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## News

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### Interim guidelines for smallpox response and management published by the Department of Health

On 2 December 2002, the Department of Health in London published guidelines for responding to a deliberate release of smallpox in the United Kingdom (UK) (1, 2). The guidelines, which are for discussion over the next month, describe vaccination strategies prior to and in the event of an outbreak, procedures for diagnosis and management of the initial cases, and other essential outbreak preparedness and control measures.

The level of threat of a deliberate release is unknown but is likely to be extremely low. While smallpox remains eradicated, the risks from adverse effects of vaccination outweigh the risks from disease. Experience in the United States in the late 1960s found that among people aged over twenty years, who were being vaccinated for the first time, there were severe adverse vaccine related events at a rate of around 1500 per million people vaccinated, with about one death per million people vaccinated (3).

The number of people to be vaccinated will therefore be limited to a few hundred specialist healthcare workers who would be required to assess and manage any initial cases. In the event of a heightened threat, for example if smallpox re-emerges elsewhere in the world, a greater number of healthcare, emergency and other essential personnel will be offered vaccination in case they are required to respond to a smallpox emergency in the UK.

Rapid diagnosis and response to the first cases is essential to limit the size of any outbreak. To help familiarise clinicians with the symptoms and signs of smallpox a diagnostic algorithm is to be distributed. A network of teams of vaccinated workers including infectious disease (ID) physicians will be available to visit and assess cases of suspicious illness. If smallpox is suspected, these emergency diagnosis and response teams will be called out to initiate laboratory investigation and further management of the patient. Regional directors of public health in England have been given responsibility for establishing the networks of ID physicians and the emergency teams. Members will be identified and then vaccinated, and it is hoped that this can be completed by the end of January 2003.

In the event of an outbreak, a search and containment strategy will be deployed, with rapid isolation of cases, and tracing, vaccination and monitoring of contacts. To prepare for this all regions have been asked to identify smallpox care centres and smallpox vaccination centres that could be opened within 24 hours to provide isolation for cases and vaccination for contacts. Search and containment measures will focus on close contacts of smallpox patients, since they are most at risk from infection.

1. Department of Health. *Interim guidelines for smallpox response and management in the post-eradication era*. London:

Department of Health, 2002. Available at <http://www.doh.gov.uk/epcu/cbr/biol/smallpoxplan.htm>

2. *Health workers to be vaccinated against smallpox*. 10 Downing Street website [online] [cited 5 December 2002]. Available at <http://www.number-10.gov.uk/output/Page6741.asp>

3. Advisory Committee on Immunization Practices. *Vaccinia (smallpox) vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001*. Atlanta, US: Centers for Disease Control and Prevention, 2001. Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/tr5010a1.htm>

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## Preliminary update on WNV surveillance in England and Northern Ireland 2002

All surveillance samples from humans in England and Northern Ireland tested for West Nile virus (WNV) during 2002 have been negative. This suggests that human cases of WNV infection have not occurred. Surveillance for WNV infection will resume from the beginning of spring of 2003.

Following the emergence of WNV in New York, and its subsequent spread in the US, an article in *CDR Weekly* (1) alerted clinicians to consider WNV as a possible differential diagnosis for unexplained encephalitis, and requested that samples be sent to the Centre for Applied Microbiological Research (CAMR) for investigation. The passive surveillance in the summer of 2001 yielded few suspect cases. Enhanced surveillance was begun in September 2002, following unpublished reports by an experienced research group of WNV transmission in non-migratory indigenous bird species in the UK. It is important to note that evidence of avian WNV infection does not necessarily mean that human cases will occur. Other factors are important, such as climate conditions, virus type, and the possible immunity of birds to infection that may mean that viraemia would not be high enough to transmit the virus from mosquitoes to humans.

The expanded surveillance in 2002 had two arms – a retrospective study of encephalitis from April to September when no causative organism had been identified cases, and prospective surveillance of suspect cases from June to the end of September (see box for case definitions).

