Acute Encephalitis Syndrome Surveillance: Challenges and the Way Forward

Aakash Shrivastava*

Abstract

Japanese encephalitis, an arboviral infection, is a serious public health problem in the Asian region. Globally, it affects 67,900 people per year, of which about a third are likely to die. The change in climate, ecological imbalance, and population growth together with related demands for change in agriculture and animal rearing practices have recently intensified its threat along with that of other viral encephalitides. However, many nations still struggle for disease burden data on acute encephalitides that can be used to plan prevention and control strategies. This review summarizes the current JE/acute encephalitides surveillance system in Asia and West Pacific region, with a specific focus on India.

Keywords: acute encephalitis syndrome, Japanese encephalitis, surveillance, sentinel surveillance, viral encephalitis

Introduction

Japanese encephalitis (JE) is the most significant form of viral encephalitis prevalent in most of the South-East Asia and the Western Pacific, putting at risk about half of the world's population. Figure 1 displays the JE risk areas, as per US-CDC estimates. It is a mosquito-borne disease, which is not only a killer, but also causes long-term disability in this region. Globally, JE inflicts a 20%-30% case fatality rate and 30%-50% residual neurological or psychiatric disability in survivors. As per an estimate based on representative incidence in the late 1990s, in the absence of immunization, the annual global JE incidence for children less than 15 years of age is about 175,000, of which there are 43,750 deaths and 78,750 disabilities; after adjusting for immunization coverage, this incidence is 125,000 cases. It is estimated that by the early 2000s JE virus had infected more than 10 million children worldwide, and led to more than 3 million deaths and 4 million long-term disabilities. A more recent estimate published in the year 2011 suggests an annual global JE incidence of about 67,900 cases and 20,400 deaths. For the year 2002, the JE global impact was estimated at 709,000 disability adjusted life years (DALYs). In India, JE has been reported from 171 districts in 19 states. The number of reported cases (deaths) for Acute Encephalitis Syndrome (AES) and JE in India for the year 2011 were 8249 (1169) and 1214 (181), respectively. The corresponding figures for the year 2012 were 8344 (1256) and 745 (140), respectively.

* Dr Aakash Shrivastava, Epidemiology Division, National Centre for Disease Control (NCDC), Delhi 110054.

E-mail: a.shrivastava@ncdc.gov.in
A major challenge in the fight against JE and other viral encephalitides, clinically grouped as Acute Encephalitis Syndrome (AES), is under-reporting; only one-sixth of the estimated annual incidence of JE in Asia region was actually reported in 2011. One of the important reasons for such under-reporting of the true incidence is non-existent or sub-standard surveillance systems in many affected countries. This article will review surveillance related issues of JE and other viral encephalitides in Asia and West Pacific region, with a focus on India.

**Epidemiological surveillance**

A strong surveillance system makes it easier to understand the disease burden and its epidemiology, as well as to plan and monitor the impact of preventive and control measures. Ideally, nationwide case-based clinical surveillance followed by laboratory confirmation of all cases would be the best to gather epidemiological information on viral encephalitides and the impact of any vaccination program. For example, in Japan, the National Epidemiological Surveillance of Infectious Diseases (NESID) is empowered through an infectious diseases control law enforced since 1999 and this makes all clinical acute encephalitis/encephalopathy cases, inclusive of JE, legally notifiable by all physicians and health centres to public health institutes (PHI) and district infectious disease surveillance centres (DIDSC) of local governments. The Infectious Disease Surveillance Centre (IDSC) of the National Institute of Infectious Diseases (NIID) is the national infectious disease surveillance centre to which all district infectious disease surveillance centres report. These DIDSCs usually placed at PHIs in the district are under respective local governments. In each prefecture (administrative division), one of these district surveillance centres is a principal surveillance centre which weekly through a computer-network system collects, collates, analyzes, onward transmits the information, and also provides a feedback on the data received from all districts in the prefecture. The PHIs and NIID perform laboratory confirmation of all cases. With this strong surveillance, Japan now reports less than ten JE cases per year in comparison to annual incidence of less than hundred cases in 1980s. Similarly in Australia, a number of viral encephalitides such as JE, Murray Valley, West Nile, Australian Bat Lyssa virus encephalitides are notifiable by all states and territories to the Department of Health, Australian Government through case-based surveillance, the National Notifiable Diseases Surveillance System, using common case definitions. For example, the Department of Health, Victorian State has a statutory (Public Health Act, 2008) requirement that a JE case be immediately notified by telephone, fax, or online upon initial diagnosis followed by a written notification within five days. All cases undergo laboratory testing at specified state laboratories.

