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all parts of the world. Around 163.9 million (7.4%) of Disability-Adjusted Life Years (DALYs) are attributable to mental and **substance use disorders**. In terms of years of life lost to premature mortality (YLLs), mental disorders accounts for 8.3 million, 0.5% of all YLLs. For years lost to disability (YLDs), mental and substance use disorders are the leading cause of disability worldwide [1].



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On the service side, public expenditure on mental health in low and middle income countries is less than US\$2 per capita; in high income states it is US\$58 [4]. Global cancer spend in 2014 was US\$100 billion[5]. In the UK,

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every £1 spent generates returns of 3/p [7], rendering this excellent value for money. When it comes to research spend we are a long way from the parity of esteem of other sectors. The NHS spends 1% of its budget on research, compared with 10% in the pharmaceutical industry. The NHS is a major funder of research, but the funding is not always directed to the areas of greatest need. The NHS is a major funder of research, but the funding is not always directed to the areas of greatest need.

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health needs throughout the lifespan, a multi-agency approach and greater involvement and empowerment of mental health service users in the planning and development of mental health policies and services. These are ambitious targets, without improved parity of esteem in the **funding of mental health**; it is hard to see how these targets can be met.

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References

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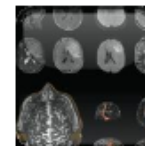
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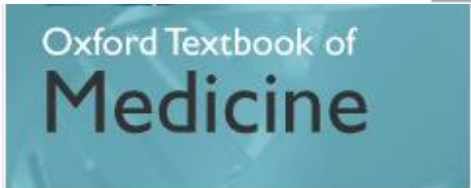
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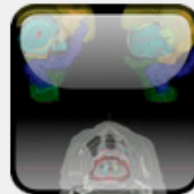
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mental health: no parity of esteem with physical health



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Potential drug therapy—failure of chloroquine.

Vaccines—continuing trials of experimental ChimeriVax-Dengue vaccine.

Updated on 31 May 2012. The previous version of this content can be found [here](#).





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Dengue

Chapter: Dengue

Author(s): Bridget Wills and Jeremy Farrar

DOI: 10.1093/med/9780199204854.003.070515_update_001

February 27, 2014: This chapter has been re-evaluated and remains up-to-date. No changes have been necessary.

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Essentials

Dengue is caused by a flavivirus and is the most important mosquito-borne viral infection of humans. Some 40 million symptomatic infections are estimated to occur annually. The disease is hyper-endemic in many large Asian cities, and is also a significant problem in the Pacific region and in the Americas. The primary mosquito vector is *Aedes aegypti*. Infection can be caused by any one of four closely related but serologically distinct **dengue** viral serotypes. Following infection with a single serotype there is life-long immunity to that serotype but the possibility of more severe disease during a subsequent infection with a different serotype.

Clinical features and diagnosis—symptomatic disease ranges from a nonspecific febrile illness through to a syndrome characterized by plasma leakage that may, if severe, result in the development of potentially fatal **dengue** shock syndrome. Thrombocytopenia and deranged haemostasis also occur, but clinically significant bleeding is unusual except in patients with profound shock. Severe hepatic and neurological complications are also seen in some patients. Diagnosis depends on viral isolation, detection of viral antigen or viral RNA, or serological testing.

Management and prevention—treatment is supportive, with particular emphasis on careful fluid management. Prompt volume resuscitation is essential for patients with shock, with regular monitoring of the pulse rate, blood pressure, and haematocrit to minimize the risk of fluid overload. No vaccine is available as yet but a number of candidates are entering

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Fig. 7.5.15.1
Global distribution of dengue .

All four serotypes can cause disease. Infection with one serotype elicits immunity to that serotype but does not provide long-term cross-protective immunity to the remaining serotypes. Severe disease occurs predominantly in patients experiencing a second or subsequent infection with a dengue serotype different from their first infection, or else in infants with transmitted maternal antibody experiencing their first infection. The generally accepted antibody-dependent enhancement (ADE) hypothesis suggests that residual heterotypic non-neutralizing antibodies bind to the new virus enhancing its infectivity by increasing the efficiency of binding and uptake of virus–antibody complexes through Fc receptors on blood monocyte or tissue macrophage cells, thus amplifying viral replication. The resulting increase in viral load drives an immunopathogenic cascade that alters microvascular function in some way, resulting in capillary leakage and coagulopathy. Rapid mobilization of serotype cross-reactive memory T cells has been suggested as an alternative mechanism to trigger the inflammatory cascade. Other factors considered to influence disease severity include differences in viral virulence, molecular mimicry, and immune complex and/or complement-mediated dysregulation, as well as age and genetic predisposition. However, the pathogenesis of the vascular leakage and coagulopathy associated with severe infections remains poorly understood and, so far, no mechanism has been identified that links the established immunological derangements with a definitive effect on microvascular structure or function.

