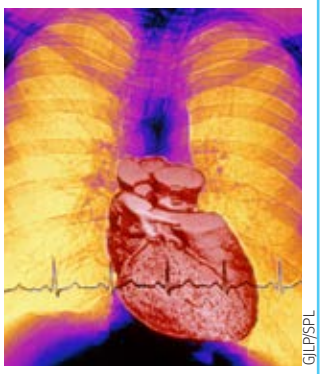
education

ART OF MEDICINE

"Troponin-negative chest pain"—a diagnostic evasion?


GJLP/SPL

Most patients who present with chest pain have acute coronary syndrome, but some have other diagnoses, such as pericarditis, aortic stenosis, and pulmonary embolism.

However, patients with such a presentation who have benign electrocardiograms and negative cardiac enzyme tests are often discharged with the diagnosis of "troponin-negative chest pain."

Why use this phrase? It acknowledges that an episode of chest pain occurred but that the pain was non-cardiac in origin, which is reassuring. But why should a diagnosis be negative? We eagerly, and rightly, focus on the heart and lungs in patients with chest pain given the suspicion of acute, life threatening disease. And when these have been ruled out, we eagerly reassure patients that "it is nothing serious" and discharge them. What answer can we give to patients who ask "But what caused the pain doctor?"

The practice of hospital medicine is centred on ruling out diagnostic uncertainty. How can we be content with a phrase so clearly steeped in it? Probably because it is a mask for "chest pain of unknown cause." Should we not seek an answer? A detailed history and examination can help identify other causes of chest pain such as gastrointestinal and musculoskeletal ones. Could there be a psychiatric component?

This phrase is not a medical diagnosis; it seems to be used as a way to evade identifying the underlying cause. Perhaps an explanation will not be elucidated, but we should not rest clinical judgement on such a phrase.

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We welcome contributions to this column via our online editorial office: https://mc.manuscriptcentral.com/bmj

CLINICAL UPDATES

Angioplasty and stenting for atherosclerosis causing refractory erectile dysfunction

New interventional procedure guidance from NICE recommends using angioplasty and stenting for refractory erectile dysfunction caused by atherosclerosis only in the research setting. Current evidence on safety and efficacy is deemed inadequate in quantity and quality. Further research with careful patient selection is advocated.

http://bit.ly/1SbUg2m

Chronic heart failure

Updated NICE quality standards on chronic heart failure in adults recommend a review within two weeks of any change in dose or type of drug prescribed. Heart failure drugs have many side effects, including hypotension, renal impairment, and dehydration, and they may worsen heart failure symptoms initially. The review should look at the efficacy and side effects of drugs. The multidisciplinary heart failure team will decide who should carry out the review.

http://bit.ly/1QGdmsc

"Minimed Paradigm Veo System" for type 1 diabetes

New NICE guidance on sensor augmented insulin pump therapies recommends the "Minimed Paradigm Veo System," which continually monitors and responds to interstitial glucose levels, as a step-up alternative for patients with type 1 diabetes receiving continuous subcutaneous insulin infusion and optimal capillary blood glucose monitoring who still have episodes of disabling hypoglycaemia. This recommendation is dependent on the manufacturer's commitment to carry out ongoing data collection, analysis, and publishing.

http://bit.ly/215Nw6C

FAST FACT—PALLIATIVE MEDICINE

Large terminal bleeds typically occur in head and neck cancers, lung tumours, and large vascular collections in varices, as well as into a viscus such as the bladder. Prescribing a pre-prepared "crisis pack in case of a catastrophic bleed" for immediate administration can bring control to the situation. The pack should include a large injectable benzodiazepine dose such as midazolam (subcutaneous), dressings for application to any external wound, and green or red blankets to camouflage the blood.

CPD/CME

You can gain CPD points from your reading by recording what you have read in your appraisal folder. You should try to link your reading back to a learning need and also consider how you plan to improve your practice as a result of your learning. http://learning.bmj.com

PRACTICE POINTER

Zika virus: management of infection and risk

Shazaad S Y Ahmad,[1 2] Tejal N Amin,[3] Andrew Ustianowski[1]

Zika virus has caused a self limiting pyrexial illness from Africa to South-East Asia for decades. Recently it has spread across the Pacific and in 2015 caused infections for the first time in South America. Though usually asymptomatic or of little clinical significance in adults, there is concern about an apparent association between infection in pregnancy and birth defects such as microcephaly.[1-3] We have no data to characterise the risks of abnormal fetal development and adverse pregnancy outcomes, or to guide testing strategies. In its absence, global health bodies have issued guidance for clinicians on how to minimise the risk of transmission to those who are, or may become, pregnant, and to monitor fetuses that may have been exposed.

We present current management advice for healthcare professionals in non-endemic countries, who may offer advice to individuals concerned about pregnancy and conception before or after travel to an area with Zika virus. Guidance is likely to change as the clinical picture and knowledge base develop, and up to date advice can be accessed from sources such as those listed in box 1 on thebmj.com.

An accompanying article[4] discusses the epidemiology and the evidence of what is currently known, including a possible association with Guillain-Barré syndrome.

