

Stimulating the development of national *Streptococcus suis* guidelines in Viet Nam through a strategic research partnership

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Problem *Streptococcus suis* is a common cause of adult bacterial meningitis in Viet Nam, and possibly other parts of Asia, yet this disabling infection has been largely neglected. Prevention, diagnosis and treatment are relatively straightforward and affordable but, in early 2007, no national diagnostic, case management or prevention guidelines existed in Viet Nam.

Approach Enhanced detection of *S. suis* infections was established in 2007 as part of a collaborative research programme between the National Hospital for Tropical Diseases, a key national hospital with very close links to the Ministry of Health, and a research group affiliated with Oxford University based in Viet Nam. The results were reported directly to policy-makers at the Ministry of Health.

Local setting Viet Nam is a low-income country with a health-care system that has seen considerable improvements and increased autonomy. However, parts of the system remain fairly centralized the Ministry of Health.

Relevant changes Following the improved detection and reporting of *S. suis* cases, the Ministry of Health issued guidance to all hospitals in Viet Nam on the clinical and laboratory diagnosis, treatment and prevention of *S. suis*. A public health laboratory diagnostic service was established at the National Institute of Hygiene and Epidemiology and training courses were conducted for clinicians and microbiologists. Ministry of Health guidance on surveillance and control of communicable diseases was updated to include a section on *S. suis*.

Lessons learnt Research collaborations can efficiently inform and influence national responses if they are well positioned to reach policy-makers.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Streptococcus suis is a bacterial pathogen that has its natural reservoir in pigs but can infect humans, causing meningitis, septicaemia, endocarditis and arthritis.¹ Infection can result in severe disease, with mortality of 3–18%, and hearing loss in up to 66% of survivors.^{2,3} It is probable that exposure to infected pigs and pork products are the main risk factors.^{2,4}

The first reports of human *S. suis* infection in south-eastern Asia were in China, Hong Kong Special Administrative Region in 1984⁵ and cases have subsequently been reported in Japan and Thailand.^{6,7} However, it was not until a large outbreak in Sichuan province, China in 2005 that interest in this pathogen grew⁸ and *S. suis* is now increasingly recognized as a major cause of bacterial meningitis in south-east Asia.^{1,2,4,9} Despite this increased interest, it is probable that the burden of *S. suis* is considerably under-estimated since clinical awareness is low and many smaller hospitals do not possess a microbiology service. Even in hospitals with a microbiology service, infection may be misdiagnosed as a viridans group streptococcus or *Enterococcus*.

Considerable scope exists for improving the prevention, recognition and treatment of *S. suis*. The clinical picture and patient demographics can be distinctive and laboratory identification is not complicated, requiring the use of biochemical tests to differentiate *S. suis* from other streptococcal species.^{2,9} *S. suis* isolates are generally sensitive to penicillin and the risk of the most important long-term sequela, deafness, can be reduced by the use of steroids.^{3,4} Therefore, *S. suis* is readily treatable with affordable and accessible drugs. The risk of infection might be

reduced through education of people who work with and butcher pigs, through enforcement of changes in butchering practices and through efforts to change dietary habits.

S. suis was detected in southern Viet Nam as early as 1997^{3,4} but by 2007 this important pathogen was still not mentioned in national guidelines on the diagnosis, treatment and prevention of meningitis. This paper presents our experience of rapidly influencing the development of national guidelines through a research partnership between an influential national institute and an external academic group.

Local setting

Viet Nam is a low-income country that has made impressive achievements in improving health. The health-care system has seen considerable changes, with improved facilities and services, increased autonomy and the implementation of a social health insurance system. However, significant challenges remain, particularly in the areas of cost containment and quality of care. Although several laws have given more autonomy to health departments and health facilities, parts of the system remain fairly centralized, with the Ministry of Health retaining responsibility for many functions, including the development of guidance on disease prevention, diagnosis and clinical management.

Challenges

The burden of *S. suis* in Viet Nam is difficult to quantify and awareness is low since most hospitals do not have the diagnos-

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tic resources to identify the organism. Although the international biomedical literature contains some publications on *S. suis*, language barriers and access difficulties mean that the information is not readily available to most Vietnamese clinicians. Alerting clinicians to the importance of *S. suis* is difficult since channels for disseminating knowledge and guidance are limited. The Ministry of Health is active in developing clinical and public health guidelines through central directives but there are few other stakeholders, such as professional associations, producing guidelines.