Clinical manifestations



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ity of illnesses ranging from inapparent infection to mild febrile illness to atypical. In the past, symptomatic disease was conventionally separated into dengue fever (DF) and dengue haemorrhagic fever (DHF), with case definitions and criteria established by the World Health Organization (WHO). The pathognomonic feature of DHF is increased vascular permeability, which may be severe enough to result in hypovolaemic shock; in addition, to qualify for a diagnosis of DHF, a patient must have some evidence of bleeding and a platelet count below $100 \times 10^9/\text{litre}$. Due to practical difficulties in using the old WHO scheme a revised classification system has recently been developed, based on prospective data collected from over 2000 children and adults with dengue from endemic areas around the world, and this has now been adopted in the latest WHO guidelines for dengue published in 2009. The new scheme classifies the disease into dengue and severe dengue, in line with several other complex diseases such as malaria and pneumonia. It is hoped that in the future this will prove to be a simpler system that will be useful for triage, aid clinical management, and improve the quality of surveillance and epidemiological data.





(a)



Fig. 7.5.15.5 (a) Major bleeding at a venepuncture site in a Vietnamese teenager with severe DSS. (b) Extensive subconjunctival haemorrhages and severe epistaxis requiring nasal packing in a Vietnamese adult with dengue.



(a)



(b)

Chapter: Dengue

Author(s): Bridget Wills and Jeremy Farrar

From: Oxford Textbook of Medicine (5 ed.)

Outcome



The majority of patients with **dengue** make a full recovery. Those with DSS and/or significant bleeding usually do well provided they receive appropriate supportive care from experienced health care personnel during the critical phase of the illness. Adults may go on to experience several weeks of extreme tiredness, weakness, skin desquamation, pruritus, and depression during convalescence after infection, but there are no permanent sequelae. In general, children recover more rapidly and do not experience such problems.

Prevention



Although major efforts are being directed towards development of safe and effective **dengue** vaccines, it seems unlikely that a suitable candidate will be available for large-scale deployment for some years. Until then prevention of epidemics will continue to rely on elimination of potential vector breeding sites together with biological control. Community control of *Ae aegypti* by eradication of mosquito larvae from standing water is difficult to achieve in contemporary tropical urban settings. Insecticide-treated bednets and repellents for mosquitoes are primarily daytime feeders. Avoidance of mosquito bites in the tropics is achieved by wearing clothing containing *N,N*-diethyl-3-methylbenzamide (DEET) or picaridin and protective measures for the traveller.

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Deen JL, *et al.* (2006). The WHO **dengue** classification and case definitions: time for a reassessment. *Lancet*, **368**, 170–3.
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Durbin AP, Whitehead SS (2010). **Dengue** vaccine candidates in development. *Curr Top Microbiol Immunol*, **338**, 129–43.
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The majority of patients with dengue make a full recovery. Those with DSS and/or significant bleeding usually do well provided they receive appropriate supportive care from experienced health care personnel during the critical phase of the illness. Adults may go on to experience several weeks of extreme tiredness, weakness, skin desquamation, pruritus, and convalescence after infection, but there are no permanent sequelae. In general, children experience such problems.

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Prevention

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Finally, non-invasive haemodynamic study represents an alternative to invasive procedures in some clinical circumstances and it is very important in the diagnostic and therapeutic decision making. Therefore, it is necessary for the cardiologist to understand how this echocardiographic study is performed, as well as its advantages and limitations.

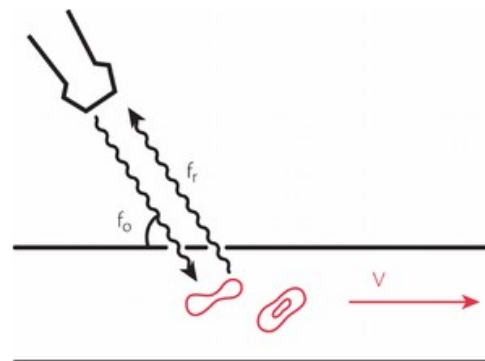
Principles of Doppler echocardiography

The Doppler effect

The Doppler effect is based on the physical phenomenon of increase of sound frequency when an object moves towards the observer and of decrease of sound frequency when an object moves away from the observer. When applied to echocardiography, it measures blood flow velocities and directions in the vessels and heart chambers, because blood cells represent moving scatterers: they produce a *Doppler effect*. When the blood moves towards the echo transducer (which is the source of ultrasounds), sound wave frequency, reflected by red cells, increases. Frequency variance (named *frequency shift*) of the ultrasound waves which encounter them depends on the transmitted frequency, on the blood velocity, and on direction of the flow, as it follows the equation (↔ Fig. 5.1):