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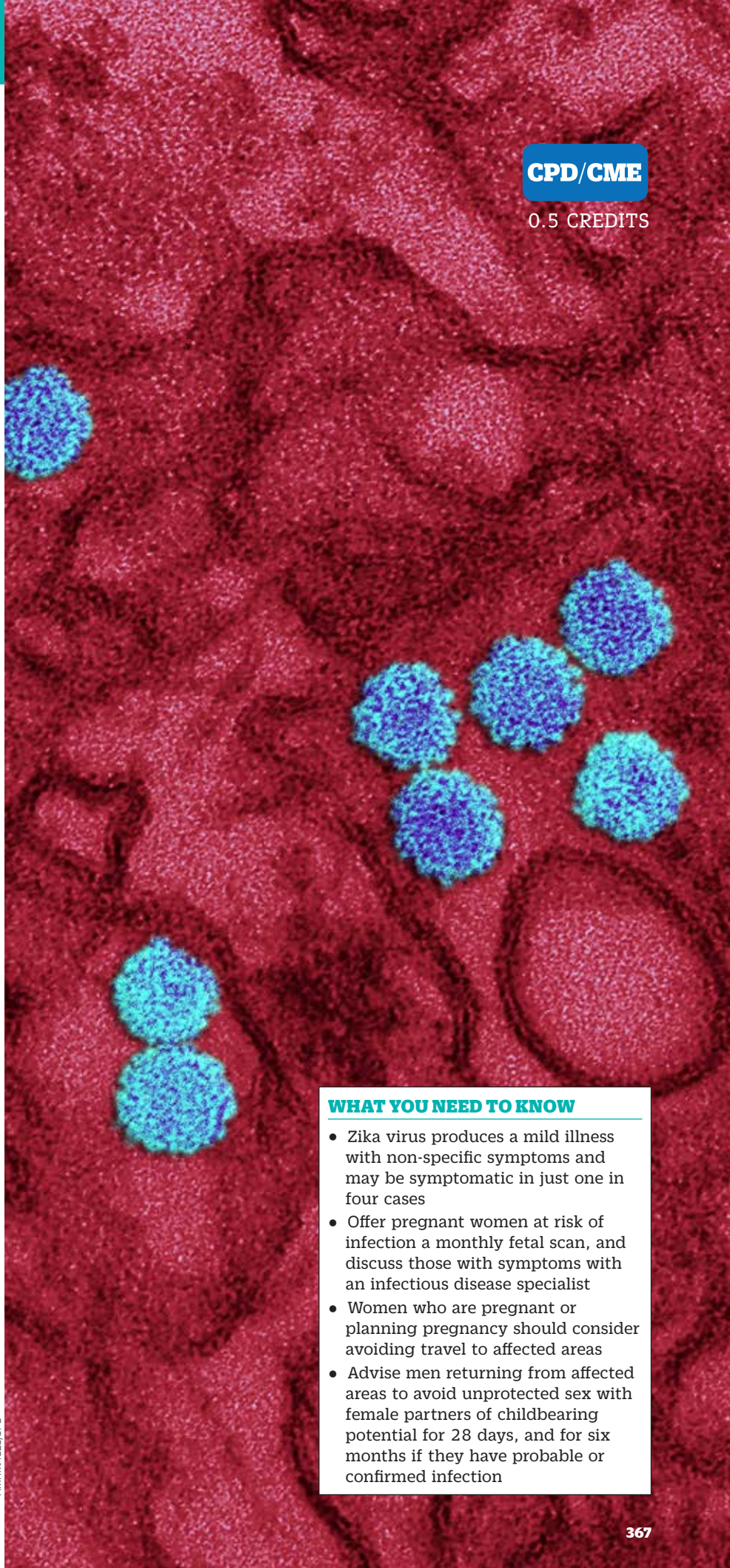

AMI IMAGES/SPL

CPD/CME
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WHAT YOU NEED TO KNOW

- Zika virus produces a mild illness with non-specific symptoms and may be symptomatic in just one in four cases
- Offer pregnant women at risk of infection a monthly fetal scan, and discuss those with symptoms with an infectious disease specialist
- Women who are pregnant or planning pregnancy should consider avoiding travel to affected areas
- Advise men returning from affected areas to avoid unprotected sex with female partners of childbearing potential for 28 days, and for six months if they have probable or confirmed infection

EXAMPLE SCENARIO 1

A 27 year old woman has just returned from Colombia. While she was there she felt mildly unwell. Yesterday she discovered that she was pregnant and is anxious about whether she had Zika virus. She has heard that it will damage her baby's brain.

Take a travel history from pregnant women concerned about, or at risk of, Zika virus infection, and from their male sexual partners. The infographi (see p 366) lists countries where Zika virus is currently present, such as Colombia. There is no evidence to suggest that Zika virus poses a specific problem for maternal health.

