

overestimation of the incidence and hence the risk of viremic donation, is more likely to occur outside an outbreak setting. The validity of the extrapolated data derived from a sentinel surveillance system estimating the total number of cases in the community should also be questioned. The serosurvey estimated that 38 percent of the inhabitants had been infected and that 32 percent had suffered from symptomatic infections. These data are consistent with the 35 percent of the inhabitants having suffered from symptomatic illness, estimated by the sentinel surveillance system and corroborate our incidence estimates.

We assumed that potential blood donors had the same risk of CHIKV infection as the general population. This assumption was supported by the findings of the serosurvey that showed similar antibody prevalences among adults of both sexes.²⁴ In addition, when we applied age-specific CHIKV antibody prevalence rates of the serosurvey to the donor population of Reunion Island, the overall seroprevalence among donors was estimated at 37.2 percent, similar to the overall antibody prevalence in the general population (38%).

One major limitation of the validity of our estimates relates to lack of a precise knowledge on the distribution of the duration of asymptomatic viremia in individuals with apparent and inapparent infection. To refine the estimates, further studies are necessary to document the kinetics of CHIKV viremia. This approach also hypothesizes that symptomatic individuals would self-defer or be excluded by the predonation examination. In real life, this may not always be the case. In the United States, among the first 14 identified donors associated with transfusion-related WNV transmission to recipients, 3 were shown to have been symptomatic at the moment of the donation.¹⁵ Nevertheless, for CHIKV infection which is characterized by sudden onset of symptoms, this assumption is more plausible than for WNV which frequently causes paucisymptomatic infection.

Lack of data on the frequency of asymptomatic infection was the most important limiting factor for the preliminary estimates. This variable has a preponderant role in the risk estimate since it contributes both in the computation of the weighted mean of the duration of asymptomatic viremia and in the estimate of the incidence of infection. Valid data were available, however, for the retrospective calculations from the seroprevalence survey. This survey provided an estimate of the proportion of asymptomatic infections obtained directly among the studied population and for the epidemic CHIKV strain circulating.

In spite of the above limitations, the retrospective estimates are likely to give a good approximation of the real risk, as suggested by the observed risk of viremic PLT donations. From January to May 2006, this observed risk was 400 per 100,000 donations, of the same order of mag-

nitude as the risk of 720 per 100,000 donations estimated over the same period.

Up to date, CHIKV infections from transfusion of blood or blood components have not been reported in the literature. On Reunion Island, no case of transfusion-transmitted CHIKV infection has been identified in spite of the estimated seven viremic donations collected before donations were interrupted. Despite the lack of data about transfusion-transmitted CHIKV infection, the high viral load during the acute phase of the infection,^{21,28} the fact that several cases of CHIKV transmission have occurred among laboratory personnel handling infected blood,²⁹ and the fact that CHIKV has been transmitted to a health care worker drawing blood from an infected patient²⁸ provide evidence that transfusion-related transmission of CHIKV is highly plausible. It is possible that transfusion-related infections have not been recognized or have not been distinguished from infection from mosquito vectors. Also, the true transmission rate from viremic donors to recipients is not known. Several issues may influence the possibility of transmission of CHIKV through transfusion, such as the stability of the virus during storage of blood and the efficiency of virus elimination of blood processing methods, as viral inactivation. Also, the presence of IgM or IgG antibodies in donor blood may neutralize infectivity, as demonstrated for other viruses, such as parvovirus³⁰ and suggested for WNV.³¹ In addition, the assessment of the risk of CHIKV transmission from a viremic donor to a recipient would need to take into account the recipient's immune status.

In conclusion, despite the absence of documented cases, blood transfusion-related CHIKV transmission is plausible and the risk of viremic donation can be substantial in an outbreak setting. During this large outbreak, the estimated risk of viremic blood donation was high, but low compared to the risk of mosquito-borne CHIKV transmission. Despite its limitations, this work provided a right order of magnitude of the risk of viremic blood donation in real time during the ascending phase of the epidemic peak. At this moment, the decision of interrupting blood collection relied on the precautionary principle. The low risk estimated for early 2007 was, however, useful to contribute to the decision making process to start again the collection of blood donations on the island from June 14, 2007. This illustrates how this approach may contribute to guiding prevention measures.

