A CLUSTER OF AIRPORT MALARIA IN BELGIUM IN 1995.

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SUMMARY

In Europe 64 cases of airport malaria have been registered between 1969 and 1996, most of them in France, Switzerland and Belgium.

In the summer of 1995 six cases of airport malaria occurred at the International airport of Brussels, Belgium. Of the six patients three were airport employees, three were occasional visitors. One patient died, the diagnosis was made by PCR amplification and DNA sequencing after exhumation. Two different species of *Plasmodium* were detected, and infections occurred on at least two different floors of the airport. An inquiry revealed that the cabin of airplanes is correctly sprayed, according to WHO recommendations, but that the inside of the hand luggage, the cargo hold, the animal compartment, the wheel bays and container flights remain possible shelters for infected mosquitoes.

In a case of fever of unknown origin, airport malaria should be considered in the differential diagnosis, especially during hot summers, and when thrombocytopenia is present. Additional antimosquito measures should be generalised, encompassing highly exposed personnel, container content and handling buildings, animal cages, wheel bays, and the boundary between the sorting and the reception of luggage.

INTRODUCTION.

Airport malaria was first described in the literature in 1977(1), although retrospectively the first case of airport malaria has been notified to the health authorities in August 1969 in France. In Europe 64 cases of airport malaria have been registered between 1969 and 1996. Most of them occurred in France (24), Switzerland (10) and Belgium (14).(2-4) The cases that have been described in Belgium before were all linked to the airport of Brussels. In 1982 two brothers who lived in the vicinity of the airport contracted malaria.(5,6) In 1983 a worker of the airport was infected.(7) In 1986 five customs officers got malaria, one of them died.(8,9) We report six cases of airport malaria that occurred during the summer of 1995 at the international airport of Brussels, Belgium Three patients were security agents working in the terminal where luggage is sorted before it is sent by conveyer belt to the travellers. One of them died. The other patients were occasional visitors to the arrival hall of the airport.

OBSERVATIONS.

Patients. (Table 1)

The first patient was a 44-year-old security agent. His symptoms started on August 19 with arthralgias and lever. Because of discrete respiratory symptoms he was put on amoxycillin-clavulanate and aspirin. The 21st he developed diarrhoea for which loperamide was started. The next day he complained of extreme weakness and could not stand on his feet. He died on August 23 while sitting on his knees in the shower.

Several weeks later, after the funeral, a colleague (case 5) made the link between their common symptoms. The body was exhumed at the cost of considerable bureaucratic efforts.

A 3 mm^2 excision from a biopsy of the left lung was homogenised, digested with proteinase K, and processed.(10) A 10 µl aliquot of the extracted DNA was submitted to standard Polymerase Chain Reaction (PCR) with a primer set specific for a sequence segment belonging to the circumsporozoite protein gene (CSP) of *Plasmodium falciparum*.(11) Primers coding for a sequence of the human 2-microglobulin gene were used as internal control and to check the quality of the extracted DNA. The single-band PCR product was purified and cycle sequenced according to the standard procedure described by Perkin Elmer.(12) A run with each of the PCR primers was sufficient to determine the integral 155 bp sequence. A DNA data bank search using the BLAST 2.0.2 pro-

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Table 1. Overview of the data of all patients.

Initials	*Sex*	*Age*	*Epidemiology*	*Onset symptoms*	*Date of diagnosis*	*Plasmodium species*	*Severe clinical signs*	*Treatment*	*Outcome*
TB	M	44	Security agent of the airport	19/8/95	post-mortem	falciparum	shock	none	died
VEN	F	42	Visitor arrival hall airport on 14/8/95	25/8/95	30/8/95	falciparum	ARDS	quinine IV doxycycline clindamycin	cured
DGE	F	28	Security agent of the airport	26/8/95	4/9/95	falciparum	/	quinine doxycycline	cured
PMJ	F	37	Visitor arrival hall airport on 14/8/95	27/8/95	3/9/95	falciparum	parasitaemia 28% DIC	quinine artemisinin doxycycline exchange transfusion	cured
JVDG	M	60	Security agent of the airport	28/8/95	5/9/95	falciparum	/	quinine doxycycline	cured
AVD	M	62	Visited 3 times the airport in August 95	9/9/95	11/9/95	ovale	/	sulfadoxine/ pyrimethamine	cured

ARDS: adult respiratory distress syndrome - DIC: diffuse intravascular coagulation

gram showed a 100 % similarity with the expected sequence segment belonging to CSP.(13)

The second patient was a 42-year-old woman who spent 3 hours in the arrival hall of Brussels International Airport on the 14th of August. Ten days later she felt unwell, with shivering and muscle aches. On August 25 she developed high fever and consulted her family doctor. She was treated with amoxycillin-clavulanate for a presumed sinusitis. Because her symptoms gradually worsened and she developed nuchal rigidity, she was hospitalised on August 28 in the University Hospital of Ghent to exclude a meningitis. The lumbar puncture was completely normal. Because of anaemia (Hb 8.1 g/dl) and thrombocytopenia (15.000/µl) the blood smear was examined and a sternal puncture was performed. Both of them revealed *P. falciparum* on August 30. Treatment with clindamycin, quinine and doxycycline was installed. On the 31st of August she developed respiratory distress. On the 1st of September her condition worsened, and mechanical ventilation was started because of an overt adult respiratory distress syndrome. She remained ventilator-dependent for 47 days. and a nosocomial sepsis and a hydropneumothorax further complicated her stay on the intensive care unit. Finally she recovered without obvious sequels.