The risk of congenital abnormalities is poorly characterised

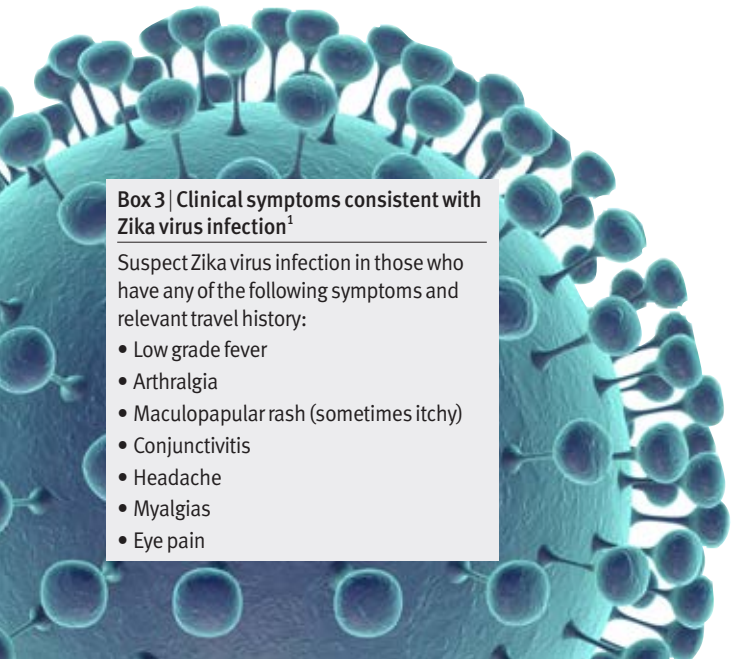
The risk of Zika virus infection to a developing fetus is not fully understood. The recent rise in such infections has coincided with an apparent increase in birth defects—predominantly microcephaly but also ventriculomegaly, cell migration abnormalities, congenital contractures, stillbirth, and neonatal death.[2 5] These abnormalities have largely been described in case reports and case series. A direct causal link has not been confirmed, but there is evidence of Zika virus infection in placentas of aborted fetuses and in the brains of babies with microcephaly who died soon after birth.[6 7] If causality is established, further data will be needed before we could tell a pregnant woman how likely it is that she would have an affected child.

Preliminary data from a small case series suggest that infection in the early stages of pregnancy may pose the greatest risk,[5] consistent with other viral infections such as rubella. No treatment is presently available to correct or alter the chances of adverse fetal outcomes.

Testing and monitoring of pregnant women is guided by symptoms

There is an absence of good evidence to guide testing and monitoring. However, expert guidance has been issued by international bodies.

The infographic (see p 366) shows UK guidance for pregnant women who have travelled to an area with known Zika virus transmission during the pregnancy.[1]



Box 3 | Clinical symptoms consistent with Zika virus infection[1]

Suspect Zika virus infection in those who have any of the following symptoms and relevant travel history:

- Low grade fever
- Arthralgia
- Maculopapular rash (sometimes itchy)
- Conjunctivitis
- Headache
- Myalgias
- Eye pain

In essence, all pregnant women who have travelled to an area affected by Zika virus should be offered a baseline fetal ultrasound scan and should be discussed with a secondary care obstetric team. If the ultrasound is normal, offer scans every four weeks throughout the pregnancy. Microcephaly and the other neurological abnormalities described may not become apparent on scans until after 20 weeks' gestation or into the third trimester. Logistically, testing and care may be led by obstetric teams or form part of joint care with midwives or primary care doctors.

Detection of any neurological abnormalities, such as a small head (more than two standard deviations below the mean for gestational age) or intracranial calcifications, warrants referral to a fetal medicine unit for further investigation. Here, alternative causes of microcephaly—such as other congenital infections, chromosomal abnormalities and undefined genetic syndromes, exposure to teratogenic substances, and maternal metabolic diseases—will also be considered.

Pregnant women who present with clinical symptoms compatible with Zika virus infection (see box 3) while in, or within two weeks of return from, a Zika virus affected area should be considered for testing for Zika virus infection and other travel associated diseases relevant to the country of travel. Those who are asymptomatic but have just returned should be advised to seek medical care if they develop any symptoms consistent with Zika virus within the next two weeks.

Interpreting tests for Zika virus is complicated

All patients undergoing testing for Zika virus infection should be discussed with infection specialists and the optimum testing strategy for this and any other infections agreed. The first line test and definitive diagnosis is made by identification of Zika virus RNA by means of PCR (polymerase chain reaction). Zika virus RNA may remain detectable in blood for the first five days of infection and probably for up to two weeks in urine.[8] Use the test in those with current or recent symptoms in liaison with the local virology laboratory. (In the UK this is generally serum and an EDTA blood sample, and also urine in sterile container if the patient is pregnant.)

If Zika virus RNA is detected, UK guidance suggests that the woman is offered direct referral to fetal medicine specialists. However, a negative PCR result cannot exclude infection (especially if the sample is sent several days after the onset of any symptoms), and follow-up with screening ultrasound scans at four-weekly intervals should be offered in this situation.

The United States uses a Zika virus IgM assay, and Australia is using IgM and IgG assays in an attempt to detect infections, including in those outside the testing window for viral RNA. The US Centers for Disease Control and Prevention advocates that all pregnant women returning from affected areas should be tested for Zika virus,[9] with PCR tests if symptomatic and serological tests if asymptomatic.

The sensitivity, specificity, and applications of such serological tests (IgG or IgM) are not established, however. They are not currently advocated in the UK, although storage of a serum sample for potential future testing (once assays have been established and validated) may be suggested.

Amniotic fluid, if sampled, may also be tested by PCR, but the utility of such testing is not firmly established at present.

EXAMPLE SCENARIO 2

A 28 year old man has returned from Brazil and has flu-like symptoms. He is worried that he has Zika virus. He is not sure he should go to work. He has also heard that it can be sexually transmitted and is worried about his partner.

