Whereas VAPP is an adverse event following a dose of OPV, VDPVs are polioviruses whose genetic properties show a prolonged replication or transmission. Three different types of VDPVs are reported: (1) circulating VDPVs (cVDPVs) from outbreaks in low OPV coverage settings, (2) immunodeficiency-associated VDPVs (iVDPVs) from persons with primary immunodeficiency and (3) ambiguous VDPVs (aVDPVs). Most cVDPVs being type 2 (88.2%), WHO advocates a global replacement of trivalent OPV with bivalent OPV containing poliovirus type 1 and 3, beginning in April 2016, preceded by at least one dose of injectable polio vaccine (IPV) into routine immunisation to maintain immunity to type 2 polioviruses.

All cVDPVs seen worldwide are identified and registered with WHO in Geneva. Among the 686 cVDPV cases reported since 2006, more than 97% were associated with $cVDPV_2$. An update on vaccine-derived polioviruses worldwide, January 2014–March 2015, has been published recently.[2] Four $aVDPV_2$s were isolated from AFP patients from four different states in India during this period. In addition, two VDPV isolates that escaped detection by screening assay by The Global Polio Laboratory Network have been reported from Mumbai, India. The first was seen in a 1.2-year-old girl with AFP in January 2008. It was identified as Sabin Type 3. The second was Type 2 VDPV found in an immunocompetent girl, 3.5 years old, in March 2014. A new confirmed case of VDPV in a 2.5-year-old child has been reported in Delhi in November 2015. This has been identified as $P_2$. Replacement of trivalent OPV with bivalent OPV will greatly eliminate the risk for circulating $VDPV_2$ cases and iVDPV infections. Maintenance of high levels of immunity through comprehensive IPV coverage will be necessary to protect against iVDPV spread. Detection of chronic iVDPV exeretors with suitable antiviral therapy is also important.

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## 2. Paediatric shigellosis

Shigellosis occurs most often in children under the age of 5 years. In South Asia and Africa, around 88.5 million episodes of diarrhoea are reported annually.[1] It occurs more often in rural than urban facilities. The risk factors are paediatric age, contaminated food and water, poor public health facilities and high fly counts. Family members of shigellosis patients have a much higher risk of developing the disease (OR 44.7, 95% CI 5.5–361.6). Some studies show that isolates of index patients and infected household contacts are invariably same. However, studies from Bangladesh found that the majority of isolates from index patients and contacts are different, thereby suggesting that the spread in contacts is attributable to both secondary transmission and shared external infecting sources. Male patient contacts are twice as likely as female contacts to develop infection. Interventions with soap handwashing reduces secondary infection rate by more than two-thirds during the first 10 days after identification of index patients. Fly control and cleanliness of stored water also show promising results in the control of spread of shigellosis.[2]

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## 3. Mixed infection with Plasmodium species

Infections with *P. vivax* and *P. falciparum* occur at approximately equal frequencies in 8 states of India where malaria is endemic.[1] The other three species, *P. malariae*, *P. ovale* and *P. knowlesi*, are reported less often. Mixed infections are reported in Peru, Brazil, Ethiopia and Papua New Guinea. Malaria diagnosis in India is based primarily on microscopy of peripheral blood smears and rapid diagnostic tests, which cannot differentiate monoinfections from mixed infections.

A total of 1521 blood samples positive only for *P. falciparum* by microscopy were subjected to species-specific nested PCR (targeted 185 rRNA gene) and 265 (17.4%) of these were positive for mixed infections. Mixed infection of *P. vivax* and *P. falciparum* was seen in 239 (16%), *P. falciparum* and malaria in 19 (1%), *P. falciparum* and *P. ovale* in 6 (0.4%) and *P. falciparum*, *P. malariae* and *P. ovale* in 1 (0.1%) samples. These mixed infections were seen in all 8 states where malaria is endemic. Misidentification of malarial parasites may prolong parasite clearance time and lead to resistance to antimalarial drugs and more severe anaemia. *P. vivax* and *P. ovale* both cause relapses and *P. malariae* can sustain at low rates in the community for decades, and complicate malaria epidemiology and subsequent control. There is thus a need for improved quality of microscopy and rapid diagnostic tests in India.