Response

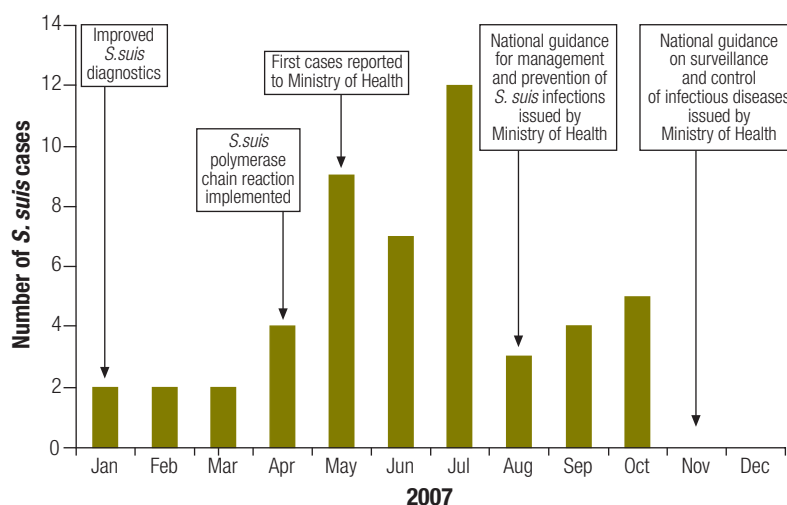
The National Hospital for Tropical Diseases (NHTD) is a 200-bed tertiary care centre for infectious diseases in northern Viet Nam. Unlike most hospitals in Viet Nam, NHTD is a specialist hospital under the direct control of the Ministry of Health and is close to the Ministry of Health both geographically and managerially. In 2006 a research partnership was established between NHTD and the Oxford University Clinical Research Unit. A key reason for developing this partnership was to maximize the impact of clinical research through the close relationship between NHTD and the Ministry of Health.

Shortly after the research unit and laboratories were operational at NHTD, an investigation was started into cases of purulent meningitis identified as being caused by *Aerococcus viridans* or *Streptococcus species*. It was decided to re-test a selection of stored strains from late 2006 with API 20 Strep (Biomérieux, Lyon, France). The strains were identified as *S. suis* and this was confirmed by a *S. suis* serotype 2 polymerase chain reaction.⁴ After this finding, it was decided that all streptococci isolates from blood and cerebrospinal fluid should be tested with API 20 Strep. Real time polymerase chain reaction diagnostics for *S. suis* were introduced in April 2007.

Impact

After introducing enhanced diagnostics, *S. suis* became the most commonly identified pathogen in adults with suspected meningitis at NHTD. Between January and May 2007, 19 cases of *S. suis* meningitis were detected and 50 cases were detected for the entire year (Fig. 1). Of 562

Fig. 1. Number of *Streptococcus suis* cases diagnosed per month during 2007 at the National Hospital for Tropical Diseases



cerebrospinal fluid specimens submitted for microbiological analysis during 2007, we identified 11 *Cryptococcus neoformans*, 3 *Streptococcus pneumoniae*, 3 *Streptococcus species*, 1 *Enterobacter cloacae* and 43 *S. suis*. An additional 7 patients had *S. suis* identified in blood cultures.⁹ Of the 50 patients with *S. suis*, 26 (52%) recovered completely, 21 (42%) recovered with sequelae and 3 patients died. Hearing loss was the most common sequela (38%).

The identification of *S. suis* as the commonest cause of bacterial meningitis at NHTD was reported to the Ministry of Health in May 2007. Within 4 months, the Ministry of Health issued national guidelines on *S. suis* (Ministry of Health Decision 3065/QD-BYT, dated 16 August 2009). The guidelines contained a description of the clinical syndrome and the organism, recommendations on microbiological diagnosis, a recommendation to treat suspected cases with ampicillin, a third generation cephalosporin and intravenous corticosteroids (methylprednisolone 0.5–1 mg/kg/day). These guidelines were sent to all hospitals in Viet Nam and received a lot of local media coverage. Although the treatment of suspected bacterial meningitis with ampicillin and a cephalosporin was standard practice before promulgation of the national *S. suis* guidelines, steroids were not recommended routinely for non-tuberculous bacterial meningitis in adults.³

In August 2007, the National Institute of Hygiene and Epidemiology, the local World Health Organization office and our research group held a meeting to discuss the public health challenges of

S. suis. The National Institute of Hygiene and Epidemiology and three regional public health institutes then received training on the identification of *S. suis* from human clinical specimens.