Discuss all those with symptoms and relevant travel history with local infection specialists

It is estimated that four out of five people with Zika virus infection are asymptomatic, and in those who do develop symptoms these are often non-specific (box 3). It is therefore important that the case of a symptomatic individual, such as described above, is discussed with a local infection specialist to allow assessment for other potential infections such as malaria and dengue.

Zika infection is not a notifiable disease in the UK, but it is in other countries such as the US and Australia.

Zika is transmitted via a type of mosquito but possibly also by semen or blood products

There is no need to avoid work or other activities of daily living. Zika virus is transmitted from human to human via a vector, the *Aedes* mosquitoes. These mosquitoes are not present in the UK, northern Europe, Canada, northwestern United States, Russia, northeastern Asia, and southern Australia, but they are widespread throughout much of the rest of the world.

It is possible that Zika virus may pass from human to human via other routes. There is a theoretical risk of transmission via infected blood or blood products.[10] The virus has been identified in semen from two men infected with Zika virus,[11 12] and, to date, there have been two reported instances of sexual transmission by male travellers to their partners in non-endemic areas (only one of these cases is presently published[13]). It is not known how long after infection the virus is detectable, or potentially infectious, in semen. There is no evidence of sexual transmission from women to men.

UK and European guidance advises that men with suspected or confirmed infection should use condoms with their partners (if pregnant or at risk of pregnancy) for six months.[1 2] Abstaining would be another option. The US advises abstaining or using condoms for the duration of the pregnancy if the partner is pregnant, but does not specify a time period if they are not.[14]

For men who have been asymptomatic during travel in affected areas and for two weeks after return, UK and European guidance suggests that they consider using condoms for 28 days after their return if their partner is pregnant or at risk of pregnancy.[1 2] The US guidelines do not specify a time period for asymptomatic men. The current advice is that condoms should be used for vaginal, oral, and anal sex. This should be discussed with patients.

These time periods are poorly evidence based. The 28 day window has been suggested to allow a 14 day incubation period and a 14 day viraemic period, even in asymptomatic people. The six month window may change once longer term data on seminal carriage is established.

Patients planning to donate blood, tissue, or semen should declare recent travel to affected areas (and Zika virus test results where known) before donation.

EXAMPLE SCENARIO 3

A 32 year old woman is planning to travel on a work trip to Brazil. She is not pregnant but is contemplating starting a family soon. She asks how long risks may persist and wonders how to minimise the chance of infection.

Risk to future pregnancies is unknown

There are few data to support advice on the duration of risk after potential exposure, but guidance has been issued. There is consensus across UK,[1] European,[2] US,[3] and Australian[15] guidance that women of childbearing potential who are travelling to Zika affected areas should ensure they are using reliable contraception and should avoid conceiving. Women who are pregnant should be strongly advised to avoid such travel if possible.

On return from endemic areas, advice in the UK is to avoid becoming pregnant for a further 28 days.[1] It is thought, though with little evidence, that a fetus conceived after a woman has cleared the virus would not be at risk of birth defects, nor should there be any risks to future pregnancies.[3] There is no known site of longer term carriage (such as in semen) in women.

Box 4 | Mosquito bite avoidance

- Wear long-sleeved shirts and long trousers
- Stay in places that use window and door screens to keep mosquitoes outside or have closed windows and air conditioning
- Sleep under a mosquito bed-net
- Use mosquito repellents that contain 50% DEET (*N*,*N*-diethyl-*m*-toluamide) (deemed safe in pregnancy)
- Apply DEET *after* sunscreen
- Treat clothing with permethrin or purchase permethrin treated items. See product information to determine how long the protection will last
- Public Health England's "Mosquito bite avoidance for travellers" information sheet is available from www.gov.uk/government/publications/mosquito-bite-avoidance-for-travellers

Advise all travellers on how to avoid mosquito bites

If travel to an affected area is unavoidable, healthcare providers should fully inform the individual on avoidance of mosquito bites. Aedes mosquitoes bite from dawn through to dusk (only rarely at night), and 24 hour preventive measures should be encouraged. DEET based insect repellents should be used and applied frequently, and other measures should be pursued (see box 4).

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CLINICAL REVIEW

Zika virus

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This is an edited version of the clinical review review, full version is on thebmj.com

CPD/CME
1 CREDIT

HOW WERE PATIENTS INVOLVED IN THE CREATION OF THIS ARTICLE?

The BMJ did not ask the authors to involve patients in the creation of this article.

Zika virus is spreading rapidly in the Americas. The virus was first confirmed in Brazil in May 2015. It has since been identified in more than 27 countries and territories in the region.[1 2] Spread to the Americas was predicted because of the abundance of the mosquito vector, *Aedes aegypti*.[3-6] Clinicians worldwide need to be aware of Zika virus infection owing to international travel and the presence of another potentially competent mosquito vector (*Aedes albopictus*) in North America and southern Europe. Some Brazilian regions experiencing outbreaks of Zika infection have reported an apparent increase in congenital microcephaly and post-infective neurological syndromes, particularly Guillain-Barré syndrome (box 1 and box 2 (see thebmj.com)).[2] The association of these conditions with Zika virus infection is currently unproved and is under investigation. On 1 February 2016, the World Health Organization declared the recent cluster of microcephaly and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia in 2014, a public health emergency of international concern.[7] If Zika virus infection is confirmed to cause congenital microcephaly, tere could be a large international burden of infant neurological morbidity. Zika virus infection should be considered in people presenting with compatible symptoms who have recently returned from countries where outbreaks of the infection are occurring.