### Figure 1

Case definitions: [http://www.phls.org.uk/topics\\_az/west\\_nile/protocol\\_wnv\\_190902.pdf](http://www.phls.org.uk/topics_az/west_nile/protocol_wnv_190902.pdf)

#### 1. Encephalitis

- Fever above 38°C
- Altered mental state (altered level of consciousness, agitation, lethargy) and/or other evidence of cortical involvement (eg, focal neurological signs, seizures)
- CSF pleocytosis with predominant lymphocytes and/or elevated protein with negative Gram stain and culture
- No alternative microbiological cause identified

#### 2. Meningitis

- Fever above 38°C
- Headache, stiff neck and/or other meningeal signs
- CSF pleocytosis with predominant lymphocytes and/or elevated protein with negative Gram stain and culture
- No alternative microbiological cause identified

The Clinical Virology Network coordinated the retrospective study which yielded 123 cerebrospinal fluid (CSF) samples from patients aged 50 years or above who had been given a clinical diagnosis of encephalitis, but for whom no organism had been detected. These patients were from a range of health authorities across England and Wales.

The prospective study yielded samples from 14 patients. During the same period, the increased publicity and awareness among doctors resulted in the laboratory at CAMR receiving samples from another 13 patients with encephalitis, but with no recent travel history and for whom testing for WNV was requested. All samples were investigated for WNV as follows: CSF samples, detection of WNV RNA by RT-PCR and detection of anti-WNV IgG by immunofluorescence (IF); serum samples, IgG-IF, with RT-PCR if sample taken in the acute phase. Further test results will be available later following work with the Centers for Disease Control and Prevention.

WNV is a member of the Japanese encephalitis complex, in the genus *Flavivirus*. It is an arbovirus, transmitted by mosquitoes primarily *Culex* species. Birds are the principal hosts and some species are competent for transmission to mosquitoes because of the high level viraemia that occurs in these birds. Horses, humans, and some other mammals are also susceptible through being bitten by infected mosquitoes but are dead-end hosts *ie* they usually do not transmit on to others (2).

Although first isolated in Uganda in 1937, WNV was not recognised as a cause of human encephalitis until 1957. Since 1994, there have been numerous outbreaks of WNV infection around the world (3). Genetic analyses indicate the WNV has a number of sub-types. In 1999 a transmittable and virulent type emerged in the United States (US) (4) where previously it had been unknown. The virus has subsequently moved south and west across the US such that it is now found in birds, horses, mosquitoes, or humans in all but five states. Up to 26 November 2002, 3737 human cases with 214 deaths have been reported in the US. (<http://www.cdc.gov/od/oc/media/wncount.htm>). A small number of cases (six proven to date) have followed in blood transfusion (5,6), but the risk of this occurring in the UK is considered to be very low (7) (either from imported blood products or from locally donated blood from a returning traveller).

1. PHLS. West Nile virus: enhanced surveillance among cases of encephalitis and viral meningitis. *Commun Dis Rep CDR Wkly*, [serial online] 2001 [cited 3 December 2002]; **11** (30): news. Available at: <http://www.phls.org.uk/publications/cdr/archive/news/news3001.html#wnv>
2. Crook PD, Crowcroft NS, Brown DWG. West Nile virus and the threat to the UK. *Commun Dis Public Health*, 2002; **5** (2):138-43.
3. Murgue B, Zeller H, Deubel V. The ecology and epidemiology of West Nile virus in Africa, Europe and Asia. *Current Topics Microbiol Immunol*, 2002; **267**:195-221.
4. Outbreak of West Nile-like viral encephalitis, New York 1999. *MMWR Morbid Mortal Wkly Rep* 1999; **48** (38): 845-9.
5. Investigations of West Nile virus infections in recipients of blood transfusions. *MMWR* 28 October 2002; **51**:1-2 (CDC Dispatch). Available at: [http://www.cdc.gov/mmwr/preview/mmwrhtml/dispatch\\_westnile.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/dispatch_westnile.htm)
6. Biggerstaff BJ, Petersen LR. Estimated risk of WNV transmission through blood transfusion during an epidemic in Queens, New York City. *Transfusion* 2002; **42**:1019-26.
7. West Nile virus: spread to new regions, association with poliomyelitis-like syndrome, and transmission through organ donation and blood transfusion. *Eurosurveillance Weekly* 2002; **6** (39). Available at: <http://www.eurosurveillance.org/ew/2002/020926.asp>

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## **Salmonella Enteritidis outbreaks in England and Wales, September to November 2002**

The largest change in the epidemiology of *Salmonella enterica* serotype Enteritidis in England and Wales since the emergence of *S. Enteritidis* phage type (PT) 4 in the 1980s has occurred during the autumn of 2002 (1). Since the beginning of September 2002, 19 outbreaks of *S. Enteritidis* have been reported to the PHLS Communicable Disease Surveillance Centre (CDSC), compared with five during the same period in 2001. In these outbreaks almost 1000 people have been affected and there have been 10 deaths (all in people with underlying illnesses and including one late death). Three outbreaks, affecting over 400 people, are national and ongoing. These are outbreaks of *S. Enteritidis* PT 14b (345 cases), *S. Enteritidis* PT 56 (31 cases) and *S. Enteritidis* PT 6d (resistant to ampicillin [Amp<sup>r</sup>]) (35 cases).