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## 4. Respiratory pathogens among Hajj pilgrims

Around two million pilgrims go to Saudi Arabia for Hajj every year from a very large number of countries. There is an overcrowding and a very close contact. This poses a major public health and infection control challenge. Respiratory diseases are a major cause for consultations in health centres and admission of more serious cases in ICUs. These individuals having returned with various viral and bacterial pathogens can be a source of spread of pathogens in their families and community. Several studies have been done in various countries to study this issue pre and post Hajj travel. Benkouiten et al.[1] in their study on pilgrims during the year 2013 in France observed that influenza virus was seen in 7.8% in post Hajj (0% pre Hajj). In addition, various other respiratory viruses, i.e. Corona viruses, Enteroviruses, Human Metapneumoviruses, human respiratory syncitial viruses and combinations of these, were seen in pilgrims on their return. Of the bacterial pathogens, Streptococcus pneumoniae was frequently acquired.

This matter needs to be considered in them if they report for a respiratory illness.[2,3]

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## 5. Management of invasive Salmonella disease in the era of antimicrobial resistance

Invasive salmonella infections are a huge global burden. Worldwide annual estimates are: typhoid fever 22 million, paratyphoid fever 5.4 million and invasive non-typhoid salmonella disease (iNTS) 3.4 million. Morbidity and mortality are high, especially in resource-limited settings and in compromised hosts. Invasive non-typhoid salmonella diseases are principally *Salmonella typhimurium* and *Salmonella enteritidis*. The routine and prospective surveillance for antimicrobial resistance is not readily available.[1] Currently resistance to chloramphenicol, ampicillin and cotrimoxazole (MDR) has declined. However, if used, there is a need for

multiple dosing, longer course of therapy (2–3 weeks), risk of chloramphenicol myelotoxicity and higher relapse rates. Fluorquinolone resistance is very common and hence unreliable for therapy. Third generation cephalosporins, oral and parenteral, are currently the mainstay, safe and effective. However, MIC creep and rarely full resistance have been reported. Azithromycin is a good alternative: oral, single daily dose, excellent tissue penetration, high intracellular concentration and almost negligible relapse rate. But resistance is already being reported. Combination therapy with third generation cephalosporins is under discussion.[2] Management of iNTS disease is as yet not fully determined, due to lack of adequate laboratory and clinical data. Third generation cephalosporins for at least 2 weeks is the conventional therapy.[3]

Improved public health hygiene, wider use of WHO approved typhoid vaccines and designs of new vaccines which target the other serovars (*S. paratyphi A*, *S. typhimurium*, *S. enteritidis*, *S. choleraesuis*) are an urgent need to reduce the burden. New approaches to develop live attenuated multivalent salmonella vaccines are also in progress.[4]

There is a high prevalence of severe disease in children under two years of age. The presently available vaccines cannot be used in these children. There is a need for conjugate vaccines which can be administered to infants and children.[5]

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## 6. Ciprofloxacin-resistant *Shigella sonnei* associated with travel to India

Shigella spp. is a major pathogen in food borne diseases. *Shigella dysenteriae* serotype 1 causes severe disease, outbreaks or even epidemics. Occasional outbreaks by antibiotic-resistant *S. sonnei* have been reported in industrialised world, especially among children. Such outbreaks are also now being reported from developing countries. In India, severe outbreaks of dysentery with high mortality were caused by multidrug-resistant *S. dysenteriae* type 1 during 1984–1985. Later, it re-emerged with fluoroquinolone resistance and caused several dysentery outbreaks. More recently, food-borne outbreaks due to *S. sonnei* have been reported in India.[1] The emergence of ciprofloxacin-resistant *S. sonnei* causing such outbreaks and spread among international travellers is a cause of serious concern.

Antimicrobial drug resistance is a serious worldwide issue more so in countries with poor sanitation and excessive use of antibiotics in humans and animals. Several studies show the emergence of ciprofloxacin-resistant *S. sonnei* in India. In view of this, ciprofloxacin can no longer be recommended for empiric therapy of *S. sonnei* infections.[2]

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## Conflicts of interest

The author has none to declare.