WHAT YOU NEED TO KNOW

- Zika virus, transmitted by mosquitoes, has spread rapidly recently in the Americas, and it is likely to spread further in the presence of Aedes mosquitoes
- Some Brazilian regions experiencing outbreaks of Zika virus infection have reported an apparent increase in congenital microcephaly. Some countries experiencing outbreaks have reported an increase in post-infective neurological syndromes, particularly Guillain-Barré syndrome. An association with Zika virus has yet to be confirmed
- The situation is changing rapidly, and up to date advice must be sought about travel to affected areas, particularly with regard to pregnancy and sexual transmission

What is Zika virus?

Zika virus is an arbovirus (arthropod borne virus). It is a member of the Flaviviridae family, genus *Flavivirus*, which includes dengue, yellow fever, and West Nile viruses. It was first identified in the Zika forest near Kampala, Uganda in rhesus macaques in 1947.[8]

Zika virus is a single stranded RNA virus with two major lineages: Asian and African.[4-10]

Few complete Zika virus genome sequences are available, and to date only two are from the current South American epidemic. Phylogenetic analysis of a Suriname Zika virus indicates that it belongs to the Asian genotype. A mutation in the Asian lineage may have led the virus to adapt to the human (as opposed to non-human primate) host.[16]

Zika virus replicates readily in skin immune cells, and a large number of receptors are able to mediate entry of the virus into cells.[18] Studies on the capability of the virus to replicate in neuronal cells are warranted to further investigate the link with neurological disorders.

Epidemiology

Between the first isolation of Zika virus in monkeys in 1947 and 2007, reports of human cases were rare and sporadic.[8-20] Evidence on the extent of human infection was based mainly on serological studies and, in some cases, isolation of the virus.[19-25] Viral isolation suggested a wide distribution in Africa and South East Asia, although no epidemics were observed.

In 2007 an outbreak caused by a strain of Asian lineage occurred on the island of Yap, an island state of the Federated States of Micronesia.[3 4]

A further outbreak occurred with a closely related Asian lineage strain in French Polynesia in 2013 in which 294 cases were confirmed by RNA detection over a 10 week period.[26 27] Locally acquired cases on Easter Island in 2014 marked the first arrival of Zika virus in the Americas.[28] This was followed in May 2015 by confirmation of cases in north east Brazil, where again the Zika virus sequence belonging to the Asian lineage was found.[14 29]

Zika virus is new in the Americas and there is no immunity within the population. Its rapid spread and large number of cases mirrors that of the recent arrival of the chikungunya virus in the Americas in 2013.

Brazilian authorities estimate that around 1.5 million cases of Zika virus infection have occurred since the outbreak began.[2] Colombia reported local transmission in October 2015, with now more than 25 000 suspected cases.

FELIPE DANA/AP/PA

How is the virus transmitted?

The key Zika virus vector is thought to be the daytime biting (indoors and outdoors), urban dwelling *Aedes aegypti* mosquito. Evidence to support this comes from detection of the virus in wild *Aedes aegypti* and by experimental transmission in rhesus monkeys.[30-32] Following laboratory feeding of *Aedes albopictus* mosquitoes with Zika virus infected blood, the virus has been demonstrated in mosquito saliva, suggesting these mosquitoes may also transmit the virus.[33 34]

Presumptive sexual transmission has been reported in two cases.[35 36] Isolation of virus in semen 17 days after a clinical diagnosis of acute infection supports potential sexual transmission, as does the detection of Zika virus RNA in semen 62 days after the onset of symptoms.[37 38]

Zika virus was detected in approximately 3% of asymptomatic blood donors during the French Polynesian outbreak,[39] suggesting that transmission might be possible through infected blood and blood products.

Evidence implies transplacental transmission and perinatal transmission during delivery, with Zika virus RNA being found in amniotic fluid[15] and in paired blood samples taken from newborn infants and mothers.[40]

There is currently no evidence to support transmission via contact with saliva, urine, or respiratory droplets.

How does Zika virus present?

Zika virus infections seem either to be subclinical or to cause a mild illness after an incubation period of three to 12 days. Symptoms, which last for approximately two to seven days include fever, conjunctivitis, arthralgia, myalgia, and widespread rash, which may be itchy. Headache, retro-orbital pain, peripheral oedema, and gastrointestinal disturbance have also been observed.[3-43]

The proportion of infected people who experience no symptoms is not known. Observation of Zika viraemia in 31 French Polynesian blood donors who reported no symptoms, during or after blood donation, suggests that asymptomatic infection does occur.[39]

Box 1 | Case reports of fetal Zika virus infection

- Zika virus detected by polymerase chain reaction (PCR) in amniotic fluid in two infants with microcephaly in north east Brazil[15]
- Serological evidence of past Zika virus infection identified in Hawaii in a baby with congenital microcephaly born to a mother who resided in Brazil during the pregnancy[57]
- In north east Brazil, Zika virus detected in brain tissue of two neonates with microcephaly who died within 20 hours of birth, and in the placental tissue of two early miscarriages. All four mothers reported illness compatible with Zika virus infection in the first trimester of pregnancy[58]
- Zika virus detected by PCR in fetal brain tissue of terminated pregnancy of microcephalic fetus in Slovenia. Mother had been in north east Brazil in the first trimester of pregnancy[59]

Shock and haemorrhage occur with other flaviviruses such as dengue, but they have not been documented in Zika virus infection. Severe acute illness seems to be rare. Fewer than 10 possible Zika related deaths have been reported in adults, and an additional three deaths from Guillain-Barré syndrome have occurred in individuals who had symptoms of Zika infection.[44 45]

Is there evidence for an association between infection and complications?