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REFERENCES

1. Robinson MC. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-53. I. Clinical features. *Trans R Soc Trop Med Hyg* 1955;49:28-32.
2. Lumsden WH. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-53. II. General description and epidemiology. *Trans R Soc Trop Med Hyg* 1955;49:33-57.
3. Jupp PG, McIntosh BM. Chikungunya virus disease. In: Monath TP, editor. *The arboviruses: epidemiology and ecology*. Boca Raton (FL): CRC Press; 1988. p. 137-57.
4. Pastorino B, Muyembe-Tamfum JJ, Bessaud M, Tock F, Tolou H, Durand JP, Peyrefitte CN. Epidemic resurgence of Chikungunya virus in democratic Republic of the Congo: identification of a new central African strain. *J Med Virol* 2004;74:277-82.
5. Thonnon J, Spiegel A, Diallo M, Diallo A, Fontenille D. Chikungunya virus outbreak in Senegal in 1996 and 1997. *Bull Soc Pathol Exot* 1999;92:79-82.
6. Lanciotti RS, Ludwig ML, Rwaguma EB, Lutwama JJ, Kram TM, Karabatsos N, Cropp BC, Miller BR. Emergence of epidemic O'nyong-nyong fever in Uganda after a 35-year absence: genetic characterization of the virus. *Virology* 1998;252:258-68.
7. Saluzzo JF, Gonzalez JP, Herve JP, Georges AJ. Epidemiological study of arboviruses in the Central African Republic: demonstration of Chikungunya virus during 1978 and 1979. *Bull Soc Pathol Exot Filiales* 1980;73:390-9.
8. Carey DE, Myers RM, DeRanitz CM, Jadhav M, Reuben R. The 1964 chikungunya epidemic at Vellore, South India, including observations on concurrent dengue. *Trans R Soc Trop Med Hyg* 1969;63:434-45.
9. Porter KR, Tan R, Istary Y, Suharyono W, Sutaryo Widjaja S, Ma'Roef C, Listiyaningsih E, Kosasih H, Hueston L, McArdle J, Juffrie M. A serological study of Chikungunya virus transmission in Yogyakarta, Indonesia: evidence for the first outbreak since 1982. *Southeast Asian J Trop Med Pub Health* 2004;35:408-15.
10. Nimmannitya S, Halstead SB, Cohen SN, Margiotta MR. Dengue and chikungunya virus infection in man in Thailand, 1962-1964. I. Observations on hospitalized patients with hemorrhagic fever. *Am J Trop Med Hyg* 1969;18:954-71.
11. Thein S, La Linn M, Aaskov J, Aung MM, Aye M, Zaw A, Myint A. Development of a simple indirect enzyme-linked immunosorbent assay for the detection of immunoglobulin M antibody in serum from patients following an outbreak of chikungunya virus infection in Yangon, Myanmar. *Trans R Soc Trop Med Hyg* 1992;86:438-42.
12. Borgherini G, Poubeau P, Staikowsky F, Lory M, Le Moullec N, Becquart JP, Wengling C, Michault A, Paganin F. Outbreak of chikungunya on Reunion Island: early clinical and laboratory features in 157 adult patients. *Clin Infect Dis* 2007;44:1401-7.
13. Lambert J, Couturier B, Vaillant V. Infection à chikungunya. Etude descriptive des cas importés en France métropolitaine, 2005-2006. Saint-Maurice: Institut de Veille Sanitaire; 2007.
14. Brouard C, De Valk H, Pillonel J; Groupe "Estimation Quantitative du Risque de Contamination d'un Don de Sang par des Agents Infectieux." Estimation quantitative du risque de contamination d'un don de sang par des agents infectieux. Saint-Maurice: Institut de Veille Sanitaire; 2007.
15. Biggerstaff BJ, Petersen LR. Estimated risk of transmission of the West Nile virus through blood transfusion in the US, 2002. *Transfusion* 2003;43:1007-17.
16. Fleiss JL. Statistical methods for rates and proportions. 2nd ed. New York: Wiley; 1981.
17. Sarkar JK, Pavri KM, Chatterjee SN, Chakravarty SK, Anderson CR. Virological and serological studies of cases of haemorrhagic fever in Calcutta. Material collected by the Calcutta school of tropical medicine. *Indian J Med Res* 1964;52:684-91.
18. Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, Suntayakorn S, Rothman AL, Ennis FA, Nisalak A. Dengue in the early febrile phase: viremia and antibody responses. *J Infect Dis* 1997;176:322-30.
19. Gubler DJ, Suharyono W, Tan R, Abidin M, Sie A. Viraemia in patients with naturally acquired dengue infection. *Bull World Health Organ* 1981;59:623-30.
20. Guzman MG, Kouri G. Dengue: an update. *Lancet Infect Dis* 2002;2:33-42.
21. Laurent P, Le Roux K, Grivard P, Bertil G, Naze F, Picard M, Staikowsky F, Barau G, Schuffenecker I, Michault A. Development of a sensitive real-time reverse transcriptase PCR assay with an internal control to detect and quantify chikungunya virus. *Clin Chem* 2007;53:1408-14.
22. Waterman SH, Novak RJ, Sather GE, Bailey RE, Rios I, Gubler DJ. Dengue transmission in two Puerto Rican communities in 1982. *Am J Trop Med Hyg* 1985;34:625-32.
23. McBride WJ, Mullner H, LaBrooy JT, Wronski I. The 1993 dengue 2 epidemic in North Queensland: a serosurvey and comparison of hemagglutination inhibition with an ELISA. *Am J Trop Med Hyg* 1998;59:457-61.