The majority of outbreaks reported during the autumn of 2002 (15/19) are not attributable to *S. Enteritidis* PT4. The non-PT4 phage types causing clinical disease are confirmed by the PHLS Laboratory of Enteric Pathogens (LEP) as PT1 (resistant to nalidixic acid and with low level

susceptibility to ciprofloxacin [Nx, Cp<sub>L</sub>], PT3 (Nx, Cp<sub>L</sub>), PT6, PT6a (Nx, Cp<sub>L</sub>), PT 6d (Amp<sup>r</sup>), PT8, PT14b, PT 21 (Nx, Cp<sub>L</sub>), and PT 56.

Shell eggs have been implicated as a food vehicle in 11 of the 19 outbreaks so far. Investigations into the food vehicles for the remaining outbreaks are continuing. To date Public Health Laboratories (PHL) (Chelmsford PHL, London Food, Water & Environmental Laboratory, and Wessex Environmental Microbiology Services Laboratory) have tested 372 pooled samples of six whole eggs (2232 eggs in total) in outbreak-related public health investigations. Thirty out of 372 pools were positive (8%). So far, the LEP has confirmed *S. Enteritidis* PT 5c, PT 6, PT 6a (Nx, Cp<sub>L</sub>), PT6d (Amp<sup>r</sup>), PT13a, PT14b, and PT 58 from the positive pools. The stated country of origin for these positive eggs is Spain. Isolates from clinical cases in the outbreaks of *S. Enteritidis* PT 6a (Nx, Cp<sub>L</sub>), PT6d (Amp<sup>r</sup>), and PT14b are indistinguishable from egg isolates of those respective phage types on plasmid profile and pulsed field gel electrophoresis analysis (PFGE), indicating that the human infection almost certainly came from the eggs.

Twenty-two of the 372 pooled samples tested as part of ongoing investigations comprised UK origin eggs (*ie.*, stated to be of UK origin) including eggs bearing the Lion Quality mark. These were all negative for salmonella. The Food Standards Agency re-iterated advice on proper cooking of raw shell eggs on 15 October 2002 (2), especially for vulnerable groups and advised all importers and wholesalers on 29 October 2002 that eggs imported from Spain should be sent for heat treatment (3). Cases continue to be reported to the PHLS.

1. PHLS. *Salmonella* Enteritidis in England and Wales: increases in unusual phage types in 2002. *Commun Dis Rep CDR Wkly* [serial online] 2002 [cited 3 December 2002]; **12** (45): news. Available at: <http://www.phls.co.uk/publications/cdr/archive02/News/news4502.html#salm>
2. FSA. Salmonella outbreak leads Agency to issue hygiene alert. Food businesses advised to use properly cooked or pasteurised eggs. Available at: <http://www.food.gov.uk/news/pressreleases/salmonellaoutbreak>
3. FSA. Agency re-emphasises advice on use and handling of all eggs, and issues guidance on use of Spanish eggs. Available at: <http://www.food.gov.uk/news/pressreleases/reemphasiseegadvice>

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## Linezolid resistance in MRSA: first case in Europe

Linezolid is an oxazolidinone antibiotic used to treat serious infection with methicillin resistant *Staphylococcus aureus* (MRSA), glycopeptide resistant *Staphylococcus aureus* (GISA) and vancomycin resistant enterococci (VRE). Mutations causing resistance have been associated with the central loop of domain V of 23S RNA. There has been one report in the United States of resistance in MRSA causing clinical infection (1). A second case has now been reported from a London hospital (2). A 52 year old man developed an empyema due to MRSA following a thoracotomy. He was treated with linezolid for three weeks as part of a clinical trial. Three weeks after the course was completed a mixed population of MRSA was isolated from the empyema fluid. Some strains remained sensitive, some were intermediate, and some were resistant to linezolid (minimum inhibitory concentration 32 mg/L). All were phage type E-MRSA 15 and of similar pulse field gel electrophoresis (PFGE) type. Increasing resistance was associated with G2576T mutations in increasing numbers of alleles. The patient was later cured using teicoplanin. Resistance to linezolid should be monitored in prolonged courses of treatment with this antibiotic.