Current epidemiological data suggest spatial and temporal links with the Zika virus epidemic and congenital microcephaly. These are supported by case reports of detection of the virus from amniotic fluid or the brain tissue of affected fetuses. Robust epidemiological studies with clear definitions of microcephaly are under way to test whether any association with Zika virus infection can be confirmed.

Microcephaly usually results from abnormal brain development (see box 3). There is no internationally accepted definition of microcephaly. The Brazilian Ministry of Health is now using a definition of head circumference of less than 2 standard deviations (3 standard deviations for severe microcephaly) below the mean for sex and gestational age at birth.[46]

Diagnostic tests for Zika virus			
Sample	**Test**	**Timing**	**Reference**
Blood	Polymerase chain reaction	Typically <5 days (occasionally up to 8 days) from symptom onset	50
Saliva	Polymerase chain reaction	Typically <5 days (occasionally up to 8 days) from symptom onset	50
Urine	Polymerase chain reaction	Very limited data: single study (6 patients)—positive in 6/6 at 10 days from symptom onset, and 1/6 still positive at 30 days	51
Semen	Polymerase chain reaction	Very limited data: RNA has been detected at 62 days after symptom onset in one case	38
Serum	IgM antibody detection	Detectable 4-7 days from symptom onset and persists for 2-12 weeks	53

Box 3 | Causes of microcephaly

- Chromosomal and genetic abnormalities
- Craniosynostosis (premature fusion of cranial sutures)
- Fetal infection during pregnancy (eg, rubella, toxoplasmosis, cytomegalovirus, varicella, herpes simplex)
- Exposure to drugs, alcohol, and toxins (eg, cocaine, antiepileptic drugs, lead or mercury intoxication)
- Severe maternal malnutrition

Pregnant women infected with Zika in Colombia

SCHNEYDER MENDOZA/EPA/CORBIS

Box 4 | Provisional case definition of suspected acute Zika virus infection. Pan American Health Organization[49]

- Rash or increase in body temperature (>37.2°C), with any of the following not explained by other conditions:
- Arthralgia or myalgia
- Non-purulent conjunctivitis
- Conjunctival hyperaemia
- Headache
- Malaise

Over 85% of the cases of microcephaly from November 2015 have been reported from the state of Paraíba, north east Brazil. Reported cases of microcephaly increased from 5.7 per 100 000 live births in 2010 to 99.7 per 100 000 live births from November 2015 to January 2016.[47] It is not yet clear whether this is a true increase, an increase in severe cases, or an increase in ascertainment. Colombia, where Zika virus has been present since October 2015, has reported over 30 000 cases of Zika virus infections, more than 5000 of which were in pregnant women. As yet, there are no reports of associated cases of microcephaly.[48]

From November 2015 to 13 February 2016, 5280 suspected cases of microcephaly and/or central nervous system malformation, including 108 deaths, were reported by Brazil—1345 of these have been investigated further: 837 of the 1345 did not have microcephaly, 421 had radiological findings such as cerebral calcifications compatible with a congenital infection, and 41 had laboratory confirmed Zika virus infection.[2]

A retrospective review of birth data in French Polynesia showed 18 cases of central nervous malformations in children born between March 2014 and May 2015, including nine cases of microcephaly, compared with the previous national annual average of none to two cases.[2]

How is Zika virus infection diagnosed?

Clinical

The clinical picture of Zika virus infection is similar to that of other mosquito borne viruses such as dengue and chikungunya, which often co-circulate in the areas where Zika virus is endemic.

The Pan American Health Organization of WHO has issued a provisional case definition for suspected acute Zika virus infection, intended for use in countries with ongoing local transmission (see box 4).[49]

The differential diagnosis of Zika virus infection is wide (see infographic). Diagnosis is guided by history (countries of travel, sexual contacts, and contact with other cases of infection) and examination. The symptoms and clinical signs do not have sufficient positive or negative predictive value.

Laboratory testing

Definitive diagnosis is based on detection of Zika virus RNA in blood (serum or, ideally, EDTA treated plasma) and other body fluids by polymerase chain reaction (PCR) (table).

After the acute phase, diagnosis by antibody detection in serum samples is compromised by considerable cross reactivity with antibodies to other flaviviruses; false positive results can be seen with past dengue infection or previous yellow fever vaccination.[52]

How is Zika virus infection managed?