24. Perau J, Catteau C, Michault A, Parain C, Favier F. Fin 2006, 300 000 personnes avaient été atteintes par le chikungunya. *Economie de la Réunion* 2007;129:16-7.
25. Renault P, Solet JL, Sissoko D, Balleydier E, Larrieu S, Filleul L, Lassalle C, Thiria J, Rachou E, De Valk H, Ille D, Ledrans M, Quatresous I, Quenel P, Pierre V. A major epidemic of chikungunya virus infection on Reunion Island, France, 2005-2006. *Am J Trop Med Hyg* 2007;77:727-31.
26. Biggerstaff BJ, Petersen LR. Estimated risk of West Nile virus transmission through blood transfusion during an epidemic in Queens, New York City. *Transfusion* 2002;42:1019-26.
27. Sanchez-Garrido L, Bernillon P, Delarocque-Astagneau E, Brouard C, Pillonel J, Santa-Olalla P, De Valk H, Desenclos JC. Modélisation du risque de contamination des dons de sang par le virus de l'hépatite A. *Journées de veille sanitaire* 2005, 29-30 November; Paris.
28. Parola P, De Lamballerie X, Jourdan J, Rovey C, Vaillant V, Minodier P, Brouqui P, Flahault A, Raoult D, Charrel RN. Novel chikungunya virus variant in travelers returning from Indian Ocean islands. *Emerg Infect Dis* 2006;12:1493-9.
29. Centers for Disease Control and Prevention and National Institute of Health. *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*. 5th ed. Washington (DC): US Government; 2007.
30. Parsyan A, Candotti D. Human erythrovirus B19 and blood transfusion—an update. *Transfus Med* 2007;17:263-78.
31. Busch MP, Caglioti S, Robertson EF, McAuley JD, Tobler LH, Kamel H, Linnen JM, Shyamala V, Tomasulo P, Kleinman SH. Screening the blood supply for West Nile virus RNA by nucleic acid amplification testing. *N Engl J Med* 2005;353:460-7. ■

医薬品 研究報告 調査報告書

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一般的名称	(製造販売承認書に記載なし)	研究報告の公表状況	Chuang VW, Wong TY, Leung YH, Ma ES, Law YL, Tsang OT, Chan KM, Tsang IH, Que TL, Yung RW, Liu SH. Hong Kong Med J. 2008 Jun;14(3):170-7.	公表国 中国	
販売名(企業名)	合成血-LR「日赤」(日本赤十字社) 照射合成血-LR「日赤」(日本赤十字社)				
研究報告の概要	<p>○1998年～2005年の香港におけるデング熱症例の検討 目的: デング患者の疫学的、臨床的知見、臨床検査知見、並びに転帰の検討。 患者: 1998年～2005年に香港の公立病院に入院したデング患者(臨床検査による確定例)全員の医療記録を後方視的に検討した。 結果: 合計126名の患者を特定した[デング熱123名(98%)、デング出血熱3名(2%)]。輸血によりデング熱が伝播した患者1名が明らかとなった。合計116名(92%)は「輸入感染」で、10名(8%)は「地域内感染」であった。RT-PCRで確定したデング症例56名のうち、もっとも多かったのはデングウイルス1型(48%)であり、ついで2型(23%)3型(16%)、4型(13%)であった。地域内感染は1、2型のみであった。患者の年齢の中央値は38歳で、入院期間の平均は6日間であった。死亡例はなく、ほぼ全員(98%)が発熱を呈した。入院時のその他の症状は次の通り: 筋肉痛(83%)、頭痛(65%)、倦怠感(59%)、皮疹(60%)。3分の1以上の患者が胃腸および上気道の合併症を発現した。もっとも多く認められた身体的所見は斑丘疹状皮疹であった。血小板減少、好中球減少、リンパ球減少は、それぞれ86%、78%、69%の患者に発現した。人口統計学的・臨床的知見、臨床検査知見、ならびに転帰は、4つのデング血清型間で差はなかったが、リンパ球数は、他の型と比べて3型がもっとも低かった($P=0.004$)。 結論: 発熱、皮疹を呈し、合致する血液学的知見を持ち、流行地への渡航歴のある患者に遭遇した場合には鑑別診断にデング熱を含めるべきである。</p>				使用上の注意記載状況・ その他参考事項等
	報告企業の意見	<p>1998年～2005年に香港の公立病院に入院したデング患者は合計126名で、うち10名(8%)は「地域内感染」であり1名は輸血による感染だった。ウイルス型は1型が最も多く、地域内感染は1、2型のみであったとの報告である。デングウイルスは東南アジアに定着しており、中国や台湾など日本に近い地域での流行状況を注視していく必要がある。</p>			
報告企業の意見		今後の対応			
<p>1998年～2005年に香港の公立病院に入院したデング患者は合計126名で、うち10名(8%)は「地域内感染」であり1名は輸血による感染だった。ウイルス型は1型が最も多く、地域内感染は1、2型のみであったとの報告である。デングウイルスは東南アジアに定着しており、中国や台湾など日本に近い地域での流行状況を注視していく必要がある。</p>		<p>日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国(入国)後4週間は献血不適としている。問診でデング熱の既往があった場合には、治療後1ヶ月間献血不適としている。また、厚生労働科学研究「献血血の安全性確保と安定供給のための新興感染症等に対する検査スクリーニング法等の開発と献血制限に関する研究」班に協力する予定である。今後も引き続き情報の収集に努める。</p>			