1. Tsiodras S, Gold H S, Sakoulas, G Eliopoulos, G M, Wennersten, C, Venkataraman, L, *et al.* Linezolid resistance in a clinical isolate of *Staphylococcus aureus*, *Lancet*, 2001; **358**, 207-8.
2. Wilson A P R, Andrews J A, Charlesworth R, Walesby R, Singer M, Farrell D J, *et al.* Linezolid resistance in clinical isolates of *Staphylococcus aureus*. *J Antimicrob Chem* 2002 (in press, <http://jac.oupjournals.org> from 12/12/02).

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## Respiratory

Last updated: 5 December 2002  
Next update due: 3 January 2003

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Laboratory reports of respiratory infections made to CDSC from PHLS and NHS laboratories in England and Wales

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### Laboratory reports of respiratory infections made to CDSC from PHLS and NHS laboratories in England and Wales

Data are recorded by week of report, but include only specimens taken since 1 October 2002 (*ie*, recent specimens)

**Table 1 Reports of influenza infection made to CDSC, by week of report, weeks 45-48/02**

Week	45/02	46/02	47/02	48/02	Total
Week ending	10/11/02	17/11/02	24/11/02	01/12/02	
<b>Influenza A</b>	2	–	3	1	<b>6</b>
Isolation	–	–	–	–	–
DIF	–	–	1	–	<b>1</b>
Four-fold rise in paired sera	–	–	1	–	<b>1</b>
PCR	–	–	–	–	–
Other	2	–	2	–	<b>4</b>
<b>Influenza B</b>	–	–	2	–	<b>2</b>
Isolation	–	–	–	–	–
DIF	–	–	–	–	–
Four-fold rise in paired sera	–	–	1	–	<b>1</b>
PCR	–	–	–	–	–
Other	–	–	1	–	<b>1</b>
<b>Influenza (untyped)</b>	–	–	–	–	–
Isolation	–	–	–	–	–
DIF	–	–	–	–	–
Four-fold rise in paired sera	–	–	–	–	–
PCR	–	–	–	–	–
Other	–	–	–	–	–

DIF = Direct Immunofluorescence.

'Other' = 'Antibody detection - Single high titre' or 'method not specified'

**Table 2 Respiratory viral detections by any method (culture, direct immunofluorescence, PCR, four-fold rise in paired sera, single high serology titre), by week of report, weeks 45-48/0**

Week	45	46	47	48	Total
Week ending	10/11/02	17/11/02	24/11/02	01/12/02	
Adenovirus*	11	11	7	7	36
Coronavirus	–	–	–	–	–
Parainfluenza **	11	7	5	8	31
Rhinovirus	4	2	3	4	13
Respiratory syncytial virus (RSV)	122	129	204	361	816

\*Respiratory samples only. Excludes diagnoses made by electron microscopy (EM)

\*\*includes parainfluenza types 1, 2, 3, 4 and untyped

Laboratory reports of respiratory syncytial virus (RSV) made to CDSC have increased in recent weeks (Table 2), signifying the start of the period of RSV activity that occurs each winter in the United Kingdom (UK) figure1. In any given year epidemics usually start in November or December, and continue until late February. RSV is best known to cause bronchiolitis in children, although can infect people of all ages. Table 3 shows that 94% of the reports received in the last four-week period related to specimens taken from children aged less than five years of age. Communicable Disease Surveillance Centre (CDSC) receives approximately 9000 laboratory reports each winter, most of which are diagnosed by direct immunofluorescence of viral antigen.

**Table 3 Respiratory viral detections by age group, weeks 45-48/02**

Age group (years)	<1 year	1-4 years	5-14 years	15-44 years	45-64 years	65+ years	Unknown	Total
Adenovirus*	5	9	1	11	8	1	1	36
Coronavirus	–	–	–	–	–	–	–	–
Influenza A	–	–	–	3	2	1	–	6
Influenza B	–	–	–	1	1	–	–	2
Parainfluenza**	18	4	–	4	2	2	1	31
Rhinovirus	8	2	–	3	–	–	–	13
Respiratory syncytial virus (RSV)	657	112	5	4	3	7	28	816

\*Respiratory samples only. Excludes diagnoses made by electron microscopy (EM)