There is currently no vaccine against Zika virus, nor specific antiviral for the treatment of Zika virus. Treatment is symptomatic, although it is not known what agents are optimal for treating the fever, itch, and arthralgia. Minimisation of the chance of mosquito bites is advised by wearing long sleeves and trousers and using mosquito repellents.[54] Specific travel advice is dealt with in the accompanying article.[55 56]

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CASE REVIEW

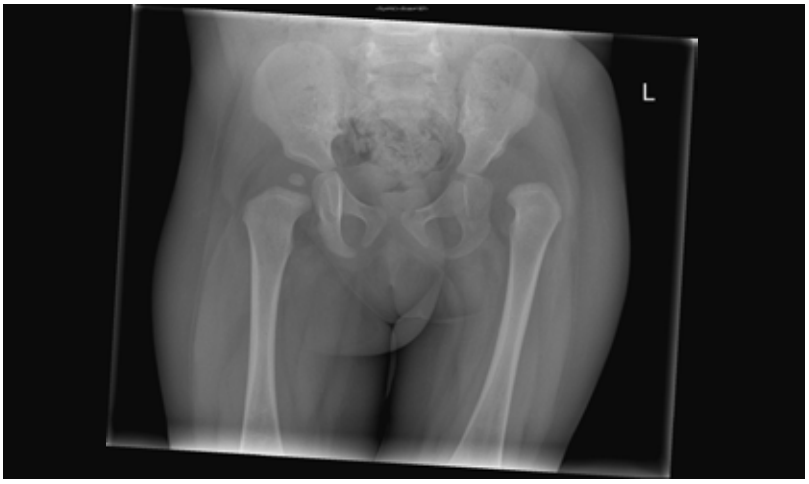
A limping child

A 15 month old girl was referred to the orthopaedics department by her general practitioner with an abnormal gait and a tendency to fall over more than her peers. There was no history of trauma or family history of note, and she was otherwise well.

She was born by uncomplicated spontaneous vaginal delivery at term and began walking independently aged 13 months. The midwife had commented to the mother during neonatal examination that the left hip was "a bit clicky," but this had not been investigated further.

On examination she walked, apparently pain free, with a left sided lurch. Her left leg was 2 cm shorter than her right leg. Hip instability tests were normal. The general range of motion in the left hip was good, but abduction was limited and the telescope test was positive. A plain radiograph of the pelvis was obtained (figure).

1 What is the diagnosis?
2 How can this condition be identified clinically?
3 How can it be assessed radiologically?
4 How is it usually managed?
5 Why has the name of this condition changed?



Submitted by David Lindsay and Sunil D'Souza

Parental consent obtained.

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SPOT DIAGNOSIS

Back pain after trauma

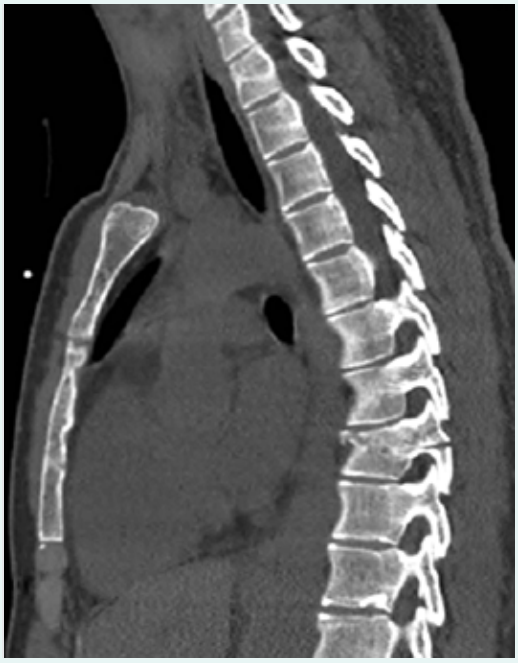


Fig 1

A 22 year old man presented because of back pain after a car crash. Physical examination identified tenderness over the mid aspect of the back. Non-contrast computed tomography of the dorsal spine was performed (fig 1). What does the scan show and what is the diagnosis?

Submitted by Layla A Nasr and Ali A Haydar

Patient consent obtained.

Cite this as: *BMJ* 2016;352:i825
Find this at: http://dx.doi.org/10.1136/bmj.i825

answers

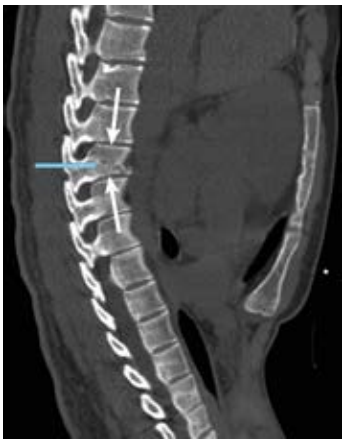
CASE REVIEW **A limping child**

1 Left sided developmental dysplasia of the hip.
2 Limited hip abduction in flexion, leg length discrepancy (above knee), Barlow's and Ortolani's tests (normal in this case because the dislocated hip has become irreducible), asymmetrical skin creases, abnormal gait, and history.
3 Ultrasound (age ≤6 months) or anteroposterior pelvic radiography (≥6 months).
4 Splinting for early presentations; late presentations may require surgery.
5 It is no longer called congenital dislocation of the hip because some cases are now known to develop after a normal neonatal examination.