However, in countries, where such national surveillance may not be financially or logistically viable, sentinel surveillance has been recommended as an alternative. Some pathogens such as JE virus are known to inflict severe illness and as a consequence most JE cases would end up in health...
facilities equipped with specialized care facilities. Routine passive sentinel surveillance based in such health facilities may suffice for providing information related to disease trends and early warning signals of potential outbreaks. India has adopted the sentinel surveillance approach for JE and its initial plan is to include selected hospitals of JE endemic districts, where most cases are usually seen, as sentinel sites. Thereafter it envisions further expansion to more hospitals and other districts of the country. On similar lines, Nepal a relatively less developed largely rural country, also established a sentinel surveillance for JE in the year 2004. 64 referral hospitals from different parts of Nepal were enrolled in the first two years for case-based syndromic surveillance of acute encephalitis, which later was increased to 125 sentinel sites by the year 2012. The laboratory specimens are transported in cold chain to one of its two national laboratories – the National Public Health Laboratory (NPHL), Kathmandu or the B. P. Koirala Institute of Health Sciences (BPKIHS) in Dharan. Nepal experiences a massive burden of JE; in the year 2005, a large outbreak resulted in almost 2,000 cases and 300 deaths.

The World Health Organization (WHO) recommends that Asian countries should strive for a nationwide surveillance to gather aggregate syndromic data through passive reporting from all health facilities, and conjoin this with sentinel case-based surveillance in a selected number of health facilities which have laboratory capacity to confirm the etiological pathogens. If the sentinel sites are carefully chosen to ensure representativeness of the general population and if they provide complete and reliable data, then the information on the proportion of syndromic cases that are laboratory confirmed for any particular pathogen can be extrapolated to aggregate data gathered from nationwide syndromic surveillance, and a national incidence estimate on pathogen-specific acute encephalitis can be approximated and monitored over time. An example of such a surveillance system can be observed in mainland China. China has a statutory requirement for reporting all clinical syndromic cases, which since the year 2004 are electronically captured through the national surveillance system of Chinese Centre for Disease Control and Prevention. However, there are only 22 sentinel surveillance sites at 13 of the 31 provinces of mainland China, which provide pathogen testing for each case. JE incidence in China decreased fourfold from 12490 cases in the year 1998 to 2975 cases in the year 2008, and more recently further decreased to 1625 cases in the year 2011; this decline can be partially credited to the constant effort made to strengthen the sensitivity of their surveillance system, which in turn improved JE control. A recent study in China suggested that use of WHO suggested clinical syndromic surveillance approach provided a strong potential for capturing most of their JE cases. India also has a possibility to implement such a conjoint effort by integrating its National Vector Borne Diseases Control Program (NVBDCP) case-based JE sentinel surveillance with the Integrated Disease Surveillance Program (IDSP) implemented nationwide passive AES surveillance. However, it is cautioned that if sentinel sites have been selected for operational feasibility reasons, then extrapolated estimates of disease burden may not be accurate.

Among cases admitted with symptoms of acute central nervous system infection, a sizeable proportion is likely to be of bacterial meningitis, which in itself is largely vaccine-preventable and treatable. Haemophilus influenzae type b (Hib), Streptococcus pneumoniae (pneumococcus), and Neisseria meningitidis (meningococcus) are a few common causes of bacterial meningitis. The incidence of just Hib meningitis in children below age 5 years in India is estimated to be 7.1 per 100,000 population. As per another estimate, India has 2,400,000 Hib cases and 72,000 deaths in children under 5 years of age, an approximate 4% of all child deaths in the country. As there are also some commonalities between recommended clinical case definitions for "AES" and "bacterial meningitis", an integrated meningo-encephalitis (acute meningitis/encephalitis syndrome) surveillance concept is envisioned and even practiced in some countries such as China, Bangladesh and Cambodia. If "AES" and "bacterial meningitis" cases were to be sorted into only one of the two parallel reporting systems, there are possibilities of incomplete case detection and inaccurate representation of disease burden. This alternative meningo-encephalitis surveillance approach has shown better sensitivity for case detection and is also useful from the perspective of clinical case management. The only challenge of integrated meningo-encephalitis surveillance is that bacteriology laboratories would require different equipments, tests, technical resources, and specimen handling as compared to virology laboratories.