\*\*includes parainfluenza types 1, 2, 3, 4 and untyped

**Table 4 Laboratory reports of infections associated with atypical pneumonia by week of report, weeks 45-48/02**

Week	45/02	46/02	47/02	48/02	Total
Week ending	10/11/02	17/11/02	24/11/02	01/12/02	
Coxiella burnettii	–	1	–	1	2
respiratory Chlamydia sp.*	2	3	1	4	10
Mycoplasma pneumoniae	18	18	14	32	82
Legionella sp.	14	9	6	4	33

\*includes Chlamydia psittaci, Chlamydia pneumoniae and Chlamydia sp detected from blood, serum and respiratory specimens

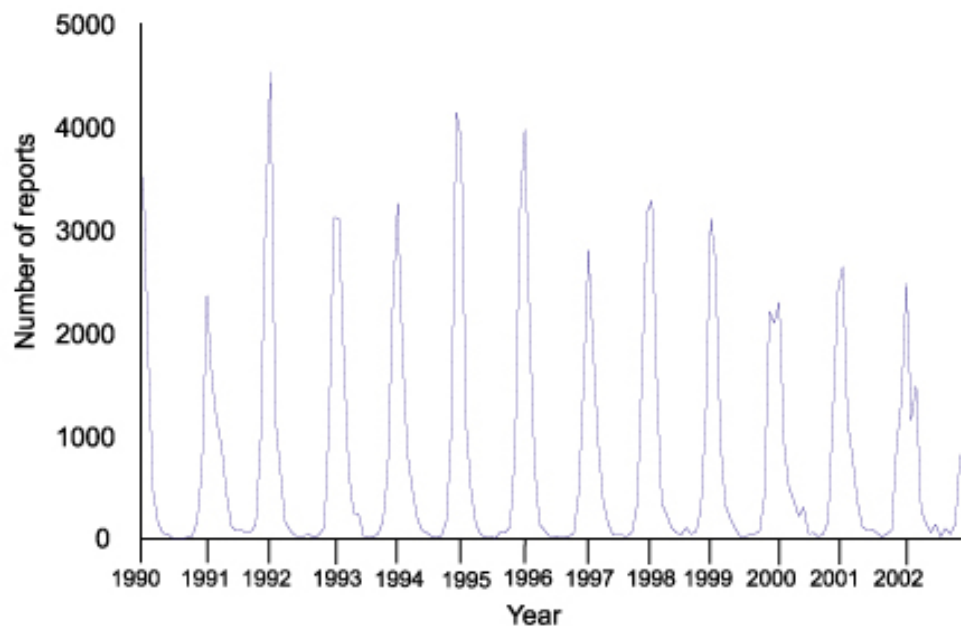
**Table 5 Reports of legionnaires' disease (pneumonic and non-pneumonic\*) cases in England and Wales, by week of report, weeks 45-48/02**

Week	45/02	46/02	47/02	48/02	Total
Week ending	10/11/02	17/11/02	24/11/02	01/12/02	
Nosocomial	–	–	–	1	1
Community	4	2	3	1	10
Travel abroad	9	6	3	1	19
Travel UK	1	1	–	1	3
<b>Total</b>	14	9	6	4	<b>33</b>
Male	12	7	4	3	26
Female	2	2	2	1	7

\* non-pneumonic cases in brackets

Thirty-three cases were reported with pneumonia. Twenty-six were males aged between aged 31 and 88 years and seven females aged between 37 and 78 years. Two male cases died, aged 64 and 77 years. Twenty-two cases were associated with travel: Spain (5), England (3), France (2), Italy (2), Croatia (1), Dominican Republic (1), Greece (1), Mexico (1), Thailand (1), and the United States (US) (1). Four cases travelled to more than one country: Austria, Belgium, France, and Germany (1), Turkey and Greece (1), Bermuda and US (1), and one case travelled to Majorca and went on a cruise. One case is associated with an outbreak in Belgium. Ten cases, nine males aged between 31 and 81 years and F 40y had community acquired infection. One was associated with a community outbreak in Cumbria. M 77y had a nosocomially acquired infection.

**Figure 1 Laboratory reports to CDSC of infections due to respiratory syncytial virus, England and Wales, by date of report 1990-2003 ( 4 weekly average)**



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## Travel health

Last updated: 5 December 2002  
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### Malaria – The Wider Picture

This article about malaria for health professionals who are advising travellers from the United Kingdom (UK), takes a broad view of malaria in the world and the most important current issues in malaria control and the research base for improving it. Previous articles (1,2,3) were focused on potential advice for preventing malaria in travellers. This one provides background, and hopefully answers, to some of the questions posed by travellers who take a wider view of the malarious countries they may be visiting.