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(5.1)



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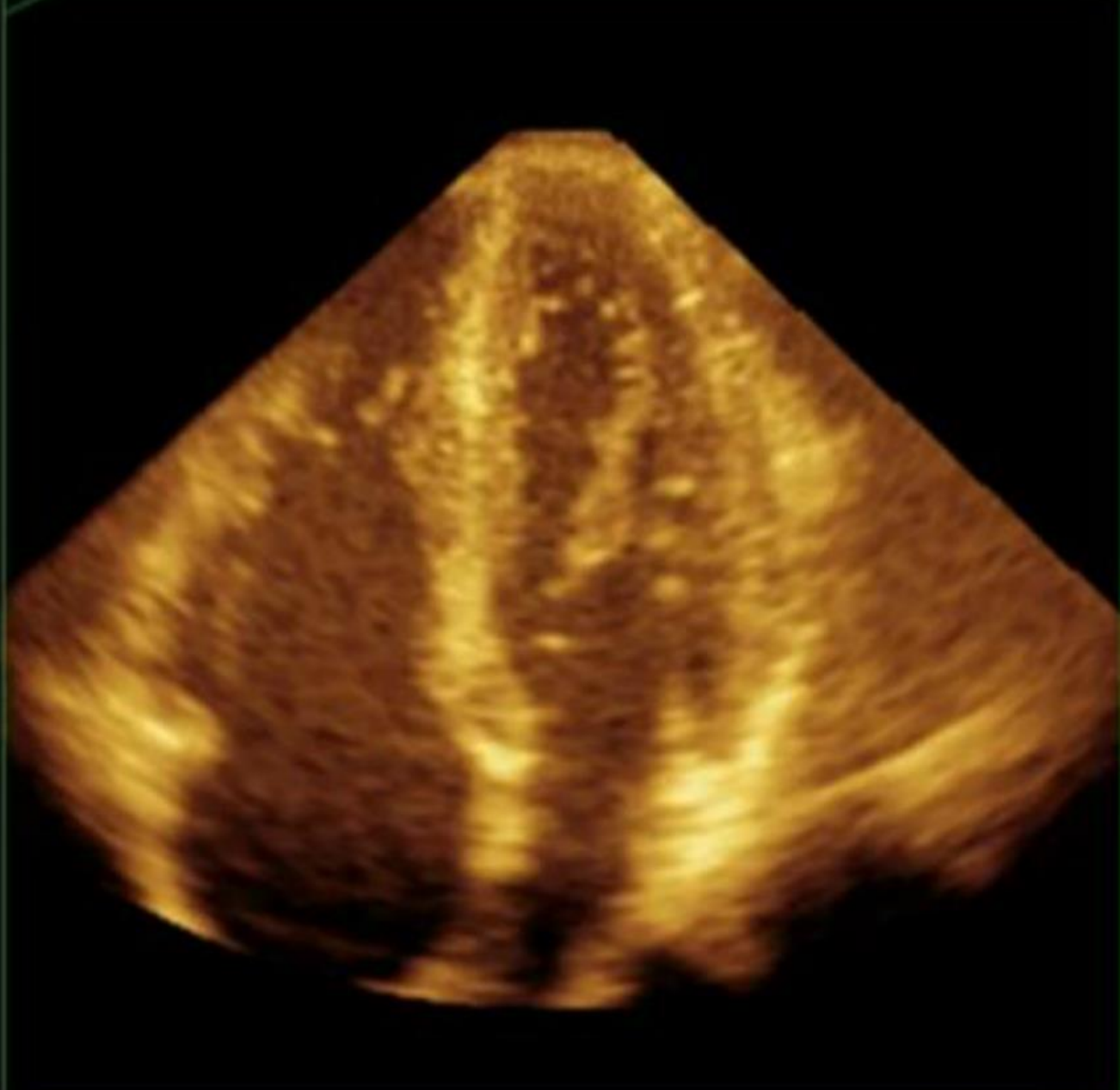
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