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VACCINE PREVENTABLE DISEASES: WHERE CLINICAL, LABORATORY, AND PUBLIC HEALTH SERVICES CONVERGE

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Disease surveillance is the monitoring of disease. It involves detection of illness by clinicians, confirmation of diagnosis by the laboratory, and disease prevention and control by public health authorities. The importance of this confluence of roles was sharply illustrated in the first cholera outbreak experienced in Papua New Guinea (PNG) between 2009 and 2011 for which PNG was not adequately prepared and in which some 15000 people were affected with 500 deaths. Clinicians were alerted to the possibility of cholera by patients with profuse watery diarrhoea. The diagnosis was initially confirmed in the PNG Institute of Medical Research (IMR) Laboratory in Madang. The public health response varied between different pockets of infection but probably prevented a nationwide and potentially devastating epidemic. Had the diagnosis not been suspected by the clinicians and the diagnosis not been confirmed, delay in the public health response would have almost certainly had disastrous consequences [1 – 4].

Good surveillance, involving the clinical and laboratory services has the potential to record disease burden, to document changes in disease patterns and to predict and confirm disease outbreaks. It is essential for adequate health planning.

This review focuses on surveillance for vaccine preventable diseases (VPDs) in PNG. In the current PNG Expanded Programme on Immunisation (EPI), vaccines should be provided free of charge to all children. The vaccines provide protection against Hepatitis B, Diphtheria, Tetanus, Whooping cough, *Haemophilus influenzae* type b (Hib), S*treptococcus pneumoniae* (pneumococcus), measles and rubella, polio and tuberculosis.

Surveillance involves the keeping and regular review of accurate records. The National Department of Health (NDoH) has a system in place - the National Health Information System (NHIS) to record disease statistics from hospitals and health centres throughout PNG. The system is however, notoriously fallible.

Diagnoses may be inaccurate, reports may not be sent at all, may be sent late or may be fabricated, and there is much room for human error. Mobile phone surveillance has been shown to be effective in the country [5] and the Health Department is currently testing out an e-based recording system using e-tablets, whereby information is entered directly onto the central data bank from the tablet.

Accurate information can also be obtained by focusing on specific areas of health. In order to obtain more precise information on childhood morbidity and mortality the Paediatric Society of Papua New Guinea set up its own Paediatric Hospital Reporting Program in 2010 and has produced annual reports each year providing valuable and easily accessible data and allowing patterns of disease in different provinces to be observed over time [6]. In the area of maternal health, the World Health Organisation (WHO) has a Maternal Death Surveillance Response programme aimed at improving reporting of all maternal deaths and focussing on appropriate responses to reduce maternal mortality [7].

To be of any value, surveillance relies on accurate diagnosis. In the absence of a laboratory test for the condition, such as neonatal tetanus, and where standard laboratory tests for confirmation of diagnosis are not available, surveillance should depend on syndromic reporting following strict criteria based definitions. But without laboratory confirmation data quality is limited. Meningitis is basically a clinical diagnosis. The paediatric reporting programme has provided accurate data on numbers and outcome for clinical meningitis [8] but it does not contain information on causation. In children the common causative bacteria are/ or were Hib, pneumococcus and meningococcus, but tuberculous meningitis is common, viral meningitis probably more common than is recorded, and other organisms such as Cryptococcus may be involved, whilst in neonates, gram negative organism such as E coli and *Klebsiella pneumoniae* are common. Unfortunately many of the provincial hospitals in the country do not have adequate laboratory facilities to determine accurate bacteriological diagnosis, and this is a matter of considerable concern not just in relation to monitoring the effect of vaccines, but of monitoring antimicrobial resistance.

The world is facing a crisis in the emergence of antibiotic resistance microorganisms [9]. In PNG the first report of penicillin resistance was reported in 1973 [10], resistance of Hib to Chloramphenicol, the mainstay of standard treatment was reported in the 1990s and increased rapidly to the extent that almost all Hib in the country is now resistant, and a change of standard management has been

required [11, 12]. A recent study reported the development of Chloramphenicol resistant pneumococcal strains [12]. There is well documented Methicillin resistant staphylococcus [13] and multiple antibiotic resistant Klebsiella strains [14]. The emergence of Multidrug resistant TB and Extensively drug resistant TB is no longer a spectre but a reality [15]. Appropriate antibiotic strategies can only be formulated when there is good data on causative organisms and their antibiotic sensitivities. Laboratories practicing at a high level of quality control are essential for bacteriological surveillance.

To return to the VPDs. Vaccination is an incredibly powerful public health strategy. The use of high quality vaccines in well-functioning health systems has resulted in extraordinary reductions in targeted disease and even in countries with poorly functioning health systems and low socioeconomic indicators, vaccination has produced remarkable effects. Smallpox was declared eradicated in1980. It is hoped that poliomyelitis will be eradicated within the next 3 years. Target dates have been set for the elimination of measles, congenital rubella syndrome and neonatal tetanus, and for a massive reduction in the number of people affected by Hepatitis B. It is estimated that between 1988 and 2016 polio vaccination prevented 16 million cases of paralytic polio [16] and that measles vaccine has prevented 20.3 million deaths between 2000 and 2015 [17]. There have been other remarkable achievements. The introduction of the conjugate Hib vaccine in high income countries in the 1990s led to the virtual eradication of invasive Hib disease, most notably meningitis [18, 19] and the introduction of the polyvalent pneumococcal conjugate vaccines has had similar, though less dramatic effects [20]. Surveillance is much more difficult in low and middle income countries, but where it has been in place, it has also shown dramatic reductions in the incidence of Hib meningitis following the introduction of Hib vaccine [21, 22]. There is good evidence that the vaccine is highly cost effective [23].