In some countries, extensive activities are already in place for poliomyelitis, acute flaccid paralysis, or meningitis surveillance; if these processes were to be synergistically linked to AES surveillance, it would gain technical and logistical benefits of existing infrastructure and investments. The global polio eradication initiative has an extensive well established surveillance network. Efforts are being made to leverage these resources for surveillance of other priority vaccine preventable diseases; initiatives have been made for measles, rubella,
neonatal tetanus, and also Japanese encephalitis. In Nepal and some parts of India, a number of JE surveillance activities have been integrated with the infrastructure and resources developed for AFP surveillance.14, 20

Components of epidemiological surveillance

Other than the problem of not having a surveillance system, there is also an apprehension about non-comparability among acute encephalitis data available from different regions. In this concern of standardizing surveillance for selected vaccine-preventable diseases, the World Health Organization (WHO) has recently recommended some guidelines.11

Clinical case definition

The WHO recommends using syndromic surveillance to clinically detect cases of acute encephalitis and then subsequently assign specific etiological classification after laboratory confirmation. This approach is recommended for the reasons that though acute encephalitis is quite a common clinical presentation of many viral infections, inclusive of JE virus, it is not easy to clinically differentiate between them. In India, the etiological pathogens identified for acute febrile encephalopathy in a sizeable proportion of cases are of bacterial origin, and among viral pathogens JE virus, Enteroviruses, and Chandipura virus have been identified frequently in both outbreaks and hospital surveillance studies. Measles, Varicella Zoster, Mumps, and Herpes Simplex viruses also form a moderate proportion of sporadic cases presenting at hospitals. The pathogens differ by the geographic location of the study.12-24 Using syndromic surveillance also makes reporting consistent and comparable in the situation where availability and capacity for diagnostic testing is not uniform.

As per the WHO recommended definition, a case of Acute Encephalitis Syndrome (AES) is clinically defined as a person of any age, at any time of year with the acute onset of fever and one or both of a change in mental status or new onset of seizures (excluding simple febrile seizures).13 In India, both the NVBDCP implemented sentinel surveillance and IDSP implemented nationwide surveillance conform to this case definition. Other than India, the following countries of Asia and West Pacific region comply with this case definition: Bhutan, Laos, Myanmar, Nepal, Papua New Guinea, and the Philippines.5

While the recommended definition allows for inclusion of a person of any age, some infections such as JE are most common in children under 15 years of age. Some nations with limited resources, such as Cambodia and Papua New Guinea, 8 may find it cost-effective to restrict JE surveillance to less than 15 years age group, but then there are possibilities of not capturing AES cases caused by other pathogens. Even the risk of JE infection is not always restricted to the paediatric population; the older age groups are possibly at risk in areas not previously affected (immunologically naive)25 and where childhood immunization has resulted in an upward shift of the naturally acquired immunity.26 This shift in average age from under 15 years age towards adulthood has been reported from Taiwan27 and Assam, India, 26 where inclusion of all age groups under surveillance has been found useful.

The recommended definition permits to include cases occurring any time of the year so as to allow for all possible pathogens and also sporadic JE cases. Typically, in endemic tropical countries, such as India, JE virus transmission is observed round the year as sporadic occurrence, and with a specific seasonal peak supposedly explained by rains and agricultural practices.28 In most of the Indian JE endemic states, this rise in case numbers is observed from July and maximizes around September-October.6

A study that evaluated a cohort of suspected central nervous system infections found that the symptoms of fever, altered mental status and/ or new onset of seizures included in the AES clinical definition made the WHO recommended case definition 65% sensitive and 39% specific.29 It was also observed that one third of the JE confirmed children which presented with acute limb paralysis or meningitis missed detection when the recommended AES clinical case definition was used. Adding acute flaccid paralysis and meningism in the clinical definition had a potential to improve the sensitivity to 89% and reduce the specificity to about 23%.29 Acute paralysis in JE virus infection has also been reported from India.30-31 Even though WHO has not recommended this addition due to issues related to loss in specificity, some nations such as China, Bangladesh and Cambodia have found it more convenient to introduce meningo-encephalitis surveillance instead of AES surveillance.20, 21

While the WHO recommended case definition of AES does not indicate what duration may be considered as “acute”, 11 an expert group on encephalitis for the Indian Academy of Pediatrics suggests that a period of up to 14 days may be accepted for the same.22 According to NVBDCP India case definition, acute onset is defined as of no more than 5-7 days duration.32
Laboratory confirmation of AES cases and case classification

For the purposes of surveillance, any clinical AES case can only be a suspect case for a pathogen-specific diagnosis unless confirmed in a laboratory; after such confirmation it may be considered a laboratory-confirmed pathogen-specific case. In an outbreak situation, whenever AES suspect cases have a time and place relationship to a laboratory-confirmed pathogen-specific case, the epidemiologically linked suspect cases may be considered as probable cases for that pathogen-specific disease. This prevents the necessity to laboratory test all suspected cases if the outbreak conforms to an epidemiological pattern well known for any particular pathogen-specific disease.