ORIGINAL
ARTICLEReview of dengue fever cases in Hong Kong during
1998 to 2005

CME

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Objective To describe the epidemiology, clinical and laboratory findings, and outcomes of patients presenting locally with dengue.

Design Retrospective review of case records.

Setting Public hospitals, Hong Kong.

Patients Medical records of all laboratory-confirmed dengue patients admitted to public hospitals during 1998 to 2005 were reviewed retrospectively.

Results A total of 126 cases were identified, 123 (98%) being dengue fever and three (2%) dengue haemorrhagic fever. One patient who had blood transfusion-acquired dengue fever was highlighted. A total of 116 (92%) cases were 'imported', while 10 (8%) were local. Among the 56 dengue cases confirmed by reverse transcription-polymerase chain reaction, dengue virus type 1 was the most common accounting for 48% of them, followed by type 2, type 3, and type 4 responsible for 23%, 16%, and 13%, respectively. Only type 1 and type 2 were present in locally acquired infections. The median age of the patients was 38 years and the mean duration of hospitalisation was 6 days. There was no mortality, and nearly all patients (98%) presented with fever. Other symptoms at presentation included: myalgia (83%), headache (65%), fatigue (59%), and skin rash (60%). More than one third of patients had gastro-intestinal and upper respiratory complaints. Maculopapular skin rash was the most common physical finding. Thrombocytopenia, neutropenia, and lymphopenia were present in 86%, 78%, and 69% of the patients, respectively. In only 29% of the patients was dengue fever included in the initial differential diagnosis. The demographic, clinical, and laboratory findings as well as outcomes did not differ significantly among the four dengue serotypes, but the lowest lymphocyte counts of type 3 was lower than the other serotypes ($P=0.004$).

Conclusion When physicians encounter patients with a relevant travel history, presenting with fever and skin rash, and having compatible haematological findings, dengue fever should be included in the differential diagnosis.

Introduction

Dengue is the most common and widespread arthropod-borne viral infection in the world today. It is recognised in over 100 countries throughout the tropics and subtropical areas and threatens the health of approximately 40% of the world's population, of nearly 2.5 billion people.¹ The highest burden of disease occurs in South-East Asia and the Western Pacific, where it is one of the 10 leading causes of hospitalisation and childhood mortality.²

In Hong Kong, dengue fever was made notifiable since March 1994 and all infections reported to the Department of Health (DH) are investigated to establish their source. The number of cases reported is showing an increasing trend in recent years; the vast majority being imported from other countries. Hong Kong experienced its first local dengue case in September 2002.³ Thereafter, several others were encountered in Ma Wan and local cases were subsequently identified sporadically in 2002 and 2003.

The epidemiology, clinical manifestations, and laboratory findings of dengue fever infections and its complications have been extensively described in the medical literature,^{4,5} but comprehensive review is lacking for our local patients.