#### Background

Interest in malaria has been cyclical, the disastrous effects of malaria upon individuals, households and communities have been continuous over much of recorded history, and so far as the tropics are concerned, malaria has been placed in a class of its own, viewed with equal comparable importance to all the other classical tropical diseases put together. The first great wave of scientific interest in malaria was a century ago, around the time that transmission of malaria was shown to be attributable to anopheline mosquitoes. It was followed by over 40 years of control aimed at preventing mosquito breeding, avoidance of being bitten, and treatment with quinine. By the end of the second world war both synthetic anti-malarials and residual insecticides were in use and opened up a new phase of interest in malaria control. Residual insecticides (DDT was the original one) are sprayed onto house walls and may remain toxic to any mosquito landing on the wall for up to six months. The dramatic effect on malaria transmission was due particularly to the way the insecticide selectively prevented mosquitoes surviving into the relative 'old age' needed to transmit malaria.

This led to the second period of global interest in malaria, when great efforts were made in the 1960s to eradicate malaria from the world completely, using residual insecticides. This was achieved in Europe, Australia, and America north of Mexico as well as in various small islands and limited areas, while in much of Asia the incidence of infection fell dramatically, so that malaria was rare, but still present in the population. Once the attempts at eradication ceased due to lack of funds among other constraints, malaria became resurgent in Asia in the 1970s. Africa remained the most malarious part of the world, with little impact being made on malaria in tropical sub-Saharan Africa, where it remained the predominant cause of childhood mortality. So although malaria was far being conquered, interest in it waned, and the World Health Organization (WHO), which had led the attack on malaria, turned its attention to primary health care and virtually ignored malaria, which spread rapidly so that cases in Asia, but not deaths, were soon back at the very high levels seen before.

From the end of the 1990s, after a 'gap of despair' lasting almost 20 years, concern for malaria became apparent at all levels, beginning from an awakened interest in research leading to a perception of how immense the global problem was. WHO re-established its leadership in 1992 with the ministerial conference on malaria which, for the first time, put the treatment of sick people as the first principle of control, following it with selective use of preventive measures, prevention and control of malaria epidemics, and having national research and operational capacity able to keep the optimal strategy for each place under review. There was no mention of eradication – once bitten twice shy – and a much less dogmatic and clearcut approach than in the 1960s.

This current concern for malaria differs from the eradication era in that it is more driven by an appreciation of need than by the opportunity given by new methods for control. That need has led, together with advances in basic science, to great progress in attempts to improve methods for

controlling malaria.

The problem of malaria today is more intractable than 50 years ago. First, and of overwhelming importance, is the spread of drug resistance. First to pyrimethamine and then to chloroquine, and subsequently to each new drug that is introduced. Resistance to antifolate drugs (pyrimethamine, proguanil, used on their own) occurs rapidly – after less than two years of widespread use in a population occurs sometimes – while resistance to chloroquine spread remarkably slowly, considering the huge amounts in use. It was first observed at the end of the 1950s but did not reach Africa till about 20 years later.

It is now very widespread in most places with high falciparum malaria transmission. The only other comparably inexpensive drug is a fixed preparation mixture of sulphadoxine and pyrimethamine (SP or Fansidar), to which resistance has occurred in south east Asia, and to which it is rapidly developing in Africa. In Kenya and Tanzania the drug has become of limited value for treatment in a few years. The patchy but widespread resistance to these drugs and the partial cross-resistance among the medicines that attack the folic acid metabolic pathway and explains why proguanil and chloroquine can no longer be recommended as good chemoprophylaxis for those visiting Africa.

### **Malaria treatment**

What is to be done then for treatment of malaria in Africa where around 1 million children die of malaria every year? WHO has been moving rapidly to the view that anti-malarial medicines should be given in combinations, and that one member of the pair should be an artemisinin derivative (one of the drugs derived from the Chinese qinghao plant, *Artemisia annua*). The logic of this is that the artemisines are the most effective drugs to rapidly bring down the parasite numbers in the blood, while the other drug given with it should prevent any artemisin-resistant strains emerging as well as helping to get rid of any remaining parasites after the very short-acting artemisinin has been excreted. One combination drug of this type, co-artemether (Riamet or Coartem) with a fixed combination of artemether and lumefantrine is now licensed for sale in the UK and can be considered for standby treatment.

