

Emerging Disease Surveillance in Southeast Asia

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Abstract

*The emergence of infectious disease causing agents/pathogens necessitates a rational surveillance approach leading to early detection and appropriate intervention. Surveillance activities with support from the US Naval Medical Research Unit No. 2 (NAMRU-2), targeting susceptible populations/areas in Southeast Asia, have been organised using a multi-design strategy: 1) systematic multi-size (usually hospital-based) study; 2) investigation of (suspected) outbreak events involving significant case populations (and associated fatalities); and 3) monitoring of unique "risk opportunities" that include pre- and post-screening of immunologically naive (susceptible) persons (including military personnel and tourists) travelling in groups to areas of likely disease transmission/occurrence. Recognition of new (or old) disease agents or emerging antimicrobial resistance requires a standardised study effort with complementary advanced diagnostic capabilities. Collaborative research involving NAMRU-2 includes surveillance of 01 and non-01 *Vibrio cholerae* strains in epidemic and sporadic transmission, profiling regional patterns of antimicrobial resistance associated with *Mycobacterium tuberculosis*, describing the molecular epidemiology of HIV genotypic spread, and investigating foci of epidemic hepatitis E virus transmission. Focused surveillance efforts, as described, provide for recognition of emerging and/or re-emerging diseases, optimising the investment of generally scarce public health resources.*

Ann Acad Med Singapore 1997; 26:628-31

Key words: Epidemiology, Indonesia, Monitoring, Resistance, Transmission

Background

The US Naval Medical Research Unit No. 2 (NAMRU-2) is located in Jakarta, Indonesia. This infectious disease research facility is part of a larger, organised network sponsored by the US Department of Defense (DoD), supporting infectious disease research worldwide. Other DoD laboratories are located in Thailand (Army), Egypt (Navy), Kenya (Army), Peru (Navy), Brazil (Army) and the United States (Navy and Army). The rationale behind this global system is to apply advanced diagnostic and epidemiological capabilities in areas burdened by infectious disease threats for research into appropriate prevention and treatment strategies. Principal funding for NAMRU-2 is through DoD appropriations, although significant support is provided via cooperative research agreements with the private sector, including companies like DAINABOT Laboratories of Japan. The Emerging Disease Program at NAMRU-2 is one of four research programme centres that include malaria, enterics, and virology. Drawing from a complement of

20 American and over 100 Indonesian health professionals, and its formal association with the Indonesian National Institutes for Health Research and Development (LITBANGKES), Ministry of Health, NAMRU-2 has developed a sophisticated surveillance mechanism to study emerging diseases in Southeast Asia. Also, NAMRU-2 recently (15 April 1997) assumed added responsibilities in association with its status as a World Health Organization (WHO) Collaborating Center for Emerging Diseases, serving member countries in the Southeast Asian region.

Surveillance Strategies

Recognition of new emerging and re-emerging viral and microbial agents/pathogens is very much a function of basic diagnostic (clinical and laboratory) capabilities and a systematic epidemiological study approach. NAMRU-2 has organised research of emerging diseases into three distinct research strategies: 1) outbreak investigations; 2) surveillance via systematic data/specimen

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collection; and 3) pre- and post-screening activities targeting immunologically naïve (susceptible) populations. Investigations involving the mentioned research designs provide for an effective and efficient use of generally scarce surveillance-type resources and personnel in the study of emerging disease occurrence.

Outbreak investigations provide a “window of opportunity” for identifying new (emerging/re-emerging/previously unrecognised) disease causing agents/pathogens. Epidemic transmission nominally involves populations somewhat “marginalised” from an immunological perspective: naïve relative to exposure history, or burdened with background infections. Consequently, surveillance efforts targeting marginalised type groups may enhance early detection of emerging or re-emerging infectious agents. Additionally, epidemic transmission uniquely profiles the natural history of disease impact in a population characterised by time, place, and risk. NAMRU-2 is sponsoring training programmes leading to improved regional outbreak response capabilities in eastern Indonesia, Laos and Cambodia.

Surveillance networks allow for the regionalisation of disease profiles, using standardised designs from multi-institutional studies. Selective monitoring of targeted events, e.g. diarrhoeal disease occurrence, in geographically representative settings, including hospital-based, provides for a mapping for the following: 1) the importance of different microbial agents in clinical disease, and 2) antimicrobial patterns of multi-drug resistance. The on-going surveillance also allows monitoring of changes over-time via trend analysis.

Pre- and post-screening activities involve identification of antibody conversions, the translation of which consti-

tutes an incidence measure. Groups (military personnel, tourists, and business people) travelling from non-infectious to uncharted areas relative to active transmission, against a background of predisposing environmental and/or climatic conditions, serve as immunologically naïve, susceptible populations from which an assessment for an area-specific infectious disease threats can be made. Study cohorts are selected on the basis of shared risk-related opportunities for exposure.

Applied Epidemiological Research

Cholera

The potential spread of *Vibrio cholerae* 0139 strain, from the sub-Indian continent (first recognised in epidemic form from India in 1992)¹ into Southeast Asia, prompted development of a surveillance mechanism, the purpose of which was to provide for early detection of *Vibrio cholerae* 0139 into Indonesia (Fig. 1). Eight hospitals from throughout the archipelago were enrolled in the cholera surveillance network between 1993 through 1994, ensuring some geographical representation (Fig. 2). Additionally, twelve diarrhoeal outbreaks involving case-fatalities were investigated (Fig. 3). Twelve per cent of the 2395 specimens from hospital-based study were culture positive for *Vibrio cholerae* 01 biotype El tor (294 were of Ogawa serotype and 1 of Inaba serotype), 0.5% (12) for non-01 *V. cholerae* and 2% (48) for *V. parahaemolyticus*. Significant geographical variability was found in the proportion of hospital admissions attributed to Ogawa serotype, ranging from <1% to as high as 22%. In contrast to hospital-based findings, Ogawa serotype *V. cholerae* was recognised as the causative aetiological pathogen in the 12 outbreaks investigated, involving an examination of 520 case subjects.