In November 2007, the preventive medicine branch of the Ministry of Health issued updated guidelines on the surveillance and control of communicable diseases. For the first time the guidelines included a section dedicated to *S. suis*. They included advice not to slaughter or consume sick pigs, to cover wounds and wear protective equipment during slaughtering of pigs, and not to consume undercooked pork.

The Ministry of Health has not established a surveillance system for *S. suis* so it is not possible to assess the impact of the guidelines on the incidence and clinical outcome of *S. suis* infections. However, 44 cases of *S. suis* were diagnosed at NHTD during 2008, so it is clear that *S. suis* remains an important health problem. The main lessons learnt are summarized in Box 1.

Recommendations

It is well recognized that developed and developing countries both have difficulties in ensuring that research findings influence policies and practices.¹⁰ However, in resource-poor settings, where the population is more vulnerable, the opportunity costs greater and the consequences of poor policy more serious, the relative importance of the influence of research on policy may be greater. Demonstration of the relevance of health research is also

essential for the grass roots credibility of the research team.

There are many obstacles to translating evidence into policies and practices that have been well documented.¹⁰ The causes are diverse and apply both to the researchers and policy-makers.¹¹ In fact, it could be argued that the duty of policy-makers to seek out the best evidence is equally weighted by the duty of publicly funded researchers to seek to influence policy. Rigorous evidence is not enough if the evidence can only be found in inaccessible journals written in impenetrable scientific language. It is not enough to publish and pray for percolation.¹² A common difficulty is that the process of policy formulation is often not well characterized or mapped. And for those sitting outside the policy-making forum, channels to formally challenge or develop policy may be obscure. But Ministries of Health often out-source expertise and it can be very useful to identify these spheres of influence. Indeed, policy-makers have identified personal contact

Box 1. Summary of main lessons learnt

- Engaging with research partners who have influence with government and policy-makers will maximize the chances of research having an impact locally.
- Reporting of simple research data directly to policy-makers can have more impact than publishing in the biomedical literature.
- It is important to identify local "pathways to policy" and use prominent figures or institutions to lobby for change.

with researchers as the most important factor influencing decisions about use of research information.¹³

Our experience illustrates that a scientific partnership between an international research group and an influential national institute closely linked to government can have an immediate impact on national policies. Identifying and using the pathways to policy and giving evidence prominence through prominent figures can profoundly improve the chances of effecting change. ■

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ملخص

حذف إعداد الدلائل الإرشادية للعقدية السوسية في فيت نام من خلال نهج الشراكة في البحوث

التغيرات ذات الصلة: أصدرت وزارة الصحة في أعقاب تحسن الاكتشاف والتبليغ عن حالات العقدية السوسية توجيهاً لجميع المستشفيات في فيت نام حول التشخيص السريري والمختبري والمعالجة والوقاية من العقدية السوسية. وتأسس التشخيص المختبري للحالات كخدمة صحية عمومية في المعهد الوطني للنظافة الصحية والوبائيات وأجريت دورات تدريبية للأطباء والمختصين في المكروبيولوجيا. وأجرى تحديث على التوجيه الصادر عن وزارة الصحة حول ترصد ومكافحة الأمراض السارية ليتضمن قسماً عن العقدية السوسية.

الدروس المستفادة: يمكن للتعاون البحثي أن يزيد بفعالية من الاطلاع المستنير على الاستجابات الوطنية للأمراض ويؤثر فيها، وذلك إذا وضع التعاون البحثي بحيث تصل نتائجه إلى راسمي السياسات.

المشكلة تعد جرثومة العقدية السوسية *Streptococcus suis* سبباً شائعاً للالتهاب السحائي بين البالغين في فيت نام، ومن المحتمل أن تكون كذلك في أجزاء أخرى من قارة آسيا، ومع ذلك فإن الإهمال الجسيم يحيط بهذه العدوى المسببة للعجز. وبالرغم من أن الوقاية منها وتشخيصها وعلاجها بسيط نسبياً وبتكلفة ميسورة، فلم تتوافر حتى بداية عام 2007 في فيت نام دلائل إرشادية وطنية خاصة بتشخيص الحالات ومعالجتها والوقاية منها. الأسلوب تأسس اكتشاف مَطَوَّر للعقدية السوسية في عام 2007 كجزء من برنامج التعاون البحثي بين المستشفى الوطني لأمراض المناطق المدارية، وهو مستشفى وطني رئيسي له روابط وثيقة مع وزارة الصحة، ومجموعة من الباحثين المنتسبين لجامعة أكسفورد ومقرهم في فيت نام. وقد أبلغ عن نتائج البحث مباشرة إلى راسمي السياسات في وزارة الصحة.