The WHO recommended laboratory standard for JE surveillance suggests that the presence of JE virus specific IgM antibody detected by ELISA (enzyme linked immunosorbent assay) in a single sample of serum or cerebrospinal fluid (CSF) will be considered sufficient to confirm JE virus infection, though the latter is considered a better diagnostic procedure. Though the presence of JE virus specific IgM in serum suggests JE virus infection, it does not necessarily confirms JE virus as the pathogen responsible for AES illness; specifically in situations: where the region is highly endemic for JE, where it may cross-react with antibodies of other flaviviruses, where there is high JE vaccination coverage, or where epidemiological findings do not conform to better known characteristics of JE transmission. Therefore, the serum based test has been deemed sufficient only when epidemiological findings support existence of a seasonal outbreak of JE. It is also worthwhile comparing the sero-positivity rate (percentage of specimens confirmed as JE positive) during the outbreak period to the baseline sero-positivity rate to suggest whether further investigations into the aetiology of the outbreak are warranted. The existence of sporadic JE infection would account for a population’s baseline sero-positivity rate. A comparison with sero-positivity rate of previous outbreaks of the same pathogen may also be useful in this regard.

In practice, a serum sample is usually obtained at the time of admission, as it is also required to guide clinical management. However, an additional serum sample after 10 days of illness onset (alternatively, where not possible, at the time of discharge or before death) is recommended to gain maximum diagnostic sensitivity; the sample collected after 10 days of illness onset has more than 95% sensitivity to capture JE virus specific IgM. When diagnosing a recently vaccinated case, it is recommended to test for JE virus specific IgM in the CSF specimen instead of the serum, because vaccine related IgM may possibly be detected in the serum of the vaccinated person for six months following JE vaccination. Accordingly, the NVBDCP JE sentinel surveillance program recommends serum collection at least 5 days after the onset of illness and a repeat collection after at least 10 to 14 days from the first sample. It also makes a provision to record the three important dates of last JE vaccination, onset of first symptom, and collection date of samples in its laboratory test request form AESF. Even though IgM detection in CSF is considered a better diagnostic procedure, being dependent on CSF diagnostics alone has not been recommended for surveillance as it misses many cases. The cohort study that assessed the new JE surveillance standards missed 20% of cases when only CSF diagnostics were considered. CSF collection rates are dependent on favourable medical, logistic and cultural conditions, and the chances of collecting a convalescent CSF sample, the one which ensures better IgM sensitivity, can be quite low as it is not a usual requirement for clinical management. Even after extensive laboratory investigations, it may not be possible to identify the causative pathogen in a considerable (28 to 85%) proportion of AES cases. Other than the limitations of laboratory procedures, this is also explained by the fact that a proportion of febrile encephalopathies are not of infectious origin.

Procedures for surveillance

WHO recommends collecting both aggregated and case-based data for AES surveillance. Aggregated data may be passively collected from all health facilities identified as surveillance reporting units. In India, its nationwide communicable diseases reporting system IDSP classifies the reporting units as “S”, “P”, or “L”. Usually, the “S” reporting units are health facilities manned by a paramedical staff, the “P” reporting units are health facilities manned by a qualified medical doctor, and the “L” reporting units are laboratories. The periodicity of reporting under IDSP is weekly. While the “S” reporting form captures the aggregate number of patients that presented with fever less than 7 days along with altered mental status, the “P” reporting form provides the aggregate number of clinical AES cases. The NVBDCP has three types of sentinel surveillance sites, first those with their own laboratories (SSSL), second those without laboratories (SSS) and third, independent informer units (IU). The NVBDCP program envisages including government or private health facilities which treat a large number of children of less than 15 years age as sentinel surveillance sites; usually medical colleges and regional or district hospitals with laboratories would qualify as SSSLs. With a long term target of at least one per district,
presently the country has 78 such SSSLs in 16 states. The periodicity of sentinel reporting is daily during an outbreak, weekly during JE transmission season, and monthly during the remaining period. This sentinel surveillance program has AESF 1 and AESF 2 reporting forms to capture the aggregate number of AES/ JE cases and deaths (gender and age group wise) reported by districts to states and surveillance sites to districts, respectively. AESF 4 is a detailed case investigation form for each AES case and AESF 3 is a line list of AES cases. Each case is provided a unique identifier that can help to find the case. Thus IDSP and NVBDCP can complement each other as a national syndromic reporting system and a case-based sentinel reporting system. There is an immense potential for both systems to synergistically, develop more comprehensive AES/ JE surveillance for the country. The reporting forms of both these surveillance systems have the provision to capture the data elements recommended in WHO surveillance standards.