The effects of introducing vaccines on the incidence of meningitis can only be determined if laboratories are able to identify these organisms [24]. Although bacteriology facilities are lacking in many hospitals, we do have evidence that the introduction of Hib vaccine has reduced considerably from data from Madang, which reported a fall in the proportion of Cerebrospinal fluids (CSFs) positive for HIB from 47% to 9% after the introduction of the vaccine [25] and from an as yet unpublished study of data from PMGH and Mt Hagen which has shown a significant reduction in the proportion of Hib isolated from CSF and estimated an 83% drop in population incidence in the years following the introduction of the

vaccine. Notable in this study was the use of latex agglutination tests for bacterial antigen detection in the years after introduction of the vaccine so that surveillance was considerably improved.

Syndromic diagnosis and laboratory confirmation are fundamental to the eradication and elimination programmes of the WHO. Acute Flaccid Paralysis (AFP) and Acute Fever and Rash (AFR) are the best known. AFP is most often the result of Guillain Barre syndrome (acute post infectious polyneuropathy) but is also caused by transverse myelitis, spinal shock following injury, or other pathology of the lower motor nerves, neuromuscular junction or muscles as well as polio. Cases of AFP are immediately notified to the health authorities. Stool samples are collected for testing for polio virus in WHO specified regional laboratories, and if polio is confirmed rapid and focussed response by Public Health authorities to vaccinate the community from which the AFP case is reported is instituted. The incidence of AFP in the absence of polio is similar in all countries of the world and an adequately functioning surveillance system will detect at least one case per 100 000 children less than 15 years of age each year. Failure to do so is indicative of poor surveillance. Adequacy of stool collection and reporting are also markers of surveillance efficiency. The system therefore is vital to the detection of individuals with polio and the control of polio outbreaks. Together with vaccination, AFP surveillance has been crucial to the massive reduction of cases of polio and will be fundamental to the achievement and maintenance of its eradication [26].

AFR surveillance is fundamental not only to the global medium term measles elimination programme, but vital for the early detection and rapid response to control measles out breaks in individual countries. Acute Fever and Rash is a syndrome which can be caused not only by measles, but also by rubella, several other viruses including parvovirus B19, and by an allergic reaction. All children presenting with AFR should have a dried blood spot or serum tested for Measles antibodies. In PNG this test is done at the Central Public Health laboratory (CPHL). The detection of IgM antibodies indicates an acute infection and should result in immediate notification of the national and provincial health authorities. In countries such as Australia with high vaccination coverage the AFR surveillance system and public health response has successfully limited the spread of measles from imported cases for many years [27]. In PNG and other countries with low routine vaccination coverage the potential for large outbreaks is ever present. PNG experienced almost a decade without measles as a result of supplementary immunisation activities but at the end of 2013 cases of AFR

confirmed to be due to measles were detected in West Sepik.

Measles is one of the most contagious diseases known. Public Health authorities responded with a mass vaccination campaign and doubtless prevented many cases and many deaths from measles but the epidemic spread through the country and then onto the Solomon Islands and Vanuatu. During 2014 2589 laboratory confirmed and epidemiologically linked cases and 73183 clinically suspected cases from all 22 provinces of PNG were reported. More than 365 measles deaths were reported from an entirely preventable disease [28, 29]. Gene-typing of the measles virus indicated that there were two importations, one related to the Hong Kong strain and the other to a Philippine strain introduced into a large and highly susceptible population of young children who had not been immunised.

The costs of surveillance need not be large. An integrated disease surveillance and response system targeting 19 priority diseases in Eritrea, Burkino Faso and Mali cost less than 50 US cents per capita; between 0.3% and 5% of the total government health spending per capita [30]. The costs of a measles epidemic, whooping cough epidemic and the costs of the high mortality and morbidity from Hib and pneumococcal disease heavily outweigh surveillance costs.

Given that surveillance is a low cost public health intervention which, when working effectively prevents disease outbreaks and saves lives and substantial costs, it follows that investment in education of all health workers about its importance, and training in the procedures necessary for detection, reporting and response, should be a priority. All provinces have Provincial Disease Control Officers (PDOs) responsible for disease surveillance, and the NDoH has run training courses for field epidemiologists. In practice these officers are given additional responsibilities, and support for their primary function is often lacking. Clinicians should work in close collaboration with the PDOs to give support and recognition to the importance of their role.

In general, surveillance systems are passive in the sense that they depend on reporting from peripheral sites to a central unit from which a response is coordinated. There are, however, situations in which active surveillance, in which activity is directed to finding cases in high risk communities, is necessary. Such surveillance activity is more costly, but in the case of diseases such as TB active case finding focussed on high risk “hot spots” is necessary for disease control. A recent study from PNG shows that such focussed active surveillance is possible with limited resources even in remote areas [31].

The dramatic reduction in morbidity and mortality from Vaccine Preventable Diseases has only been possible because of clinicians, laboratories and public health authorities working together. There is still much to be done in PNG. The country is a risk of a further measles outbreak unless vaccination levels are substantially increased. It will be clinical health workers alert to AFR and the laboratory staff which will give early warning allowing preventative measures to be taken against another disastrous epidemic. Vaccination coverage for all the EPI antigens must be improved and the highly significant reductions in incidence of Hib not only in high income countries but also in low and middle income countries including PNG should be widely acknowledged and should provide encouragement to all those involved in disease prevention. It is important for all health workers, particularly those working in the forgotten front lines of rural PNG to know that their work in vaccinating children makes a major difference. Laboratory capabilities in Provincial hospitals need support to enable good bacteriologic surveillance for monitoring of VPDs and antimicrobial sensitivity.

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