Fig. 1. The spread of *V. cholerae* 0139 (Bengal strain).

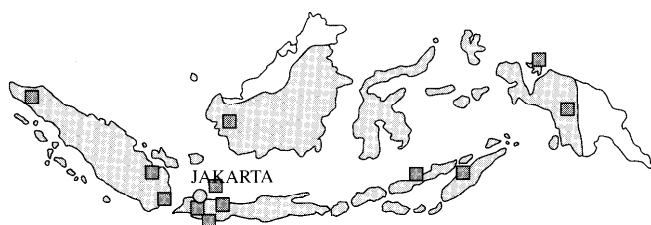


● Hospital-based ongoing studies

* *V. cholerae* (Ogawa) identified as principal agent in every outbreak.

** No *V. cholerae* 0139 identified yet in Indonesia.

Fig. 2. Hospital-based *V. cholerae* 0139 surveillance in Indonesia.



■ Outbreak investigations

Fig. 3. *V. cholerae* outbreak investigations in Indonesia.

Clearly, *V. cholerae* remains an important cause of debilitating diarrhoeal disease in Indonesia, particularly during epidemic transmission.

Tuberculosis

Surveillance of primary (versus secondary) multi-drug resistant *Mycobacterium tuberculosis* is of interest given outbreak reports from hospitals, correctional institutions and other facilities, involving broad spectrum resistance in overall healthy (non-immunocompromised) populations.² The potential for emergence of primary drug resistance is exaggerated in areas with large immunosuppressed (HIV positive) populations. In Indonesia and Vietnam, surveillance efforts are underway (since 1995) in identifying regional resistance patterns, and differentiating resistance between primary and secondary cases (Fig. 4).

Viral Hepatitis

Foci of epidemic hepatitis E virus (HEV) transmission have been recognised in Indonesia³ and Vietnam (unpublished observations). In Indonesia, two large HEV outbreaks were reported from West Kalimantan (Borneo) in 1987 and 1991. The prevalence of HEV infection 7 years after the first outbreak was 50% ($P < 0.0001$) higher than that found among a control, non-outbreak

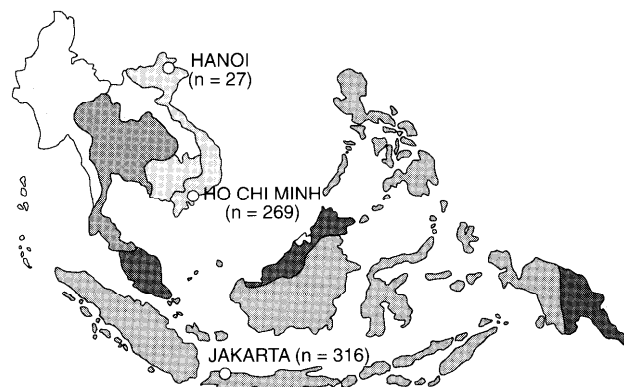


Fig. 4. Surveillance of multidrug-resistant for *Mycobacterium tuberculosis* in primary and secondary cases in Indonesia and Vietnam.

affected population (23%). In the second outbreak, the prevalence two years later was 59%. The first evidence of epidemic HEV transmission in Indo-China was recognised in 1994 along the Cambodian border. Findings from these investigations suggest that HEV is the aetiology responsible for most waterborne (enteric) hepatitis outbreaks while cross-sectional studies found that more than 90% rural populations in Southeast Asia have been exposed to hepatitis A virus in early childhood. NAMRU-2-supported investigations recently provided first time recognition of GBV-C in Indonesia and Laos.⁴ New efforts are being planned to identify new viral agents of jaundiced disease in acute hepatitis patients, in cooperation with the National Institutes of Health in the United States.

HIV Infections

High reported prevalence of HIV infections among local sex workers prompted the Indonesian military to screen 3627 soldiers participating in UNTAC peace-keeping operations in Cambodia. Surveillance involved two groups of peacekeepers: 1658 pre-screened and post-screened soldiers and 1929 post-screened soldiers only. Serological analysis defined HIV-1 seropositive individuals and the diagnosis was confirmed by Western Blot techniques. A combination of PCR, RT-PCR and nested PCR followed by SSP and sequencing allowed for defining genotypes of HIV-1 based on HIV-1 env sequences. The overall annual seroconversion rate was 6.3 per 1000 soldier-years. HIV-1 subtype E was identified from HIV seropositive individuals associated with exposures during deployment to Cambodia.⁵ The genotypic evidence of subtype E is compatible with data from the geographical distribution of HIV-1 genotype in the area, the likely source of HIV spread into Cambodia, where E is the predominant subtype. In contrast, preliminary findings from other Indonesian risk groups demonstrate the presence of subtype B as being the most representative. A similar type of pre- and post-screening activities is being sponsored by NAMRU-2, targeting US

soldiers involved in humanitarian activities in Indo-China, for the study of area risk to rickettsial and flavivirus infections/disease.

Conclusion

Surveillance of new and/or re-emerging disease agents requires, first and foremost, a focused strategy with clearly delineated objectives. Early recognition of disease-causing agents and/or environmental events that can enhance opportunities for rapid disease spread contributes to the effectiveness of preventive and therapeutic health measures. Minimal resources can be efficiently applied as described in this review.

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