Under NVBDCP, each district has a designated vector borne disease officer who within 2 days of notification is supposed to personally visit and verify the case, ascertain if the case qualifies for the case definition, gather the case history and examination information using the form AESF-4, and also organize laboratory confirmation of the case. A possible improvement to monitor this case verification process would be to introduce a few additional indicators in the weekly reporting form as available in the weekly summary (part II) of the H 399 form used in Sri Lanka AES surveillance. These indicators such as AES cases notified but awaiting verification, cases found untraceable, cases classified as under another administrative region, cases confirmed as not AES, would be useful in monitoring case ascertainment. In each Indian district there also is a designated surveillance officer and a rapid response team under IDSP, who are trained to perform similar activities for any notified infectious disease, which may require investigation. A synergistic approach from both NVBDCP and IDSP would allow pooling of such specialized manpower resources.

In India, the IDSP electronic reporting system allows online submission of data through a specifically designed web portal and these facilities are available at block or district level of each state. Such compilation of surveillance data facilitates availability of data at once to everyone connected to this surveillance portal. For NVBDCP, sentinel surveillance data are largely compiled at block, district, and state level as they flow along the vertical reporting system. Therefore each block, district or state has only access to data pertaining to their own administrative unit. Though it may not be possible to accommodate all case-based data required under the NVBDCP JE program through the IDSP surveillance portal, this portal holds the potential for compiling other than aggregate data, a case-based basic line list of laboratory confirmed cases, which unfortunately has not been used in this manner.

The AES surveillance standard recommends certain aggregate and case-based data analyses which if periodically reported can improve understanding of disease burden and impact of immunization. Some relevant analyses would be to display incidence of syndromic and laboratory confirmed cases by time intervals (week, month, year) place and person (age and gender groups, immunization status) characteristics, vaccination coverage status by time and place, proportion of cases vaccinated/ unvaccinated, number of deaths/ case fatality ratio, and proportion of AES attributed to JE and other etiological agents. Under NVBDCP, at each district and state there are vector borne disease consultants and data managers who undertake some of the aforementioned analyses and guide their programme officials in preparing programme implementation plans (PIPs). Similarly, in each district and state there also are epidemiologists and data managers under the IDSP programme to analyze the surveillance data. The IDSP portal is specifically designed to provide certain distribution analyses as output tables and graphs. These aggregate analyses are available by administrative blocks, districts and states, and by surveillance weeks. However, a useful improvement in the reporting module of this software would be to have a possibility to display the spatio-temporal distribution of the information, as available with “Nivrāna” software of Sri Lanka.

Using and analyzing performance targets for improving data reporting and laboratory functioning is also recommended. Such performance targets hugely benefited the poliomyelitis surveillance in this country. Some of these would be attributes of completeness and timeliness in monthly reporting, percentage of AES cases for which specimens were collected (and collected at the right time), reached laboratory in acceptable conditions, were tested, and timely reported. NVBDCP has only recently in its updated guidelines introduced a number of such monitoring indicators. The IDSP web portal allows ready retrieval of information regarding attributes of completeness, consistency and timeliness for reporting. This information is available for different types of reporting formats and for all levels of reporting units, blocks, districts and states. One critical performance indicator suggested for AES surveillance is that the minimum annual
incidence reporting should be 10, 2 and 6 AES cases per 100,000 children who are under 15 years of age, adults and all age group populations, respectively; these figures correspond to the minimum AES incidence reported in most robust, prospective studies conducted \(^5^\) and may be accepted as the baseline incidence in these age groups.

Dissemination of analyzed results and feedback is an important component of disease surveillance. Though both NVBDCP and IDSP organize some formal (meetings, official communications) and informal (telephonic) feedback to the lower levels of administration, not much is done for routine dissemination of results. The NVBDCP uploads the state-wise annual incidence of AES and JE cases and deaths on its website (www.nvbdcp.gov.in). A weekly summary of disease outbreaks, inclusive of AES/ JE reported from across the country is uploaded on the IDSP website (www.idsp.nic.in). However, India needs to strengthen this component and learn from experiences of Asian and Western Pacific partners. In Sri Lanka, over 300 Medical Officers of Health (MOH) provide a weekly summary of reported and confirmed cases to the Epidemiology Unit at Colombo, where these data are analyzed and published weekly, quarterly and annually in the form of weekly epidemiological reports and quarterly/ annual epidemiological bulletins respectively, and these reports are disseminated to all MOH offices and other stakeholders and uploaded on their website (www.epid.gov.lk). \(^35^, ^36^\) Since the year 2009, the “Nivārana” software, which has an inbuilt dissemination module, sends out these reports through emails. \(^35^\) It also sends out brief alerts through short messaging service (SMS). The Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health in Thailand disseminates through its website (www.boe.moph.go.th) a weekly disease surveillance report (report 506) which other than the usual distribution characteristics also provides a comparison of disease incidence to the average incidence from preceding weeks and also to the average incidence from the similar historical period, so as to recognize any possible change in incidence. The website of the Infectious Disease Surveillance Centre of the National Institute of Infectious Diseases of Japan (http://idsn.nih.go.jp) similarly publishes weekly, monthly, and annual epidemiological reports and also the sero-prevalence and vaccination status for each year. These epidemiological reports include graphs on historical trends. It also disseminates information on geo-spatial trends for sero-prevalence in pigs.