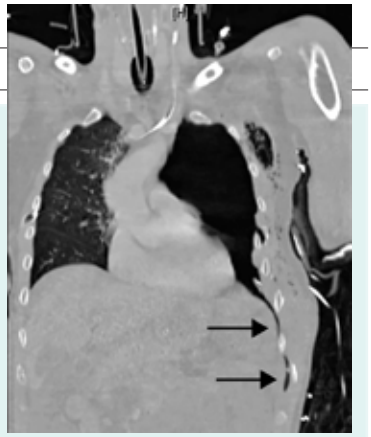
SPOT DIAGNOSIS **Back pain after trauma**

The sagittal computed tomogram on bone window shows a wedge shaped fracture of the anterior aspect of the T8 vertebral body (arrows) with the fracture line extending horizontally to affect both the transverse processes and the pars interarticularis (blue line; fig 2). There is associated minimal retropulsion. It is a flexion distraction (Chance) fracture of the T8 vertebra.

Fig 2



Deep sulcus sign in chest trauma



A polytrauma patient had a left sided chest drain to treat a pneumothorax. During computed tomography performed the next day he became acutely unwell. The scan shows a large left pneumothorax with mediastinal shift indicating tension and "deep sulcus" sign, a rare but specific finding of a pneumothorax in supine patients, more usually seen on supine chest radiographs. Air collects in the anterolateral pleural space and pushes the diaphragm inferiorly, forming the deep sulcus of pleural air (arrows). This resolved with manipulation of the chest drain. It is important to remember that chest drains do not entirely prevent tensioning of a pneumothorax.

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Patient consent obtained.

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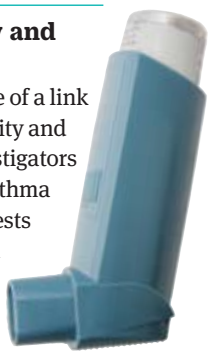
Female infertility and asthma



Intrigued by evidence of a link between female fertility and asthma, Danish investigators prospectively gave asthma questionnaires and tests for atopy and asthma to 245 women attending a clinic with unexplained subfertility (*Eur Resp J* doi:10.1183/13993003.01389-2015). Women with asthma had fewer successful pregnancies during fertility treatment (39.6% *v* 60.4%), and the median total time to pregnancy was 32.3 months in the 149 non-asthmatic women versus 55.6 months in the 96 with asthma.

Sibling caregivers

It's relatively uncommon for brothers or sisters to become caregivers, although demographic trends mean it may become commoner. Using data from the national survey of midlife development in the US, investigators compared the experiences of 61 sibling caregivers with 570 other family caregivers (*Gerontologist* doi:10.1093/geront/gnw008). Siblings were less affected by caregiving than parent or spouse caregivers, but of all ethnic groups, white (non-Hispanic) Americans experienced the greatest burden of depression and loss of life satisfaction.

Taking arms against Ebola

Chinese military staff recently fought alongside the British in Africa. The common enemy was Ebola virus and their weapons were field hospitals and medical supplies. The UK Ministry of Defence chose the mighty acronym GRITROCK for its operation to protect Ebola-facing clinical staff, despite which there were several exposures and one case (*J R Army Med Corps* doi:10.1136/jramc-2015-000516). The Chinese military medical team was the first ever deployed on a humanitarian mission. Its report does not mention its own casualties but gives a good account of its learning curve and its success rate of over 50% (*J R Army Med Corps* doi:10.1136/jramc-2015-000562).

Bowel cancer across the world

Incidence and mortality rates of colorectal cancer vary up to 10-fold worldwide, according to the GLOBOCAN database (*Gut* doi:10.1136/gutjnl-2015-310912). The highest incidence is still found in the richest countries, although it is now levelling or decreasing; meanwhile both incidence and mortality are rising rapidly in many low and middle income countries. Its burden is expected to increase by 60% by 2030—to more than 2.2 million new cases and 1.1 million deaths.

Obesity paradox after MI

The paradox of body mass index related survival after myocardial infarction (MI) continues. The Cooperative Cardiovascular Project provides data from 124 981 Medicare beneficiaries hospitalised with MI with 17 years of follow-up (*Am Heart J* doi:10.1016/j.ahj.2015.10.024). Overweight and obese patients showed a better rate of survival across the whole timespan than those classified as normal, and differences were more pronounced in younger patients.

Don't use our drug

Drug companies often use the dubious endpoints of progression-free survival and non-inferiority to sell products for cancer treatment. A recent trial supported by Janssen to test its own product, epoetin alfa (EPO), does the opposite (*J Clin Oncol* doi:10.1200/JCO.2015.63.5649). By ordinary statistical criteria, EPO was non-inferior to usual care (red blood cell (RBC) transfusion) for treating anaemia in women receiving chemotherapy for breast cancer (hazard ratio 1.09, 95% CI 0.99 to 1.20). But because investigators had tightened the non-inferiority criteria to a maximum upper bound of 1.15, they conclude that RBC transfusion should be the preferred approach for managing anaemia in this population.

Nitrates and survival in acute HF

Acute heart failure (HF) is the sort of emergency that makes doctors do everything they can, which is always dangerous for patients. In North America doctors often use nitrates as first line treatment to promote vasodilatation, but a propensity matched retrospective study of 11 078 admissions for acute HF in Canada shows no short or long term survival benefit from these drugs (*J Am Heart Assoc* doi:10.1161/JAHA.115.002531).

Soda cure for stones

Baking soda dissolves up to half of radiolucent renal tract stones, according to a case review from Colchester (*J Clin Urol* doi:10.1177/2051415816631856). But you have to take enough sodium bicarbonate to keep your urine alkaline, which at up to 10 g/day is quite a lot.

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