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Human African trypanosomiasis in travellers to Kenya

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In this issue, two cases are described of human African trypanosomiasis (HAT) due to *Trypanosoma brucei rhodesiense*. They occurred recently in European tourists returning from Masai Mara area, Kenya, to Germany and Belgium, respectively [1,2]. These are, to our knowledge, the first two HAT cases described in travellers to Kenya in the last 12 years, while several cases were reported mainly from Tanzania (Serengeti and Tarangire game parks), Zambia, Zimbabwe and Malawi [3]. HAT, also known as sleeping sickness, is caused by a flagellated trypanosome protozoan, which is transmitted by *Glossina* (tsetse) flies. *T. b. gambiense* – found in western and central Africa – is transmitted mainly by *G. palpalis*, which prefers areas of vegetation near rivers and cultivated fields; *T. b. rhodesiense* – found in eastern and southern Africa – is transmitted predominantly by *G. morsitans*, which feeds on wild animals in savannah areas, far from human settlements [4]. While humans are the only substantial reservoir of *T. b. gambiense*, *T. b. rhodesiense* HAT is a zoonosis and humans occasionally visiting affected areas (usually for hunting or tourism) are accidental hosts. *T. b. gambiense* HAT is usually characterised by a chronic course of illness, lasting months to years, whereas *T. b. rhodesiense* HAT causes a more acute and aggressive course, clinically resembling acute septicaemia or severe falciparum malaria, with death occurring within days, weeks or months of the untreated disease. HAT of both forms is characterised by two distinct phases: the early or haemo-lymphatic stage and the late or meningo-encephalitic stage, with trypanosome invasion of the central nervous system of patients surviving the early stage [5].

Although *T. b. gambiense* accounts for more than 90% of all reported cases of HAT worldwide, *T. b. rhodesiense* has been the cause of most imported cases [6]. From 2000 to 2010, there were reports of 94 HAT cases diagnosed in non- endemic countries, of which 72% were due to *T. b. rhodesiense*: of them, 82% were diagnosed at the first stage. For comparison, among 26 cases of *T. b. gambiense* HAT cases, 77% were diagnosed at the second stage [3]. The diagnosis of HAT requires demonstration of the parasite in peripheral blood, lymph node aspirate or cerebrospinal fluid. Cerebrospinal fluid examination is mandatory for the disease staging, even in the absence of neurological signs, particularly because the treatment of the two stages is different [7]: for *T. b. rhodesiense* HAT, suramin is the drug of choice in the first stage and melarsoprol (both are highly toxic drugs) in the second, while for *T. b. gambiense*, pentamidine is used in the first stage, a combination of nifurtimox and eflornithine in the second [8]. Serology is commercially available for *T. b. gambiense* only and PCR has not yet come into routine use.

The occurrence of two imported cases of *T. b. rhodesiense* HAT, who were returning from the Masai Mara area, in south-west Kenya, is not really surprising, considering that several cases were reported in the last decade from the Serengeti Park in north-west Tanzania. Although located in two different countries, the two parks constitute a single geographical entity, artificially divided by the Kenyan–Tanzanian border. Up until now, transmission of the parasite occurred sporadically in the southern part (Serengeti) and seems to have now extended northward, probably following migration of infected game. The whole area should therefore be considered at potential risk. In 2001, the almost simultaneous occurrence of HAT in two Italian patients returning from Tarangire and Serengeti national parks was promptly reported to ProMED and to the European Network for Tropical Medicine and Travel Health (TropNet), allowing the detection of a cluster of several cases occurring in a short space of time in tourists who had been in the same locations [9]. The importance of networks in Europe, such as the European Travel Medicine Network (EuroTravNet) and TropNet, to detect rare diseases and to disseminate the relevant information, cannot be overemphasised. Besides offering advice on travel and prevention measures, such networks are also crucial for the local public health system in endemic countries, where tourism in the parks represents a fundamental income. For example, in 2001, after the alert was issued, surveillance of domestic cattle in the Serengeti and Tarangire areas was conducted by the chief veterinary officer in order to ascertain if they might have played a role in transmission of the parasite to humans [9].

Awareness of HAT is an essential prerequisite to prompt diagnosis and disease management, thus avoiding the potentially fatal complications of the disease [3]. For every patient coming from Sub-Saharian Africa, HAT, although rare, must be included in the differential diagnosis of any febrile patient returning from areas at potential risk. Patients often recall tsetse bites but this is not always the case as for example in the recent German case. Urech et al., in a review of the published cases [5], reported the presence of fever in the vast majority of cases of HAT due to *T. b. rhodesiense* (98%) and *T. b. gambiense* (93%). A trypanosomal chancre, which consists of a tender, purplish, indurated area that develops at the site of the tsetse fly bite [7], is a very important clue, occurring more frequently in *T. b. rhodesiense* disease (84% versus 47% in T.b. gambiense HAT). While its presence is virtually pathognomonic, its absence should not exclude the disease. Gastrointestinal and hepatic symptoms such as nausea, vomiting or jaundice are not rare in travellers infected with T.b. rhodesiense HAT and could mislead the physician to a gastrointestinal infection [5]. In HAT patients, cardiac involvement with typical ECG alterations, as seen in the German case, is frequent. HAT cardiomyopathy generally subsides with treatment [10].

Even in the absence of any accompanying symptoms, a fever in a patient coming from Sub-Saharan Africa should prompt all clinicians to exclude malaria. If a thick blood smear is used for this, *T. b. rhodesiense* infection should not be missed, if present, as the sensitivity of a thick smear is high in the acute phase of the disease [3]. However, in 11% of travellers infected with *T. b. rhodesiense*, trypanosomes could not be detected in the first blood smear and repeated blood examinations were necessary [5]. An excessive reliance on malaria rapid diagnostic tests – which are increasingly suggested as a useful diagnostic tool, especially outside specialised, referral centres – might lead to *T. b. rhodesiense* HAT cases being missed, as well as other conditions such as relapsing fever caused by *Borrelia*. In the German case the reason why HAT was not diagnosed on presentation could be that malaria thin smear only was initially performed at the local hospital, which is a frequent practice in non-specialised centers, without doing the more sensitive thick smear. Whatever the reason, we argue that all travellers (including people who are long-term residents abroad and migrants) should have access to specialised (clinical and diagnostic) management if presenting with fever or other relevant symptoms This is even more important for the gambiense form of the disease, for which diagnosis is often more problematic. Moreover, while *T. b. rhodesiense* HAT cases have generally been tourists who have relatively easy access to appropriate healthcare, *T. b. gambiense* HAT outside endemic countries is typically observed in people who have been long-term residents overseas for missionary or work-related reasons or in migrants or refugees from endemic countries, including undocumented migrants who may have limited access to healthcare in the host country [3]. Clinical networks such as TropNet, with its vast experience from its 62 centres spread over Europe, can also offer advice and support for diagnosis and management of HAT.

As far as treatment is concerned, distribution of HAT drugs is the exclusive responsibility of the World Health Organization (WHO), as, except for pentamidine, they cannot be obtained on the market. To treat patients with imported HAT, hospital pharmacy services have to request drugs from WHO and provide patient data. The drugs are then received from WHO within 24 and 48 hours. However, to enable prompt start of treatment – which is particularly important for the acute rhodesiense disease – a few hospitals have requested and have been given anti-trypanosomal drugs and thus are repositories of these drugs [3]. Ideally, at least one such repository should be present in every European country, in order to avoid unnecessary delay in drug procurement, which can also arise due to custom procedures [11]. For some patients with first-stage *T. b. rhodesiense* HAT, treatment was initiated with the more readily available pentamidine, switching to suramin upon availability [7, 12].