Progress and shortcomings of JE/ AES surveillance in this region

In 2012, a report attempted to summarize the status of JE surveillance in 24 Asian and Western Pacific countries known to be at risk for JE virus transmission; 18 of these were found to conduct JE surveillance. \(^5^\) The five nations (Australia, Japan, Singapore, South Korea, and Thailand) with relatively better health systems had either a nationwide or appropriate at-risk area surveillance along with laboratory capacity for routine confirmation of cases. Another six nations (China, Laos, Malaysia, Myanmar, Sri Lanka, and Vietnam) also had national level surveillance but lacked the provision for laboratory confirmation of every case. The remaining seven (Bangladesh, Bhutan, Cambodia, India, Nepal, Papua New Guinea, and Philippines) conducted only surveillance at sentinel sites. While most of them (16) conducted surveillance for all age groups, two countries (Cambodia and Papua New Guinea) limited it to only children. The recommended AES case definition was being used in only seven countries (Bhutan, India, Laos, Myanmar, Nepal, Papua New Guinea, and the Philippines). The remaining countries had different surveillance case definitions, with some allowing an inclusion of meningoencephalitis (Bangladesh, Cambodia, and China). This report concluded that JE surveillance in this region has improved in terms of new surveillance programs being established, increase in number of surveillance sites, integration into national health systems, use of recommended standards, and quality of data. It further suggested that the availability of surveillance data has improved these countries’ insights into their disease burden and spread, recognition of JE as a public health concern, decisions on preventive and control issues, and monitoring the effectiveness of JE immunization programs. However, the persistent challenges faced were about incomplete and inaccurate reporting, limited coverage of sentinel reporting, and inadequate collection and testing of laboratory specimens. The report observed that lack of disease burden data when bundled with competing priorities prevented some countries, especially those with financial constraints, from implementing JE vaccination programs.

There are very few studies available that have evaluated JE/ AES surveillance in India. One such study that reviewed the quality of AES surveillance data for year 2011–2012 from Kushinagar, an endemic JE district of Uttar Pradesh, found that there were serious shortcomings in completeness and accuracy of sentinel surveillance data, inclusive of vaccination history information. \(^37^\) They also noted a propensity to test only sera samples and a considerable delay in availability of laboratory results.
The postgraduate students of NCDC, MPH (field epidemiology) 2012-2014 batch, evaluated the NVBDCP JE/ AES surveillance systems at Muzaffarpur district, Bihar (unpublished project report, 2013) and found that there were shortcomings in terms of availability of data management staff, operational manuals, and provisions of all reporting forms. There was no routine surveillance reporting, though during outbreaks the district authorities would assemble a simplified line list from designated SSSL and SSS hospitals and transmit it to the state government. Non availability of adequate staff and vehicle support along with competing requirements for Malaria and Kala Azar control activities were the cited constraints. Though the SSSL in the district was conducting JE serology, the same was not being routinely reported to either the NVBDCP or IDSP. The team observed that on account of better availability of designated data management staff, and reporting forms and registers at the major reporting units, the IDSP weekly surveillance reporting was relatively more operational at Muzaffarpur, though far from satisfactory. Data analysis, interpretation for action, and dissemination were missing in both surveillance systems. Monthly meetings were the standard form of feedback.

The NVBDCP in collaboration with WHO India organizes a Joint Monitoring Mission (JMM), of which the recent ones have been organized during Jan-Feb 2007, and March 2014. The JMM, 2007 visited Kerala for JE surveillance evaluation and observed the following weaknesses in the system:

- Physicians were not familiar with the JE case definition,
- Participation of the private sector in JE surveillance was not regular,
- Strategy for laboratory specimen collection, JE testing and reporting was not well defined,
- Analysis, interpretation and use of the JE surveillance data at both the peripheral and district levels was minimal or practically non-existent,
- Feedback from state to district and lower levels was also negligible,
- Neither the entomological data was being analysed for decision making nor the same was been monitored for data quality.

