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An analysis of imported infections over a 5-year period at a teaching hospital in the United Kingdom

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KEYWORDS Malaria; Overseas travel; Hospital admission	Summary Background. Imported infections are an important cause of morbidity and mortality in the United Kingdom. <i>Methods</i> . A 5-year analysis of cases seen in a large teaching and district general hospital in the Eastern Region of the UK was performed using ward records correlated with Hospital coding data and Hospital Episode Statistics from the Department of Health. <i>Results</i> . A surprising number (301) and diversity of imported infections was diagnosed. Prophylactic measures were, where assessable, generally inadequate. <i>Conclusions</i> . These data warrant renewed efforts to educate travellers of the risks of infection acquired abroad. The continued rise in global travel along with emergence of new infectious diseases emphasises further the need for expanded infectious diseases services incorporating accessible travel advice services in the UK which are currently
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Introduction

The number of people travelling overseas from the United Kingdom (UK) is estimated to be increasing at a rate of around 8% a year. In 2002 there were over 59 million visits abroad.¹ This fact coupled with increasing immigration, has led to a steady rise in the incidence of imported infections that includes diseases rarely seen in the UK, some of which are life-threatening. Furthermore, these infections may have public health implications for the UK due to the risk of ongoing transmission to other people.

The recent Severe Acute Respiratory Syndrome (SARS) epidemic has highlighted the need for close monitoring of emerging infections and vigilance

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over all imported infections.^{2,3} Moreover, the speed of international travel enhances the threat of diseases such as SARS in the UK.

The most frequently encountered, potentially fatal imported infection into the UK is malaria, with 1081 cases notified to public health in 2001.⁴ Due to under reporting this is believed to be an underestimate with the actual number of cases more likely closer to 2000 annually. Most predictions suggest that this statistic is also set to rise further. Like many other imported infections it can be a diagnostic challenge. Cases of malaria often present as a 'fever in a returning traveller', which is a heterogeneous group of diseases. Clinical assessment of imported infections has been recently reviewed by Spira.⁵ Hospitals close to ports and major airports are traditionally accepted as seeing a disproportionate caseload of infections in returning travellers. We were interested in the caseload

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seen in a typical large UK hospital away from a major entry route since our impression was that the number of cases of imported infection seen in Cambridge is substantial. A five-year 'look-back' was therefore carried out.

Materials and methods

The analysis includes all imported infections seen on the infectious diseases ward as recorded in the ward data book, at Addenbrooke's hospital in Cambridge, UK over a 5-year period 1998-2002. The records were checked against hospital case coding and the Hospital Episode Statistics data validation information from the Department of Health. All three gave a very similar data set. Cambridge is a University town in the Eastern Region with a population of around 120,000. The population catchment area of Addenbrooke's hospital is approximately 500,000, shared partly by two smaller district hospitals. There is a nearby international airport but with no transatlantic or longhaul flights. The ward is a 12-bedded dedicated infectious diseases unit in a large (1000 + bed)teaching hospital, which acts as a local district general hospital but is also the regional infectious diseases referral centre. Only cases directly seen, investigated and treated by the infectious diseases team were included. Outpatient cases seen in clinics only were excluded. Those infections which were self-limiting presenting to other physicians were not covered. Also excluded was an analysis of sexually transmitted infections acquired abroad seen only by the sexually transmitted disease service. All cases of malaria were diagnosed initially by blood films, though non-falciparum cases additionally had an HRP-2 antigen test to further rule out *falciparum* infection in the advent of a dual infection being overlooked.

Results

A summary of imported infections seen between 1998 and 2002 on the infectious diseases ward at Addenbrooke's hospital is shown (Table 1). Cases are shown both as specific diagnoses, when a causative organism is determined, and grouped as symptom complexes (gastroenteritis, fever, rash etc.) or by haematological indices such as eosinophilia, where no specific pathogen was identified but the clinical picture was of an imported infectious disease.

Discussion

The data indicate clearly that imported infections are an important cause of disease seen at this teaching hospital in the UK despite being relatively distant from large international airports or coastal ports. Given the relatively small population catchment it seems likely the diversity and number of diseases seen may have been bolstered by the large academic contingent associated with the large university population amongst whom are many postgraduate students from abroad.