As no vaccination is available, travellers to HAT-endemic areas should be alerted of this important albeit low risk and take general protective precautions [12]. The tsetse fly is active during daytime and is particularly attracted by motion and blue and black surfaces [13]. The patient reported in Germany used insect repellents, but wore shorts and short-sleeved shirts, while for the Belgian patient, this information is lacking [1,2]. Bites can be prevented by wearing wrist- and ankle-length clothing of thick material and avoiding dark-coloured clothing [6]. The fly is able to bite through thinly woven fabric: therefore the impregnation of clothing with permethrin is recommended, along with the application of a skin repellent [14].

These measures should be particularly kept in mind now that transmission has recently occurred, and more cases might be expected. Moreover, all referral centres for imported tropical diseases should stay alert and any new case should be promptly reported to the concerned networks, as this would concur to a better knowledge of the local situation. The authors of the German paper report that the local authorities in Kenya have been duly informed and that a WHO team of experts has been sent to the area, therefore we hope to receive further information in the coming weeks.

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Trypanosoma brucei rhodesiense infection in a German traveller returning from the Masai Mara area, Kenya, January 2012

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In January 2012, a case of Human African Trypanosomiasis (HAT) has been identified in Germany in a traveller returning from the Masai Mara area in Kenya. The 62-year-old man had travelled to the Masai Mara game park from 18 to 19 January 2012 and developed fever on 28 January. The infection with *Trypanosoma brucei rhodesiense* was confirmed by laboratory testing three days hereafter.

Case report

On 28 January 2012, a 62-year-old man was hospitalised after a sudden onset of fever with temperature up to 39°C in a local hospital near Frankfurt, Germany. The fever started after his return from a holiday trip to Kenya from 8 to 28 January. Upon arrival in Germany and admittance to a local hospital, the patient was suspected to have malaria and treatment with Atovaquon / Proguanil was administered for two consecutive days. The diagnosis was made on the basis of a thin smear, which was later re-evaluated after the patient's transfer to the Infectious Diseases Department of Frankfurt University Hospital and no Plasmodium parasites were detected.

He had travelled by airplane directly from Frankfurt to Mombasa and back and spent all the time at a beach resort south of Mombasa except for a trip to the Masai Mara area from 18 to 19 January. For this trip, he flew from Mombasa to the Ol Kiombo airstrip, stayed at a camp in the area, and then went on safari excursions within a radius of approximately 50 km from the camp. He wore shorts and short sleeved shirts most of the time and used insect repellents.

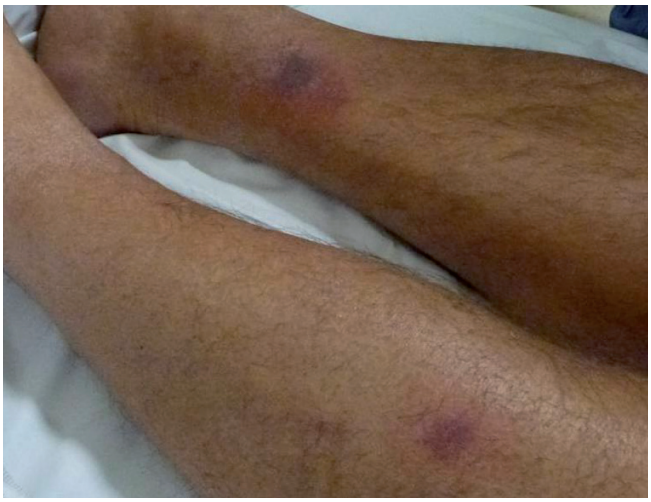
Despite anti-malarial treatment, the patient was still febrile on 31 January and was transferred to the Infectious Diseases Department of Frankfurt University Hospital. By then, the clinical symptoms had become more severe, with strong frontal headaches, vertigo, nausea and arthralgia. Fever was still high at 39.1°C. He had two distinct, painless skin lesions over both tibiae (Figure 1), but no localised or disseminated lymph node enlargement.

Malaria parasites were not confirmed in Quantitative Buffy Coat, Giemsa-stained thin or thick blood smears and the malaria antigen test (BinaxNow) was negative. However, *Trypanosoma brucei rhodesiense* was detected in thick blood smears stained with Giemsa (Figure 2) on 1 February.

Treatment was started three hours after diagnosis of trypanosomiasis with 1 g of suramin as a continuous infusion over one hour. As the substance was not readily available, it was brought to Frankfurt University Hospital from the "Missionsärztliche Klinik" Würzburg, Germany, where a regular stock of suramin is kept. In parallel, the patient was given prednisolone to prevent

Figure 1

Chancres due to infection with *Trypanosoma brucei rhodesiense* in a German traveller returning from the Masai Mara area, Kenya, January 2012



allergic reactions. The treatment was followed on day 1, 3, 7, 14 and 21 without complications.

A lumbar puncture performed on day 2 of therapy revealed a normal cerebrospinal fluid (CSF) pattern and a PCR with *Trypanosoma spp*. specific primers was negative from CSF as opposed to the peripheral blood, where it was found to be positive. The patient had leuko- and thrombopenia, an elevated complement regulatory protein (CRP) and aspartate and alanine transaminase levels two times the upper limit of normal. Electrocardiogram and echocardiography did not show any pathological findings.

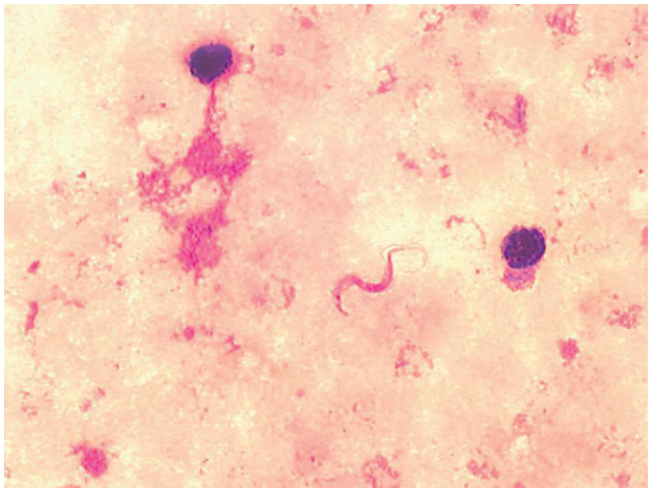
The fever subsided on day 2 of treatment and no parasites were detected from day 3 of the treatment onwards. *T. b. rhodesiense* antibodies were detected by immunofluorescence testing performed at the reference laboratory (Bernhard Nocht Institute, Hamburg, Germany) on day 8 of treatment, 12 days after the first symptoms whilst having been negative on day 1 of treatment. The patient concluded his treatment as planned on day 21 without any residual problems and left the hospital.

Discussion

Following the detection of a case of Human African Trypanosomiasis (HAT) we screened the literature for recent alerts of HAT in Kenya and only ProMED had previously published a report on the occurrence of HAT in Kenya. This however, was documented almost 11 years before the current case [1,2]. About a month after the occurrence of the case described here, there was a further case of HAT from the Masai Mara area described in this issue of *Eurosurveillance* [3].