The JMM 2007 recommended integrating the NVBDCP implemented JE surveillance with the IDSP surveillance to facilitate early detection of outbreaks. Though the report of the JMM 2014 is awaited, they have recommended collaboration between NVBDCP and NCDC, which is also the headquarters for the IDSP, in AES surveillance.

This recommendation is well founded considering that combined aggregated reporting of IDSP and case-based reporting of NVBDCP could largely improve representativeness of AES surveillance. As of now there is inconsistency in AES and JE cases data reported under these surveillance systems. While the number of AES cases for the year 2011 and 2012 reported by the NVBDCP were 8249 and 8344 respectively, the corresponding figures reported by the IDSP portal (www.idsp.nic.in) were 11436 and 9063 respectively. Similarly, while the JE confirmed cases for these two years reported by the NVBDCP were 1214 and 745 respectively, the estimates provided by IDSP portal were 686 and 465 respectively. Pooling resources with IDSP surveillance system could improve the timely detection of AES outbreaks, both of JE and non-JE aetiologies. Rapid response teams formulated under IDSP can be useful to investigate AES outbreaks. Laboratories strengthened under both programs can support timely diagnosis of pathogens. Case and vector management support provided under the JE control program, NVBDCP, can be valuable in controlling the outbreak.

**Laboratory network for surveillance**

One of the important requirements to improve surveillance is to establish a network of pathogen testing laboratories and strengthening them through internal and external quality assurance procedures. Under NVBDCP, 78 sentinel surveillance laboratories in 16 states of India are provided supplies of laboratory kits and equipments, wherever not available. They conduct laboratory IgM capture ELISA confirmation for AES cases identified at SSSLs and SSSs. 12 national level apex laboratories such as National Centre for Disease Control (NCDC), Delhi, National Institute of Virology (NIV), Pune and others provide technical support and advanced diagnostics for viral strains.

Based on the poliomyelitis and measles/ rubella laboratory network models, WHO coordinates JE laboratory networks in the South East Asian Region (SEAR) and Western Pacific Region (WPR). This standardizes the protocols of JE diagnosis in participating countries. The network promotes use of validated assays, monitors performance targets, provides technical resources, establishes referral support with regional and global laboratories, and sets up quality assurance and quality control measures, which eventually facilitates accreditation of participating laboratories by WHO.

In 2006, the JE laboratory network (LabNet) was established in SEAR which comprises of one global specialized laboratory (GSL) in US CDC,
two regional reference laboratories (RRLs) in India (National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore and NIV, Pune), and thirteen national laboratories (NLs) from six countries, inclusive of India. Their analysis shows that only 10% of tested AES specimens are positive for JE, and therefore specimens are also tested for other bacterial and viral pathogens. In 2008–2009, a similar network was established in WPR consisting of one GSL in Japan, two RRLs in China and the Republic of Korea, and seven national laboratories (NLs).

A crucial issue for laboratory surveillance is determination of the sensitivity and specificity of the commercially and in-house available IgM ELISA diagnostic kits and assays using standard validation panel of specimens and also assessing their quality and appropriate usability with serum and CSF. Using the CDC results as reference, the NIV, India developed assays have demonstrated 71% sensitivity, 75% specificity for serum testing and 75% sensitivity, 95% specificity for CSF testing. Though commercially available kits have high specificity, their sensitivity for serum specimens is quite low.

Environmental surveillance

Viruses such as JE virus are a part of the ecosystem with several hosts and vectors, and therefore, its surveillance has to be a multi-pronged approach. Several measures may be useful in predicting epidemic transmission of these viruses at different times of transmission cycle. The meteorological factors that influence vector population may be the earliest possible signals. A comparison of current vector and animal host population densities with usual averages and a laboratory evidence of virus transmission in the natural cycle would be next stage indicators of transmission. The evidence of virus spill-over to sentinel bird and animals would be late stage predictors of an impending outbreak.

Climatological data surveillance

Recent changes in climatic conditions, such as rainfall patterns, temperature and humidity, may affect the reproduction, population density, survival, biting behaviour, seasonality and distribution of some insect vectors. These changes may also influence the incubation period of pathogens inside vectors, their susceptibility, and infectivity. Change in climate also influences the habitation and food sourcing behaviours of animal reservoirs and humans and thus increases their chances of contact. Climatological surveillance would involve monitoring meteorological indicators against location-specific long-term averages and also against other host and vector specific parameters.