The number of imported infections necessitating hospital admission is surprisingly high, yet it is likely that this is 'the tip of an iceberg' with many cases treated by general practitioners or non-specialist hospital physicians in this and other local hospitals and some not seeking medical attention. In addition cases of sexually transmitted infection acquired abroad including some early presentations of HIV infection such as seroconversion illness are missing from this survey. The cases documented here represent a diverse group of diseases, a reflection in part of the wide geographical distribution over which people now travel. There is an increasing trend in the number of cases seen per annum as borne out by national statistics.

Malaria remains the most frequent imported infection throughout the study with 85 cases over 5 years, 28% of the total. When investigated as cases of fever in the returning traveller, this percentage rises further (Fig. 1). The strong concordance between local and reference laboratories supports well the current diagnostic approach. Overall the increasing numbers of cases accorded a diagnosis, is an impressive reflection of the diagnostic services.

All admissions to the infectious diseases ward are placed in negative pressure ventilated rooms that are regularly assessed to ensure that a secure flow is maintained. This is especially important for the rising numbers of suspected cases of tuberculosis often associated with the human immunodeficiency virus (HIV) infection. Two cases of multi-drug resistant tuberculosis (MDRTB) were admitted over this period, one an imported infection in a refugee. These infections pose a particular threat to public health and require considerable resources to manage. The newer definition of suspected MDRTB for all cases of tuberculosis acquired outside the UK, means numbers and need for isolation beds is certain to rise. The introduction of molecular techniques for the early detection of rifampicin resistance is a useful and cost effective advance.⁶

Amongst the group of HIV diagnoses: one presented with a rash, fever and lymphadenopathy

Diagnosis	1998	1999	2000	2001	2002	Total
Malaria—Plasmodium falciparum	16	6	15	11	8	56
Malaria–P. vivax	2	3	3	4	1	13
Malaria—P. ovale	1	1			1	3
Malaria—P. malariae				1		1
Malaria-species unidentified	4	2	1	1	4	12
Fever-no diagnosis	13	17	16	8	14	68
Tuberculosis	3		7	5	2	17
HIV/AIDS	1	1	6	10	5	23
Legionella pneumonia			1			1
Gastroenteritis	2	2	4	7	9	24
Liver abscess			1	1	1	3
Acute Hepatitis A	1	1			2	4
Acute Hepatitis B		1				1
Dengue fever		1	2	3	1	7
Typhoid					2	2
Hydatid disease	1			1		2
Amoebic dysentery				1		1
Giardiasis				1		1
Schistosomiasis-asymptomatic	1	2	7	3	1	14
Cutaneous larva migrans	1	1	3	5	1	11
Filariasis	2					2
Strongyloidiaisis				1		1
Tapeworm—Taenia solium					1	1
Eosinophilia—unknown aetiology				1	2	3
Cysticercosis			1	1		2
Toxoplasmosis			1			1
Lyme disease			1		1	2
Viral meningoencephalitis				1		1
Tick typhus	2		1			3
Tick bite		2	2	2		6
Miasis—Tunga penetrans					2	2
Cutaneous leishmaniasis	1	1	2			4
Rash			4	1	4	9
Total	51	41	78	69	62	301

 Table 1
 Imported infections seen on the infectious diseases ward at Addenbrooke's hospital in Cambridge, UK between 1998 and 2002.

and was diagnosed with an HIV seroconversion illness and there were five children who acquired HIV through vertical transmission.

Gastroenteritis as a category is certainly underrecorded since many cases are managed by general physicians in separate rooms in the general medical wards of the hospital. Ideally all of these infectious diarrhoea cases should receive the same infection control measures as on the specialist unit. The two cases of typhoid both had full screening of family members as directed by the public health physicians with no evidence of carriage.