Figure 2

Giemsa-stained *Trypanosoma brucei rhodesiense* in a thick blood smear from a German traveller returning from the Masai Mara area, Kenya, January 2012



64x magnification

A literature research on PubMed revealed two publications that reviewed the epidemiology of HAT in non-endemic countries. A review of HAT cases imported into Europe between 2005 and 2009 included 11 cases, five of which were infected with *T. b. rhodesiense*. There were no cases described from Kenya, but two infected patients had travelled to the Serengeti, which directly borders Masai Mara [4]. In another report, the bibliographic data were supplemented by the World Health Organization (WHO) data on requests of antitrypanosomal drugs from hospitals in non-endemic countries treating travellers. These data showed that 94 cases of HAT were identified between 2000 and 2010, 72% of which were caused by *T. b. rhodesiense*. Although 59% of the cases were identified in Tanzania, with the vast majority of cases being tracked back to the Serengeti, no cases have been reported from Kenya [5].

Trypanosomiasis is a disease that occurs in local clusters, and one such cluster was identified in 2002 through the TropNetEurop Sentinel Surveillance network when two index and seven consecutive cases were identified in non-disease endemic countries in Europe and South Africa [6]. These cases originated in the Serengeti and Tarangire National Parks in close proximity to Masai Mara, but with no documented case originating from the latter.

The above mentioned reports documented imported cases that were diagnosed in non-endemic countries. There are data on the cases diagnosed within the country however. The Kenyan reference hospital for sleeping sickness in Alupe, which is on the Ugandan border north of Lake Victoria, reported 31 patients with HAT caused by *T. b. rhodesiense* between 2000 and 2009. Twenty-two of the patients were diagnosed at the late stage of the diseases and coinfections and comorbidities were frequent [7]. Additionally, WHO extensively mapped the epidemiology of HAT in Africa between 2000 and 2009. For Kenya, sporadic cases were described in the very western provinces Bungoma, Teso and Busia, again on the Ugandan border, as well as in the Nyanza province. Epidemiological analysis of HAT in Kenya between 1950 and 2007 showed that infections occurred exclusively in these Western provinces, and the prevalence is altogether estimated to be low with only sporadic infections the 1990s onwards [8, 9].

Conclusion

We identified a case of HAT due to *T. b. rhodesiense* infection in a traveller who had returned from the Masai Mara area, Kenya. After this case, another report of an imported HAT infection from this area was diagnosed one month later and communicated worldwide [10]. This is noteworthy, as there were no cases described from Masai Mara in the last decade. Previously, there was documented disease activity in Kenya which was limited to the western provinces, as well as Serengeti which is essentially in direct vicinity to Masai Mara.
This report should alert clinicians to be aware of HAT when dealing with travellers from the area concerned.

We have been in contact with WHO in Geneva, Switzerland, who confirmed that the local authorities in Kenya have been informed and a WHO team of experts has been sent to the area to elucidate the situation.

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Human African trypanosomiasis in a Belgian traveller returning from the Masai Mara area, Kenya, February 2012

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A Belgian traveller was diagnosed with human African trypanosomiasis (HAT) due to *Trypanosoma brucei rhodesiense* nine days after visiting the Masai Mara area in Kenya. He presented with an inoculation chancre and was treated with suramin within four days of fever onset. Two weeks earlier, HAT was also reported in a German traveller who had visited the Masai Mara area. Because no cases have occurred in the area for over 12 years, this may indicate a focal cluster of HAT.

Case report

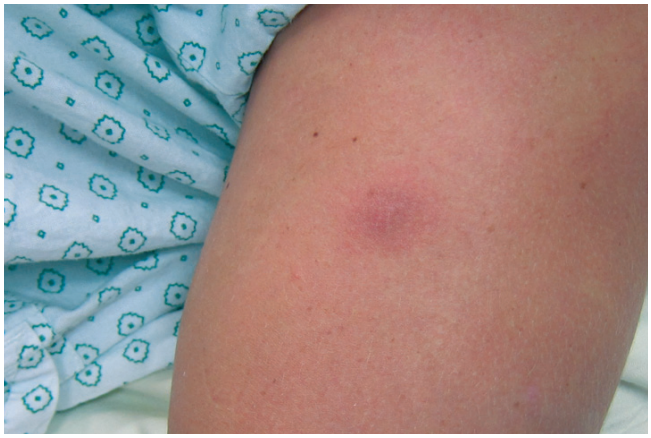
We report here the diagnosis of human trypanosomiasis (HAT) due to *Trypanosoma brucei rhodesiense* in a Belgian man who visited the Masai Mara National Reserve in Kenya from 7 to 9 February 2012. A summary of this case was reported through ProMED-mail on 22 February 2012 [1]. A similar case had been reported from Frankfurt, Germany, in a traveller who had visited the Masai Mara area in January 2012 [2], which is described further in this issue [3].

The Belgian patient stayed at a lodge at the southern end of the Mara River for one night and participated in game tracking excursions on two occasions in the Reserve. He returned to Belgium on 13 February. He presented at the St. Jan's Hospital in Bruges on 19 February with a history of high-grade fever, malaise and headache that had been present for three days. He also had a painless and discrete chancre on his arm that he had noticed only two days earlier (Figure 1). The patient was suspected to have malaria and a Giemsa-stained thick blood smear was prepared for microscopy. No malaria parasites were seen, but instead trypanosomes were identified on the thick smear, and subsequently confirmed on a thin smear (Figure 2). The patient was immediately transferred to the Tropical Diseases Unit at the University Hospital Antwerp for treatment. Pre-treatment blood analysis showed a high parasitemia (of more than one trypanosome per field on microscopy at 100x magnification), marked thrombocytopenia (47,000 platelets/µL), alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) at three times the upper limit of normal, and moderately increased C-reactive protein. The trypanosome species was identified as *T.b. rhodesiense* by PCR detection of the serum resistance-associated gene [4].

Treatment with suramin (1g) was initiated on 20 February, after a test dose of 100 mg was well tolerated. In our setting, suramin is given once weekly for five weeks. After 12 hours, an electrocardiography showed diffuse but transient S-T elevation often seen in acute *T. b. rhodesiense* trypanosomiasis. However, the levels of cardiac enzymes remained within normal limits and no cardiac dysfunction was seen on echocardiography. Trypanosomes were cleared from the blood 24 hours after suramin was given.

Figure 1

Inoculation chancre of human African trypanosomiasis in a Belgian traveller returning from the Masai Mara area, Kenya, February 2012



A generalised papulopruriginous rash appeared 36 hours after the start of treatment, lasting for four days. The patient became afebrile two days after treatment; the chancre persisted until the fifth day. He recovered clinically by the seventh day and a platelet count and liver function tests had returned to near normal values by then. A cerebrospinal fluid examination performed on the seventh day, when the second dose of suramin was given, showed a normal cell count and no trypanosomes.

The time lapse from presumed inoculation until the onset of fever was 11 days. Treatment was initiated on the 13th day after presumed inoculation. Such relatively early treatment should prevent invasion of the brain by the parasite [5].

The trypanosome inoculation chancre observed on admission is an important clinical sign present in about two thirds of patients [6]. As in our case, it may be discrete and easily overlooked by physicians unfamiliar with this rare disease.