Entomological surveillance

Entomological surveillance helps to understand vectors (such as mosquitoes), their behaviours, and impact of vector control measures. Entomological surveillance includes identification of vectors, their spatial and seasonal distribution, monitoring the vector and larval density, survey of their breeding, feeding, and resting behaviours, susceptibility and resistance to insecticides and vector control measures, and laboratory detection of virus activity in vectors. These activities require specialised skills and sufficient trained manpower, which unfortunately is not usually available; for example, over 30 mosquito species are recognized as potential vectors of JE virus alone.

In India’s JE surveillance program, there is a provision for fortnightly survey of a few affected and non-affected villages for vector identification, as well as monitoring larval and adult vector density. The breeding sites and larval density per dip are to be documented in a specific AESF 6 form and mapped. The AESF 7 and AESF 8 forms record the adult vector density for all indoor, outdoor, daytime, and night time landing collections from both human and animal dwellings using per-man-hour-density measure. These forms also capture feeding and parity status of the adult vectors. The AESF 9 form records information on susceptibility of vector mosquitoes/ larvae to insecticides/ larvicides and this is also to be mapped. A number of national laboratories have been identified for vector sero-surveillance, a few of which such as NIV, Pune and Centre for Research in Medical Entomology (CRME), Madurai have more advanced capacities to undertake virus isolation in vectors. These tests confirm involvement of identified insect species as vectors for the given pathogen in a given area.

In recent times, better vector surveillance techniques have become available internationally. Laboratories have real-time PCR protocols that allow for more rapid, sensitive and specific detection of viral nucleic acid, which can be sequenced for genetic characterization. Satellite-based remote sensing of vector breeding sites and their proximity to human or animal habitation are more rapid and useful tool for monitoring vector populations. Geographical Information Systems (GIS) simplify the process of mapping larval and vector habitats, location of known virus foci, plotting areas at risk, etc., which can be readily shared among collaborators.
Veterinary Surveillance

A number of viral encephalitides are zoonotic diseases with animals and birds as natural or amplifying reservoirs. Some veterinary based surveillance measures such as prevalence and density of reservoir animals and birds, their density in relation to human habitation, monitoring unusual increase in sickness and deaths of birds and animals, periodic serological surveillance and detecting viral activity in reservoirs, may even be useful as early warning signals. Increased crow deaths during West Nile virus transmission and sickness among horses during Eastern Equine Encephalitis virus transmission have been previously reported. Serological monitoring of strategically positioned domestic and wild avian and mammal species can alert against virus transmission in a specific region. The number of natural and amplifying hosts can be large; for example, over 90 avian species are known to be hosts of JE virus alone. Also, there would be regional differences in host species. Therefore, sentinel birds and animals are carefully chosen on certain criteria such as their local abundance, disease effects, susceptibility and immunological response to pathogens, exposure to vectors, and ease of capture. In India, the state government animal husbandry departments collaborate with veterinary research institutions such as Indian Veterinary Research Institute (IVRI), Bareilly and Veterinary Biological Research Institute (VBRI), Hyderabad to conduct such veterinary sentinel surveillance.

Way forward

Having a robust surveillance system that can provide a valid and reliable estimate of JE and other pathogen-specific encephalitides still remains a challenge for many countries of this region. Considering availability of newer vaccines, which now promise a simpler schedule, improved quality, safety, efficacy, and affordability, the need for a strong surveillance system that can measure the impact of these vaccines has become crucial. A stronger political, technical, and financial commitment from government and implementing agencies can substantially improve the JE surveillance system. The major challenges would be in ensuring consistent reporting, completeness of data, and timely collection and processing of laboratory specimens. A multi-disease approach where surveillance and possibly interventions could be integrated with other diseases having similar epidemiological characteristics would save costs and improve case detection, case confirmation, and case management. In India, concerted effort of NVBDCP and IDSP could produce such synergistic effects.

surveillance system, similar to the ArboNET in United States, which allows linkages between human surveillance data and surveillance data from veterinary and other sectors would be useful to plan strategies for these infections. The fight against vector-borne viral encephalitides requires an investment into developing the public health, entomology workforce, and laboratories. Setting up a laboratory network, on the lines of the Association of Public Health Laboratories in United States, where laboratories representing different specialities collaborate to share their expertise would strengthen the diagnostic testing. All efforts invested in improving surveillance systems would eventually strengthen the health systems capacity to fight this small bite big threat.

References


7. Response to the 15th Lok Sabha unstarred question no.1776 regarding number of cases and deaths of Japanese Encephalitis.
Response Annexure available at http://164.100.47.132/Annexure_New/lsq15/14/au1776.htm