In endemic countries the push is towards combination treatments and getting these to household level, where much of the child mortality is occurring. There are new drugs on the way, but far less than are likely to be needed. Tafenoquine has chemoprophylactic potential for travellers and is very long acting, but is still under development. Of greater interest to resource poor countries is a new treatment combination of lapudrine and dapsone, Lapdap, which has been deliberately developed as a very low cost drug combination. It has been successful in trials, but a combination of Lapdap and artemisin is now being further explored to fit the trend towards combination therapy.

### **What about a malaria vaccine?**

There will not be a malaria vaccine for a few years yet – as people have been saying for decades! The situation, however, has changed in recent years because:

- (i) the genome of *P. falciparum* has now been sequenced
- (ii) the methods of genetic engineering can be used to produce key sequences of parasite proteins without the need for massive cultures of parasites
- (iii) it is also possible to use parasite DNA as a vaccine
- (iv) it is possible to induce cellular as well as antibody responses to the parasite antigens
- (v) there is now a range of different candidate vaccines being produced by researchers

In other words, the scope and pace of generating possible vaccines has greatly increased. Hope is much greater, but a usable vaccine is still awaited.

Of particular recent interest have been the vaccine made of several polypeptides from *P. falciparum* by Dr Pattaroyo, which after some promising early results failed to protect the Africans to a useful extent, and a more recent candidate vaccine, RTSS, that achieved up to 60% protection against malaria in The Gambia albeit only transiently. A novel candidate vaccine currently in trials uses parasite DNA to prime the immune system to produce anti-malarial specific T-cells of the immune memory system. A subsequent boost using malaria antigen in a recombinant virus has led to a large cellular immune response, but only the field trials will show whether effective protection of people in a malarious area takes place. The diverse approaches being explored, combined with evidence of partial success from several, makes one hopeful that a useful vaccine may be achieved within a decade.

## Preventing mosquito bites

The use of insecticide-treated mosquito nets (ITMN), has been the main advance in transmission control since the 80s. The most important African malaria vector, anopheline mosquitoes, tend to bite indoors at night so the person sleeping under the net acts as a bait to lure the mosquitoes towards the insecticide net surface (they fly towards various fatty acids and carbon dioxide given off by people). ITMN have been dramatically successful in trials, where they have achieved as much as a 30% fall in all-cause infant mortality, as well as halving the number of clinical attacks of malaria in children living in highly malarious places. The very many practical problems, from net production on a commercial scale to changing people's behaviour, have taken years to solve but national programmes are now getting under way in several countries.

Resistance to the pyrethroid insecticides used on nets has begun to emerge in west and east Africa either as a consequence of systematic ITMN use in communities or use of pyrethroids in agriculture, but is so far not a major problem for malaria prevention (but resistant nuisance insects, such as bed-bugs are re-emerging as a problem and have tended to deter indigenous people from using their ITMN). Research on alternative safe insecticides for net treatment is under way. The use of ITMN by travellers, as well as the inhabitants of malarious areas, will significantly reduce the risk of contracting malaria, as well as facilitating a good night's sleep, especially for backpackers, and act as an important complement to chemoprophylaxis.

## Changing the mosquitoes

A research dream for many years has been to try to make anopheline vectors resistant to malaria parasites, so breaking the transmission cycle. This is a formidable task as not only do we need to genetically engineer a change in the vector that will make it resistant, but also there needs to be a way to spread that genetic change through the vast natural populations of mosquitoes. Some microparasites of the genus *Wolbachia*, however, have spread through global populations of fruitflies in recent years, so this could prove to be less intractable than; appears at first sight.

It was recently announced that the genome of an *Anopheles* mosquito had been sequenced. Consequently there is now a much firmer basic science base for seeking suitable genetic loci that could be altered to make the mosquitoes resistant to malaria. Since no *Culex* mosquitoes (the commonest nuisance biters) can transmit human malaria, there must be a genetic basis for susceptibility to malaria infection in mosquitoes. Experimental approaches include attempting to develop anophelines that produce antibodies to kill malaria parasites that are taken up in the blood meal, or alternatively trying to prevent the later stages invading the mosquito salivary glands, a necessary step if the malaria parasites are to be inoculated into a person bitten by the mosquito.