Background

Trypanosoma brucei rhodesiense is endemic in East and southern Africa and is transmitted to humans and game alike by tsetse flies of the *Glossina morsitans* group, which feed during the day. It accounts for the majority of imported HAT cases [6]. In Kenya, HAT is rare, in Kenyans and travellers alike. Until the cases reported this year, the last two autochtonous cases reported date from 2006 and 2009 and originated from the north-west part of the country (P. Simarro, personal communication, 21 February 2012). The Masai Mara Conservation Area in south-west Kenya receives about 300,000 visitors annually. Nowadays, the area also includes adjacent farms around the original Masai Mara National Reserve. In the last 12 years, HAT has not been seen in travellers visiting Masai Mara, in contrast to the situation in the adjacent Serengeti National Park in Tanzania [7].

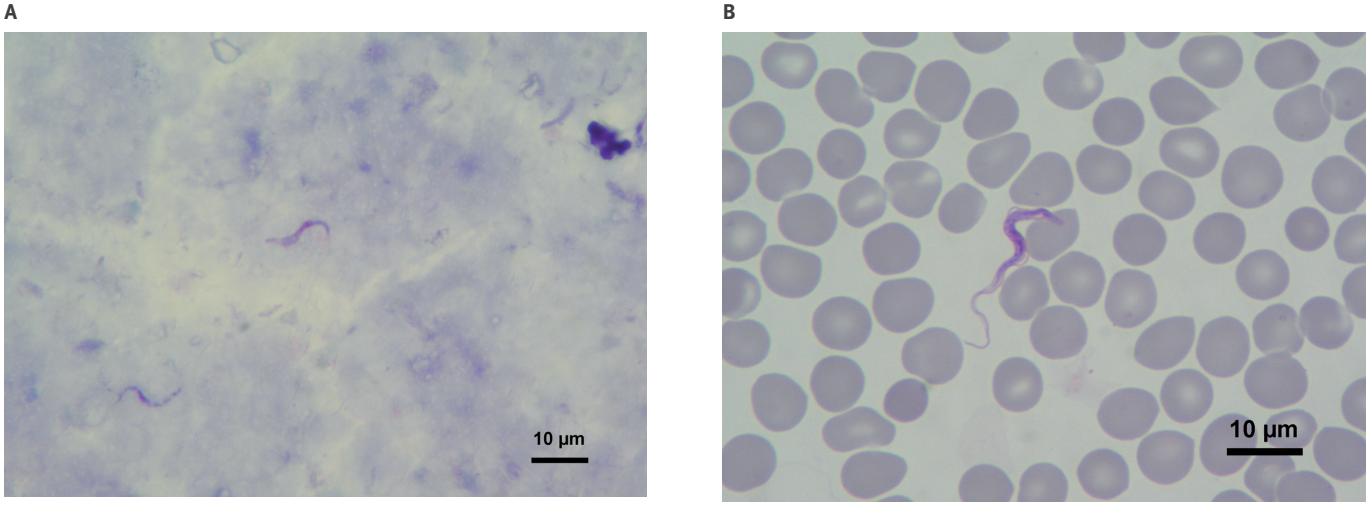
Among patients presenting fever after a travel in the tropics, *T. b. rhodesiense* HAT remains a very rare event [8]. Parasitemia is usually elevated during the acute febrile phase. This aids diagnosis, as even for microscopists unfamiliar with the parasite, trypanosomes can be easily seen on a Giemsa-stained routine thick blood smear, and often on a thin blood smear too. Trypanosomes have an unmistakable shape (Figure 2).

Discussion

Acute *T. b. rhodesiense* HAT is a medical emergency. Multi-organ failure may occur early in the course of the febrile phase with a high mortality risk, similar to that of severe malaria. In a large series of imported *T. b. rhodesiense* HAT cases, the case fatality rate was 4.3%, associated either with late diagnosis during the acute febrile stage or with meningo-encephalitic stage treatment toxicity [6]. In 2007, a German patient infected with *T. b. rhodesiense* HAT in the Serengeti, Tanzania, died of multi-organ failure five days after the onset of the acute febrile phase. The diagnosis had been missed by another physician in Zanzibar, where trypanosomiasis does not occur, four days before the patient died despite fever and the presence of a chancre. The patient was treated with antimalarials without a blood test having been done [9]. Patients require immediate treatment with suramin, after a test dose to observe any hypersensitivity to the drug. If suramin cannot be obtained within a day, immediate treatment with pentamidine has to be considered. Although not the first choice for *T. b. rhodesiense* HAT, pentamidine was effective in a few imported *T. b. rhodesiense* HAT

Figure 2

Trypanosomes in (A) thick and (B) thin blood smears at diagnosis from a Belgian traveller returning from the Masai Mara area, Kenya, February 2012



The smears were stained with Giemsa

cases as the sole treatment given [6,10,11]. Suramin and other HAT medications can be obtained from the World Health Organization headquarters in Geneva, Switzerland, at very short notice.

Our patient had stayed overnight in a lodge close to the Mara River, in the south of the Masai Mara area, whereas the German patient had stayed in another lodge about 30 km further north (P. Simarro, personal communication, 21 February 2012) (Figure 3). However, both travellers may have visited the same area during one of the daytime game-watching excursions.

The coincidence of two *T. b. rhodesiense* HAT cases infected after visiting the Masai Mara area suggests a possible, incipient focal cluster, similar to the onset of an outbreak seen in travellers visiting the adjacent Serengeti in 2001 and 2002 [7]. *T. b. rhodesiense* HAT is endemic in both game reserves and game migrate annually between both areas. The ecosystems of the Masai Mara area and the northern part of the Serengeti are nearly identical. At any given time, only very few tsetse flies are infected with *T. b. rhodesiense*, which can infect humans. Most carry zoonotic species (*T. congolense, T. vivax, T. b. brucei*) that do not have the serum resistance-associated gene required to resist parasite lysis after inoculation in humans.

Although *T. b. rhodesiense* HAT remains an exceptionally rare imported infectious disease, early recognition and treatment assures a favourable outcome.