الوضع المحلي: فيت نام بلد منخفض الدخل وقد شهد النظام الصحي فيه تحسناً هائلاً وزيادة في الاستقلالية الذاتية. إلا أن النظام مازال مركزياً نوعاً ما ومرتباً بوزارة الصحة.

Résumé

Stimulation du développement de directives nationales concernant *Streptococcus suis* au Viet Nam par le biais d'un partenariat de recherche stratégique

Problématique *Streptococcus suis* est une cause courante de méningite bactérienne chez l'adulte au Viet Nam et potentiellement dans d'autres parties de l'Asie, même si cette infection invalidante a été largement négligée. La prévention, le diagnostic et le traitement sont relativement classiques et abordables mais, début 2007, il n'existait, au Viet Nam, aucune directive nationale pour le diagnostic et la prévention de cette maladie, ainsi que pour la prise en charge des cas.

Démarche Un dépistage amélioré des infections à *S. suis* a été mis en place en 2007 dans le cadre d'un programme de recherche auquel

collaboraient l'Hôpital national pour les maladies tropicales, un hôpital national important entretenant des liens étroits avec le Ministère de la santé, et un groupe de recherche affilié à l'Université d'Oxford et basé au Viet Nam. Les résultats ont été rapportés directement aux décideurs politiques au niveau du Ministère de la santé.

Contexte local Le Viet Nam est un pays à faible revenu, doté d'un système de santé qui a vécu des améliorations et un accroissement de son autonomie considérables. Néanmoins, ce système reste relativement centralisé autour du Ministère de la santé.

Modificaciones pertinentes Suite à l'amélioration du dépistage et de la notification des cas de *S. suis*, le Ministère de la santé a publié des directives à l'intention de tous les hôpitaux du Viet Nam sur le diagnostic clinique et analytique, le traitement et la prévention des infections à *S. suis*. Un service de santé publique pratiquant des diagnostics en laboratoire a été mis en place à l'Institut national d'hygiène et d'épidémiologie et des cours de formation ont été dispensés aux cliniciens et aux microbiologistes.

Les directives du Ministère de la santé sur la surveillance des maladies transmissibles et la lutte contre ces maladies ont été actualisées pour inclure une partie sur *S. suis*.

Enseignements tirés Les recherches menées en collaboration peuvent étayer et influencer efficacement les réponses nationales si elles sont bien positionnées pour atteindre les décideurs politiques.

Resumen

Fomento de la elaboración de directrices nacionales sobre *Streptococcus suis* en Viet Nam mediante una alianza de investigación estratégica

Problema *Streptococcus suis* es una causa común de meningitis bacteriana en adultos en Viet Nam y posiblemente en otras zonas de Asia, pese a lo cual esta infección discapacitante ha permanecido muy desatendida. La prevención, el diagnóstico y el tratamiento son relativamente sencillos y asequibles, pero a principios de 2007 no había en Vietnam ningún tipo de directrices nacionales sobre su diagnóstico, tratamiento o prevención.

Enfoque En 2007 se fijó el objetivo de mejorar la detección de las infecciones por *S. suis* como parte de un programa de investigación colaborativa entre el Hospital Nacional de Enfermedades Tropicales, un importante hospital nacional vinculado muy estrechamente al Ministerio de Salud, y un grupo de investigación afiliado a la Universidad de Oxford que trabajaba en Viet Nam. Los resultados se notificaron directamente a las instancias normativas del Ministerio de Salud.

Contexto local Viet Nam es un país de ingresos bajos con un sistema de salud que se ha beneficiado de mejoras considerables y de una creciente

autonomía. Sin embargo, el sistema sigue estando bastante centralizado en el Ministerio de Salud.

Cambios destacables Tras la mejora de la detección y notificación de los casos de *S. suis*, el Ministerio de Salud transmitió a todos los hospitales de Viet Nam indicaciones sobre el diagnóstico clínico y de laboratorio, el tratamiento y la prevención de la infección por *S. suis*. Se creó un servicio de diagnóstico de laboratorio de salud pública en el Instituto Nacional de Higiene y Epidemiología, y se llevaron a cabo cursos de formación para médicos y microbiólogos. Las orientaciones del Ministerio de Salud sobre la vigilancia y el control de las enfermedades transmisibles fueron actualizadas para incluir un apartado sobre *S. suis*.

Enseñanzas extraídas Las investigaciones en colaboración pueden fundamentar de manera eficiente las respuestas nacionales e influir en ellas si se logra situarlas adecuadamente para que lleguen a las instancias normativas.

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