## Paying for the global fight against malaria

Renewing the attempt to control malaria worldwide does not come cheaply. To get medicines to all those who are ill with malaria is a daunting task, and the medicines needed against parasites resistant to chloroquine and sulphadoxine/pyrimethamine cost over ten times more than chloroquine. The populations most affected, in Africa, are not only very poor but also their mosquito vectors are very efficient, so that there may be over a hundred-fold more transmission than is needed to enable the parasites to infect everyone.

African countries in the 1990s made a great effort to give priority to malaria. A global initiative from WHO called "*Roll Back Malaria*" then followed, and recently the richer countries, including the UK, set up a Global Fund to transfer substantial resources, from the UK among other donors, for the control of malaria, HIV, and tuberculosis. Research funds have also been greatly increased, not only by the world's major research councils and such charities as the Wellcome Trust, but also by the Gates Foundation. As a result, malaria research is moving at a rapid pace. Transforming the results into operational control programmes is proving more difficult and slower, and needs sustained rather than transient funding, but at least malaria is now getting some of the worldwide attention it deserves. As the risk to travellers depends on local transmission rates in the countries visited, these global efforts should reduce the hazards that travellers are exposed to. The risk in poor, highly-endemic areas, such as Africa south of the Sahara will, however, remain high, with drug resistance an increasing problem, so that bite avoidance and chemoprophylaxis remain essential for the traveller.

1. PHLS. Malaria prevention in travellers, particularly to Africa. *Commun Dis Report CDR Weekly* [serial online] 2002 [cited 3 December 2002]; **12** (40): travel. Available at:

<http://www.phls.org.uk/publications/cdr/archive02/travelarchive02.html#malaria>

2. PHLS. Deaths from malaria in travellers. *Commun Dis Report CDR Weekly* [serial online] 2002 [cited 3 December 2002]; **12** (18): travel. Available at:

<http://www.phls.org.uk/publications/cdr/archive02/travelarchive02.html#deaths>

3. PHLS. Who is at risk of imported malaria?

*Commun Dis Report CDR Weekly* [serial online] 2002 [cited 3 December 2002]; **12** (6): travel. Available at:

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## Zoonoses

Last updated: 5 December 2002  
Next update due: 3 January 2003

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### Common animal associated infections, England and Wales: laboratory reports, weeks 45-48/02

Organism	Total reports for weeks 45- 48		Cumulative totals for weeks 01- 48	
	2002*	2001	2002*	2001
<i>Borrelia burgdorferi</i> *#	10	7	183	259
<i>Leptospira hardjo</i> **##	–	–	3	3
<i>Leptospira icterohaemorrhagiae</i> **##	3	3	9	12
<i>Leptospira other</i> **##	4	3	18	10
<i>Pasteurella haemolytica</i>	2	2	4	6
<i>Pasteurella multocida</i>	18	16	183	258
<i>Pasteurella pneumotropica</i>	–	3	4	7
<i>Pasteurella</i> spp	6	7	52	67
<i>Toxocara canis</i>	–	–	3	–
<i>Toxocara cati</i>	–	–	–	–
<i>Toxocara</i> spp	–	–	–	1
<i>Toxoplasma gondii</i>	3	4	27	30
<i>Toxoplasma</i> spp	4	7	48	53

\* provisional data; \*\* by specimen date; # Lyme Disease Reference Laboratory and CDSC;  
## Leptospira Reference Laboratory and CDSC.

**Common imported infections, England and Wales: laboratory reports, weeks 45 - 48/02**

Organism	Cumulative total reports for weeks 45 - 48		Cumulative totals for weeks 01 - 48	
Arbovirus	-	-	-	-
Dengue virus	-	1	12	1
<i>Ascaris</i> spp	2	16	92	117
Hookworms (unspecified)	3	7	122	54
<i>Leptospira</i> spp	2	-	5	13
<i>Ancylostoma duodenale</i>	-	-	-	-
<i>Necator americanus</i>	-	-	-	-
<i>Hymenolepis diminuta</i>	-	-	-	1
<i>Hymenolepis nana</i>	1	3	21	43
<i>Hymenolepis</i> spp	-	-	-	-
<i>Schistosoma haematobium</i>	1	3	37	50
<i>Schistosoma intercalatum</i>	-	-	-	-
<i>Schistosoma mansoni</i>	-	2	17	18
<i>Schistosoma</i> spp	3	5	20	35
<i>Strongyloides stercoralis</i>	-	2	12	27
<i>Strongyloides</i> spp	-	-	3	2

\* Provisional data