Acknowledgments

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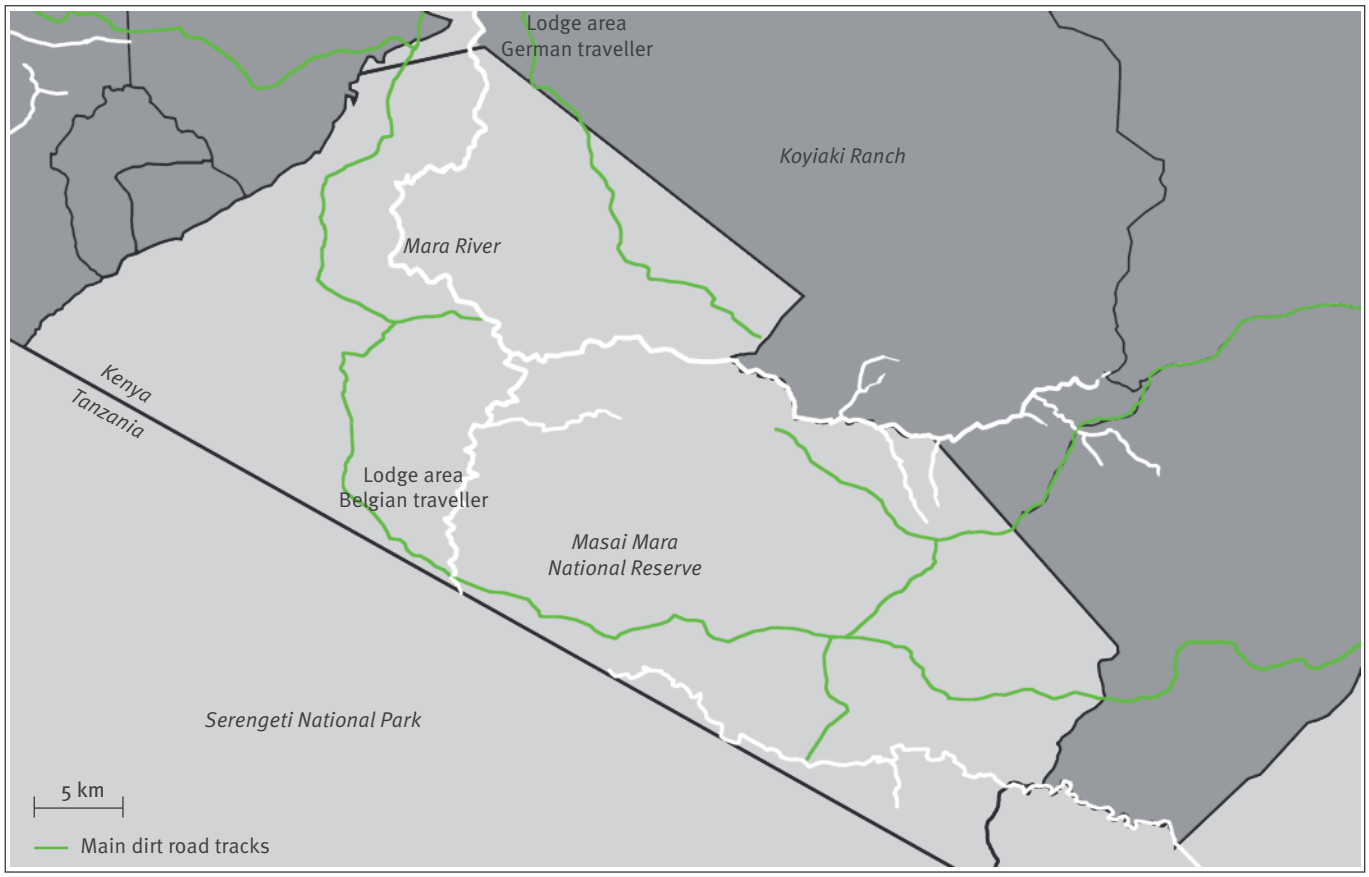
Figure 3

Masai Mara area, Kenya, with the approximate location of the lodges where the German and Belgian travellers stayed, January–February 2012



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Rabid puppy-dog imported into the Netherlands from Morocco via Spain, February 2012

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In February 2012 a rabid puppy dog was imported into Amsterdam, the Netherlands from Morocco via Spain. In a joint action between the Netherlands' Food and Consumer Product Safety Authority, the Public Health Service of Amsterdam and the Centre for Infectious Disease Control all exposed human and animal contacts were traced and, when necessary, provided with post-exposure prophylaxis. During the importation, the international legislations with respect to vaccination requirements were not fully obeyed by veterinarians and custom services.

On 28 January 2012, a Dutch couple residing in Morocco obtained an eight-week-old puppy at a parking lot. They took the dog to a local veterinarian who micro-chipped the dog and issued a certificate of good health, yet no vaccinations were given. On 4 February 2012 the couple travelled by car and ferry from Morocco to Spain. At a veterinary clinic they acquired a European pet passport. On 11 February they returned to the Netherlands by air. Although the dog was cuddled by three Spanish customs officers at Malaga Airport, the dog passport was not examined by customs in Spain, nor in the Netherlands. Upon arrival the couple immediately introduced the puppy to friends and family. It showed normal behaviour at the time, yet became increasingly hostile over the following days. On 14 February, the owners contacted the veterinary practice after they had been bitten by the dog. The puppy was assumed to suffer from 'puppy stress' caused by the new environment and was given sedative medication. In the morning of 15 February the dog's behaviour became uncontrollable. When they realised that the puppy originated from Morocco, the veterinarians contacted the Netherlands Food and Consumer Product Safety Authority (NVWA). As clinical signs indicated rabies, the NVWA advised to euthanise the dog for investigation. Rapid post-mortem rabies diagnostics were performed by the Central Veterinary Institute (CVI). On the evening of 15 February rabies (classical rabies virus, genotype I) was confirmed.

After the notification on 15 February, the NVWA, the Public Health Service of Amsterdam (PHS Amsterdam) and the Centre for Infectious Disease Control (CIb/RIVM) initiated a joint action to identify and trace all humans and animals with possible exposure to the dog's saliva in order to provide post-exposure prophylaxis and assess the risk to the general population. The dog was considered to be infectious to others during the two weeks prior to the day of onset of symptoms and until its death (28 January through 15 February).

Contact tracing

The owners were interviewed about their travel history since the date they acquired the puppy on 28 January. Throughout their journey, they had constantly supervised the puppy, and no unobserved exposure had taken place. In Morocco, no contacts were identified except for the local veterinarian. During the journey to Spain no other people or animals were in contact with the dog. In Spain, the couple stayed with two Dutch friends, visited a Spanish friend and a veterinary clinic, and stayed in four different hotels in two different towns. Apart from the three custom officers, the dog was stroked by an unknown person at a restaurant and one at Malaga airport. During the flight to Amsterdam, the dog was kept in a basket on the owners' lap, and no contacts were reported. At Amsterdam Airport they were collected by car by two friends and their dog. On 11 and 12 February they met with numerous family, friends and their children at four private locations. In one location, two cats were present. The remaining days they mostly stayed at home, except for the last visit to the veterinary clinic. A total of 43 contacts (including the two owners) residing in the Netherlands

were identified among family, friends and the animal clinic. On several occasions, unidentified people in the street were petting the dog.

Public health action in the Netherlands

Upon notification the PHS physician on call immediately arranged post-exposure treatment for the owners (rabies vaccination with human diploid cell rabies vaccine (HDCV) and human rabies immunoglobulin (HRIG) at the emergency department of the Academic Medical Centre (AMC). On the same evening most known contacts were informed by telephone. Within 24 hours their risk for transmission was assessed, and according to national and international guidelines post-exposure prophylaxis was recommended (Table) depending on the type of contact and category of exposure [1,2]. As it is known that children's recollection of exposure might be unreliable, all nine children were considered as having had a category III exposure. Casual petting on the street was categorised as category I exposure. No treatment was deemed necessary for these contacts.

As the investigations revealed no risk of rabies transmission to the general population, warning messages to alert the public were deemed unnecessary. Instead, an informative joint press statement by the PHS and NVWA was issued on 16 February describing the incident.

International public health action

The CIb/RIVM issued an EWRS (Early Warning and Response System) message to inform the Member States of the European Union about this incident.

Bilateral contact was established with Spain in order to facilitate contact tracing there. In Spain three known contacts were informed directly by the PHS. The couple's Spanish friend, considered to have category I exposure, had been previously vaccinated against rabies. Their Dutch friends, a category II and a category III contact, received treatment at a local hospital in Spain. As HRIG was not available locally, they returned to Amsterdam so that the category III contact could receive HRIG the following day. The contact details of the Spanish veterinarian and a picture of the dog were provided to the Spanish EWRS contact point. Unfortunately, it was not possible to obtain additional information on the other contacts who stroked the puppy, nor on how many contacts were traced or vaccinated in Spain overall.

The CIb/RIVM established a bilateral contact with their counterpart in Morocco, providing them with the contact details of the veterinarian that had seen the dog prior to its departure. We have as yet no information on the actions taken there.