A detailed geographical history as part of the clinical assessment is vital since 90% of all cases of *falciparum* malaria were in travellers to Africa and all seven cases of dengue fever originated in Asia reflecting the higher endemicity of these infections in these tropical regions. The two cases of Lyme disease were acquired in North America and Western Europe, respectively, with the former presenting as

a carditis and the latter as localised cutaneous involvement of erythema chronica migrans and arthralgia, reflecting the differing pathogenesis of *Borrelia burgdorferi sensu stricto* causing carditis, compared to strains more frequently found in Europe, *B. garinii* and *B. afzelii*, which cause late neurological sequelae.

A small group presented as asymptomatic cases of schistosomiasis, part of a nationwide rise mainly from Lake Malawi, as reported elsewhere,⁷ and unusually a patient-led epidemic. In most of these



Figure 1 Distribution by diagnosis of fever in the returning traveller.

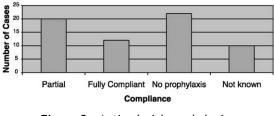


Figure 2 Antimalarial prophylaxis.

cases the diagnosis was made on antibody-based tests.

Three of the cases of malaria were second presentations of the same disease at a later admission possibly due to repeat exposure, poor compliance with medication or drug resistance and in two cases dual infection occurred. Prophylaxis is recommended for travellers to malarious regions as set out by The Hospital for Tropical Diseases guidelines.⁸ It is noteworthy that only 22% of cases admitted received a full course of prophylaxis whilst 41% did not receive any prophylaxis (Fig. 2). Similar data are reported from Communicable Disease Control in the USA on a study of 4685 cases of imported malaria in which 56% took no chemoprophylaxis.⁹ In our series there was one death in a 95-year old who had visited Kenya in the month preceding admission without taking prophylaxis then contracted Plasmodium falciparum malaria complicated by the development of pneumonia.

In conclusion, this local analysis illustrates the surprising number and diversity of imported infections seen at a hospital away from major ports of entry despite which it largely mirrors the national situation. Diagnosis and management of these conditions are optimised by having a specialist unit with experience. Individual physicians in nonspecialist units are unlikely to see these conditions frequently to become familiar with their management. Prevention is a key component of future efforts to contain these infections along with better diagnostics and enhanced surveillance. Hence, there is a requirement for expertise and the need for all large centres to have clinical infectious diseases staff. The UK is underprovided compared with most countries especially the USA but also closer comparators like Australia. The lack of prophylactic measures against malaria is very worrying. This suggests inadequate availability of advice or lack of knowledge by general practitioners and physicians or a lack of advice seeking by the general public. Over the past decade there have been 100 deaths from malaria in the UK, hence this is the most important area to target preventative efforts.⁴ This merits a Department of Health driven education effort. The first steps have been taken with the formation of The National Travel Health Network and Centre, which is a government, funded initiative launched in 2003 in response to this need.¹⁰

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References

- Office for National Statistics. MQ6 Transport and Tourism, Overseas travel and tourism, Quarter 4, 2002. London: HMSO; 2003. [Available at http://www.statistics.gov.uk/ downloads/theme_transport/MQ6_Q4_2002.pdf].
- Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med 2003; 348(20):1986–1994.
- Lipsitch M, Cohen T, Cooper B, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science* 2003; **300** (5627): 1966–1970.
- Public health laboratory service. http://www.phls.co.uk/ topics_az/malaria/menu.htm
- Spira AM. Assessment of travellers who return home ill. Lancet 2003;361(9367):1459–1469.
- Drobniewski FA, Watterson SA, Wilson SM, Harris GS. A clinical, microbiological and economic analysis of a national service for the rapid molecular diagnosis of tuberculosis and rifampicin resistance in Mycobacterium tuberculosis. J Med Microbiol 2000;49(3):271–278.
- 7. Day JH, Grant AD, Doherty JF, Chiodini PL, Wright SG. Schistosomiasis in travellers returning from sub-Saharan Africa. *BMJ* 1996;**313**(7052):268–269.
- Hospital for tropical diseases. http://www.uclh.org/ services/htd/index.shtml
- Communicable Disease Control. http://www.cdc.gov/ travel
- 10. The National Travel Health Network and Centre (NaTHNaC). http://www.nathnac.org/