Veterinary action

The investigation revealed only few exposed animals. One dog and two cats were traced within 24 hours. The dog (imported from Greece in 2010 and vaccinated against rabies) received a booster vaccination. The two cats received vaccination on 15 February and quarantine was indicated. As a suitable quarantine place was not available, it was decided to euthanise both cats.

Conclusions

This is the first case of rabies (caused by the classical rabies virus) in domestic and/or wild animals in the Netherlands since 1988.The accidental import of a rabid puppy led to a resource-intensive and costly public health response. A total of 48 known contacts in three different countries needed to be traced, of whom 45 required post-exposure treatment. Including the imported dog, three animals were euthanised.

The owners tried to import the dog in a legal way, yet the international legislations were not followed properly by the consulted veterinarians in Morocco and Spain and customs in Spain and the Netherlands. In hindsight, the European dog passport was incorrectly issued by a Spanish veterinarian as, according to the EU legislation, dogs/animals from outside the European Union should be vaccinated for rabies and kept in quarantine for three months upon arrival [3,4]. Customs at three locations upon arrival and leaving in Spain and arrival in the Netherlands failed to check the vaccination status of the dog.

The NVWA is evaluating this course of events. Lessons learnt from the evaluation should be communicated internationally to urge veterinarians and customs departments to follow international legislation appropriately.

Veterinarians and customs officials across Europe should be aware of the risk of rabies importation by animals from within and outside Europe. Particular attention should be given to puppies under the age of three months, which must be vaccinated against rabies and consequently cannot be imported into Europe [3].

Illegal importation of animals from rabies-endemic countries outside the European Union probably occurs

Table

People exposed to the rabid dog and treated by PHS Amsterdam and/or AMC, the Netherlands, February 2012 (n=43)

Exposure category[a]	Treatment given	Number of exposed people
Category I	Not indicated	1
Category II	Vaccination	21
Category III	Vaccination and HRIG	21

HRIG: human rabies immunoglobulin; PHS Amsterdam: Public Health Service of Amsterdam; AMC: Academic Medical Centre.

[a] Category I: touching animals, licks on intact skin; Category II: nibbling of uncovered skin, minor scratches or abrasions without bleeding; Category III: transdermal bites or scratches, (saliva from) licks on broken skin or on mucous membrane.

frequently. France reported nine illegally imported rabid puppies and dogs over the last ten years, of which seven were imported from Morocco [5,6]. Therefore the public should be made aware of the risks involved in bringing home a living souvenir, and of the rules and regulations governing such an action.

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The authors would like to thank the public health nurses of the Public Health Services in Amsterdam for their efficient contact tracing and the fast provision of post-exposure prophylaxis and psychological support to all contacts involved.

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Increased reports of *Mycoplasma pneumoniae* from laboratories in Scotland in 2010 and 2011 – impact of the epidemic in infants

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In common with reports from other European countries, we describe a substantial increase in the number of laboratory reports of *Mycoplasma pneumoniae* in Scotland in 2010 and 2011. The highest number of reports came from those aged one year and younger. However, reports from young children were more likely to come from PCR testing than serological testing.

In light of the increasing incidence of *M. pneumoniae* in other parts of the United Kingdom (UK) and Europe in 2010 and 2011, we examined the numbers of *M. pneumoniae* laboratory reports in Scotland from January 2008 to December 2011. Here we describe the temporal distribution of reports and the age groups most affected.

Background

Mycoplasma pneumoniae causes upper and lower respiratory tract infection in all age groups. However, it is a particularly important bacterial cause of community-acquired pneumonia in children [1]. *M. pneumoniae* is endemic worldwide, but epidemics are common; historically in the UK, these usually occur once every four years [2]. The most recent increase in the incidence of *M. pneumoniae* was seen in England and Wales in 2010 and 2011 [3,4]. Similar increases have also been noted in many other countries in the same period, particularly in northern Europe [5-12].

Although the main burden of infection is typically found in school-age children [4,6,10], *M. pneumoniae* has also been noted as a significant cause of respiratory tract infection in children under the age of five [13-15]. As the possibility of *M. pneumoniae* infection may be overlooked in young children, recent UK clinical guidelines emphasise that *M. pneumoniae* is not uncommon in those aged one to five years [1]. However, the local availability of different testing methodologies for *M. pneumoniae* may determine how frequently *M. pneumoniae* is diagnosed in particular age groups.

National laboratory-based surveillance and reporting

In Scotland, some diagnostic laboratories carry out PCR testing for *M. pneumoniae* as part of a multiplex real-time PCR screening approach for respiratory viruses [16]. Therefore, young children presenting with presumed respiratory viral infection to hospitals served by these laboratories also receive concomitant testing for *M. pneumoniae*. In hospitals served by other laboratories, serology is still the mainstay of *M. pneumoniae* diagnosis. However, serology is less convenient for diagnosis in young children, since obtaining a blood specimen from an infant is more difficult than obtaining an upper respiratory tract specimen.

Reports of *M. pneumoniae* from National Health Service (NHS) laboratories in Scotland are collated centrally by the national public health body Health Protection Scotland (HPS), via the Electronic Communication Of Surveillance in Scotland (ECOSS) non-mandatory reporting system. Reports from 1 January 2008 to 31 December 2011 inclusive were analysed in this study. Denominator testing data and clinical diagnosis were not recorded via ECOSS. Data were anonymised and analysed by week of year reported, age group (year of age was available in 2010 and 2011), sex, submitting laboratory and specimen type. Estimates of incidence were based on the most recent mid-year population estimate for Scotland [17]. Reports were submitted from all NHS microbiology laboratories in Scotland which carry out *M. pneumoniae* testing. These are based in hospitals in nine locations: Aberdeen, Ayr, Dundee, Dunfermline, Edinburgh, Fife, Glasgow, Inverness and

Lanarkshire. In the case of Glasgow, results from two laboratories in the city were combined. Respiratory specimens were tested by PCR and blood specimens by serology. Laboratories used a number of different commercial and in-house PCR and serological tests. Reports of positive serology were either from a diagnostic rise in *M. pneumoniae*-specific IgG antibodies or detection of *M. pneumoniae*-specific IgM.

Analysis of laboratory reports

Temporal distribution

During the study period, there were 1,232 laboratory reports of *M. pneumoniae* in Scotland; of these, 76 (6.2%) were from 2008, 125 (10.1%) from 2009, 290 (23.5%) from 2010 and 741 (60.1%) from 2011. The highest number of reports were found in the fourth quarter of 2011 (432 reports); this was nearly three times higher than in any other quarter in the study period. The number of reports began to rise from the autumn of 2010 through the winter of 2010/11, with a second and larger rise towards the end of 2011 (Figure 1). The peak reporting frequency was 48 reports in week 47 of 2011. The estimated national incidence of *M. pneumoniae* in 2011 was 14.2 per 100,000 population.

Laboratory testing

Reports of *M. pneumoniae* were issued from nine laboratories, with the two laboratories serving the largest populations (Edinburgh and Glasgow) issuing 77.0% of the reports. Testing methods differed across Scotland, with five laboratories using PCR only and four using serology only. Overall, 77.4% of reports were from respiratory specimens (PCR detection), 18.0% from serology, and the specimen type was not known in 4.6% of reports. Of the respiratory specimens, 92.1% were from the upper respiratory tract.

Patient demographics

The male:female ratio was 1:0.94; there was no significant difference in the number of reports from males and females (p=0.30; chi-squared test). Approximately half of the reports (53%) were from children under the age of 15 years, with the age group of 0–4 year-olds accounting for 24.9% of all reports (Table). The estimated incidence of *M. pneumoniae* in 2011 was highest in the 0–4 year-olds (67.5/100,000 population), declining to 52.2 per 100,000 in the 5–9 year-olds and 22.6 per 100,000 in the 10–14 year-olds.

Due to improvements in the quality of information provided from laboratories via ECOSS, data on individual year of age were available from 2010 onwards. The mean age of patients was 20.0 years (standard deviation (SD) +/-19.8 years; range: <1 month to 89 years), however, 16.2% of the reports from 2010 and 2011 came from patients aged one year or younger (Figure 2).

Patient age and sample type

Between 2008 and 2011, *M. pneumoniae* reports from young children were more likely to come from PCR testing than serological testing: 28.8% of reports from respiratory specimens were from 0–4 year-old children, compared to 10.4% of serology specimens (p<0.01 Fisher's exact test) (Table).

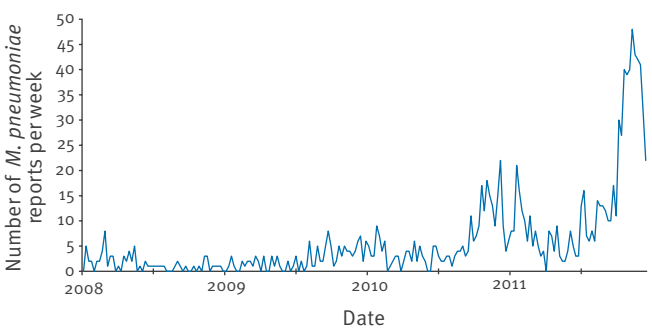
An analysis of year of age data from 2010/11 demonstrated that the mean age for PCR reports was 18.6 years (SD +/-19.4 years; range: <1 month to 89 years). In contrast, the mean age for serology reports during the same period was 27.8 years (SD +/-19.9 years; range: 1 year to 88 years).

Macrolide resistance

A full analysis of the presence of mutations in the 23S rRNA gene associated with macrolide resistance is currently underway in PCR-positive specimens.

Figure 1

Mycoplasma pneumoniae reports by week of year, Scotland 2008–2011 (n=1,232)



Table

Mycoplasma pneumoniae reports by age group and specimen type, Scotland, 2008–2011 (n=1,232)

Age group (years)	**Total *M. pneumoniae* reports (%) n=1,232**	*M. pneumoniae* reports from respiratory specimens (%) n=954[a]	*M. pneumoniae* reports from serology (%) n=222[a]
0–4	**307 (24.9)**	275 (28.8)	23 (10.4)
5–9	**218 (17.7)**	173 (18.1)	40 (18.0)
10–14	**128 (10.4)**	97 (10.2)	28 (12.6)
15–19	**67 (5.4)**	45 (4.7)	14 (6.3)
20–24	**60 (4.9)**	41 (4.3)	15 (6.8)
25–29	**55 (4.5)**	45 (4.7)	6 (2.7)
30–34	**75 (6.1)**	55 (5.8)	20 (9.0)
35–39	**75 (6.1)**	59 (6.2)	12 (5.4)
40–44	**73 (5.9)**	45 (4.7)	22 (9.9)
45–49	**43 (3.5)**	31 (3.2)	8 (3.6)
50–54	**39 (3.2)**	24 (2.5)	11 (5.0)
55–59	**26 (2.1)**	19 (2.0)	6 (2.7)
60–64	**17 (1.4)**	12 (1.3)	4 (1.8)
≥65	**49 (4.0)**	33 (3.5)	13 (5.9)

[a] 56 reports were from specimens of unknown type and are therefore excluded here.

However, preliminary results indicate genotypic evidence of resistance in at least one specimen; a paediatric patient re-presenting to hospital with ongoing respiratory symptoms following first-line treatment with a macrolide for *M. pneumoniae* infection (data not shown).

Discussion

An examination of the current epidemiology of *M. pneumoniae* in Scotland was considered timely given the recent increasing incidence seen in other countries in the UK, Europe and elsewhere [3-12]. We found a substantial peak in the number of *M. pneumoniae* laboratory reports submitted to the national surveillance programme during the autumn/winter of 2011, following a smaller peak in the previous autumn/winter of 2010. The *M. pneumoniae* activity had been low from 2008 until the autumn of 2010. As expected, this picture is consistent with an increase in *M. pneumoniae* laboratory reports in England and Wales in the same period [3,4]. The estimated overall incidence of *M. pneumoniae* in Scotland in 2011 was around 10-fold lower than that reported in other northern European countries [8,10]. However, we found that the incidence was highest in the youngest age group, in contrast to a recent study in which incidence was highest in 5–14 year-olds [10]. Reporting of *M. pneumoniae* in the UK is not mandatory and reports only arise from the active microbiological investigation of patients with respiratory symptoms, mainly those presenting to hospitals. Therefore, our figures are likely to underestimate the true extent of the epidemic in Scotland, particularly in the community.

Low levels of macrolide resistance have been reported in Europe [11,18] but not from other countries in the UK [3,4]. In a preliminary analysis as part of the present study we found one genotypically resistant isolate, however, a full assessment of the level of macrolide resistance in Scotland is required and is now underway.

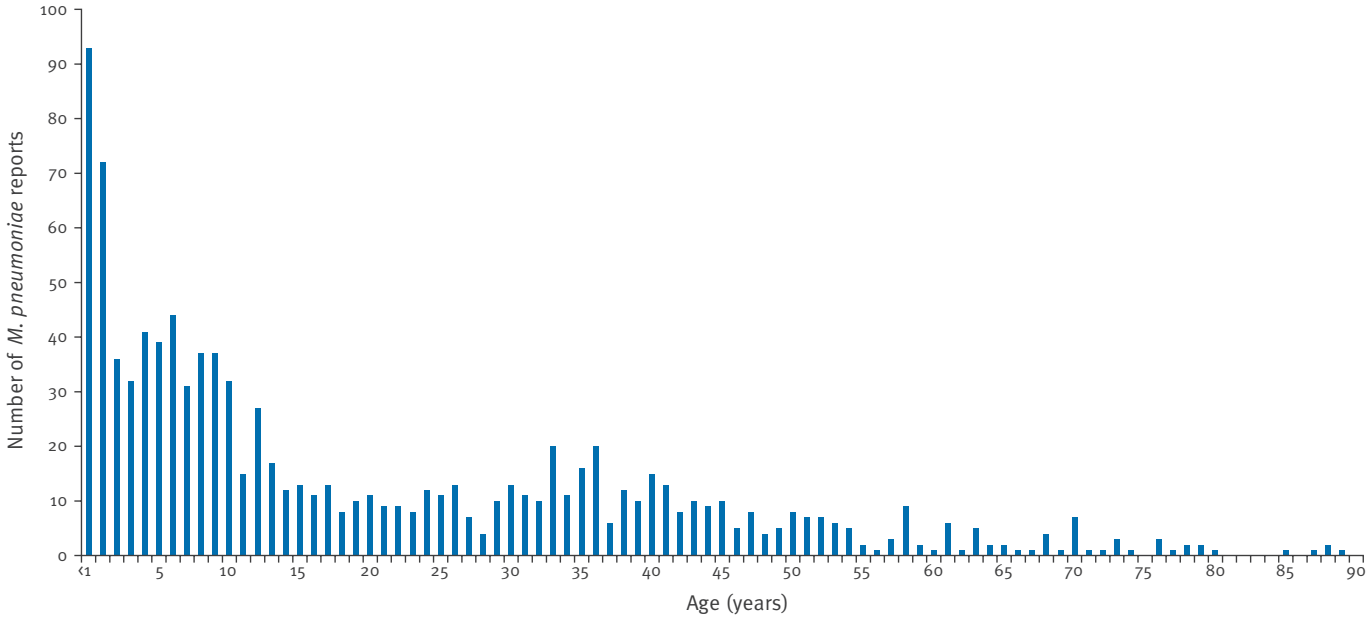
As we were able to differentiate reports into narrow age bands, it was clear that in Scotland, *M. pneumoniae* was most frequently reported in the youngest children, particularly those one year and younger. The incidence was also highest in the age group of 0–4 year-olds, with 67.5 per 100,000. A limitation of this study is that denominator testing data is not currently captured by the surveillance programme, so we are unable to determine if the proportion of *M. pneumoniae*-positive children in this age group was less than that in older age groups, as found in other studies [4,6,10]. Numerically however, we have found a significant burden in infants, which has previously been under-appreciated. A study examining the clinical course, treatment and outcomes of *M. pneumoniae* infection in infants is now underway.

We also found significantly fewer *M. pneumoniae* reports from serology compared to respiratory specimens in children aged 0–4 years. This may be due to the ease of obtaining upper respiratory tract specimens for PCR, compared to blood specimens for serology, in the youngest patients. Therefore, in hospitals where only serological testing is available, *M. pneumoniae* infections in young children may be under-diagnosed.

The majority of *M. pneumoniae* reports in Scotland originated from two large laboratories which test almost exclusively by PCR as part of in-house multiplex

Figure 2

Mycoplasma pneumoniae reports by year of age, Scotland, 2010–2011 (n=1,031)



real-time PCR screens for respiratory pathogens. In the future, as this molecular syndromic screening approach becomes more widespread, more infants are likely to be tested for *M. pneumoniae*, and more infections found. During *M. pneumoniae* epidemics, there may be a requirement to change empirical prescribing for community-acquired pneumonia from beta-lactam antibiotics to macrolides in the most affected age groups. However, further work is required to determine the clinical consequences of *M. pneumoniae* infection in infants and the need for antibiotic treatment.

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Letter to the editor: Commitment needed for the prevention of congenital rubella syndrome in Europe

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The ongoing outbreak of rubella in Romania as reported by Janta et al. [1] highlights the public health efforts that are yet necessary to meet the World Health Organization (WHO) Regional Office for Europe target for the elimination of measles and rubella and prevention of congenital rubella syndrome (CRS) by 2015 [2].

Ongoing measles outbreaks being reported in the European Union/European Economic Area (EU/EEA) countries is a reminder that rubella outbreaks may be ongoing concomitantly despite apparent lower number of cases reported through routine surveillance in the EU [3].

Rubella vaccines have been used in the EU/EEA countries for more than 20 years. Currently all EU/EEA countries have adopted a combined measles-mumps-rubella (MMR) vaccination with two doses in the childhood vaccination schedule.

At initial implementation, rubella vaccination followed two general approaches: either a targeted immunisation of adolescent girls and/or women of childbearing age, with the aim of reducing the incidence of CRS, or a more global approach that targeted young infants, susceptible adolescents and adults in order to interrupt rubella transmission and eliminate rubella as well as CRS. The first approach requires that virtually every susceptible woman should be immunised to reach elimination of CRS. The latter approach is the current standard for MMR vaccination in EU/EEA countries. Currently available MMR vaccines are not expensive, highly efficacious and well tolerated in all age groups [4].

To ensure the benefits of universal vaccination with two doses of MMR, a strong long-term public health and political commitment is vital. This is required for achieving and maintaining high vaccination coverage, for ensuring continuous vaccine supply and delivery and also for having adequate surveillance activities to monitor trends in CRS and rubella and the effects of interventions.

Screening for rubella antibodies - as part of pre-conceptual or antenatal care to identify unprotected women - enables for active rubella vaccination offer in order to protect future pregnancies. This might represent an additional tool for CRS prevention [5]. However, high vaccination coverage in childhood and reliable immunisation records should be the primary aim to strive for.

In the past, outbreaks in young adults in EU/EEA countries led to children being born with CRS [6]. This situation is likely to repeat if women of childbearing age are infected with rubella. All possible efforts should be undertaken to prevent any case of CRS in Europe in the future. Commitment is now needed at political and public health level in order to ensure that the potentially debilitating consequences of rubella infection in pregnancy for children born in the EU represent a story of the past.

The epidemiology and profile of population susceptibility for both measles and rubella are different and require different catch-up strategies to reach the elimination goal. In many countries, rubella vaccination was introduced later than measles, with different segments of the population being initially targeted by vaccination – therefore leaving cohorts of individuals unprotected. By contrast, measles vaccination has always been targeting toddlers, young children and adolescents. The initiatives undertaken in delivering measles vaccination programmes and the use of combined vaccines may provide an opportunity for synergy in activities towards rubella and CRS elimination. However, rubella deserves its own attention and public health initiatives, as susceptible population groups might be different than those unprotected towards measles.

The European Centre for Disease Prevention and Control (ECDC) is committed to support the EU/EEA Member States in the measles, rubella and CRS elimination goal. In the coming months and years, ECDC will work closely with the Member States, the European Commission and the WHO Regional Office for Europe to help ensure that appropriate measures are implemented and adequate

virological and epidemiological surveillance mechanisms are in place for rubella, as well as for measles.

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The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2010

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On 8 March 2012, the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) launched their annual report on zoonoses and food-borne outbreaks for 2010, the 'European Union Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Food-borne Outbreaks in 2010' [1]. The report provides a comprehensive overview of zoonotic infections and disease outbreaks caused by consuming contaminated food. According to the report, 5,262 food-borne outbreaks were recorded in the European Union (EU), a slight reduction from 2009. *Campylobacter, Salmonella* and viruses such as norovirus were the most frequently reported causes of food-borne outbreaks.

In 2010, campylobacteriosis was the most commonly reported zoonosis. A total of 212,064 human cases were reported which constitutes an increase of 7 % compared with the figures reported in 2009. This is an increase for the fifth year running. *Campylobacter* was most often detected in fresh broiler meat.

A total of 99,020 salmonellosis cases in humans were reported in 2010 and the decreasing trend in case numbers continued from previous years – 108,618 cases were reported in 2009 [2]. This is a drop of nearly 9 % and marks a decrease for the sixth consecutive year. Most Member States met their *Salmonella* reduction targets for poultry, and *Salmonella* is declining in these populations. The report states that the most likely reason for the decrease is the successful adherence of Member States to the EU *Salmonella* control programmes for reducing the prevalence of the bacteria in poultry populations, especially in laying hens [3]. In foodstuffs, *Salmonella* was most often detected in fresh broiler and turkey meat.

The report also presents data on other food-borne diseases such as Shiga toxin/verotoxin-producing *Escherichia coli* (STEC/VTEC). Human cases of STEC/VTEC have been increasing since 2008 - a total of 4,000 confirmed VTEC infections were reported in 2010.

The number of human listeriosis cases decreased slightly to 1,601.

The full version of the report covers a total of 15 zoonotic diseases including Q fever, brucellosis, bovine tuberculosis, rabies and the parasitic zoonosis echinococcosis.

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