The third case was a 28-year-old female security agent who was working in the same location as case 1 and 5. She developed fever and arthralgias on August 26. Treatment with clarithromycin was started by an attending physician. Because daily spiking fever up to 40°C continued under this treatment, she was hospitalised on the 1st of September in the University Hospital of Leuven. Blood examination showed haemolytic anaemia and a marked thrombocytopenia (54.000 platelets/mm^3). On the 4th of September a thick and thin smear showed trophozoites of *P. falciparum*. She was treated with oral quinine and doxycycline and made an uneventful recovery.

The fourth patient was a 37-year-old woman who visited the arrival hall of the airport on August 14. On August 27 she developed diarrhoea, nausea and fever. Her general practitioner started amoxycillin but her symptoms worsened and she developed jaundice. She was hospitalised in the hospital of Genk, where a thrombocytopenia of 34.000/mm^3 was found. A blood film on the 3rd of September revealed *P. falciparum* with a parasitaemia of 10%. She was transferred to the University Hospital of Antwerp where she stayed 6 days in the Intensive Care Unit because of very high parasitaemia (28%), haemolytic anaemia and diffuse intravascular coagulation with thrombosis of several toes. She was treated with a partial exchange transfusion with 6 units of packed cells, intravenous quinine, oral artemisinin and doxycycline. She was discharged cured on September 15 without further treatment.

The fifth case, a 60-year-old security worker, colleague of the first and the third, was on night duty during the month of August. His symptoms started on August 28, with vomiting, fever and myalgias. From the 1st of September on he took antipyretics, prescribed by his general practitioner. Because of persisting symptoms he was hospitalised in Ronse on the 4th of September. He presented with fever (39°C), jaundice, and splenomegaly. Laboratory examinations showed a severe thrombocytopenia (11.000/mm^3), hyponatraemia, immeasurable haptoglobin and positive fibrin split products. On the 5th of September a thick smear yielded the diagnosis of *P. falciparum*.

The patient received a first dose of mefloquine but vomited soon after. He was transferred to the University Hospital of Antwerp, where a parasitaemia of 3,3% was found. He presented with confusion, possibly provoked or enhanced by mefloquine. He received IV quinine and doxycycline and recovered completely.

The sixth case was a 62-year-old man who visited the airport three times during the month of August. He became ill on the 9th of September. A thick smear ordered by his general practitioner yielded the diagnosis of *P. ovale*. He was treated on an ambulatory basis with stilfadoxine/pyrimethamine. As the original slide was not available any more for revision, the species was confirmed by the presence of antibodies against *P. ovale* (titre 1:80).

Neither of these patients had travelled to a malaria endemic region in recent months, nor had received a blood transfusion or was an IV drug user. The only common risk factor was that they were present in the airport around the 14th of August 1995.

Transmission

The six cases must have been bitten by one or more infected Anopheles in the airport of Brussels, other risk factors being absent. The weather conditions in Belgium at that time were favourable for the survival of tropical Anopheles and for the completion of the *P. falciparum*'s sporogonic cycle in the Anopheles that supposedly arrived with one of the flights out of a tropical country, most probably from sub-Saharan Africa. During a visit of the airport the problem of malaria vector control was discussed with employees and health officials (Elsen P., unpublished report). Apparently, on departure from endemic countries, the cabins are correctly treated with an insecticide, the crew, the passengers and their hand luggage being present. On the contrary, the compartment where live animals are transported is not treated at all for fear that they might not support the insecticides. Given the exposure histories of the patients, the two locations likely to be involved in the transmission of malaria are the underground luggage sorting terminal and the arrival hall, where families welcome travellers. In between these two halls is the luggage distribution hall, where travellers pick up their luggage. This hall is separated from the public in the arrival hall by automatic doors.

Handling of cargo is done at the other side of the airport and is therefore less probably involved. However, interviewed employees report that often swarms of mosquitoes escape while opening the containers.

DISCUSSION.

Patients

Six patients were diagnosed with airport malaria in the summer of 1995. Although their number is small compared with the total number of imported malaria cases, it is an important problem because of the exceptionally severe course of the disease: in a review published in 1989 the case fatality rate was 16,7%.(14) This can be explained by several factors: in the same review 93% of cases were caused by *P. falciparum*, airport malaria occurs in non-immune subjects, the lack of history of travel to a malaria-endemic country causes a considerable delay in the diagnosis, and the automation of blood counts and differential counts precludes the accidental finding of trophozoites in blood films.

Transmission

Probably infections were transmitted by at least three mosquitoes: two different species of *Plasmodium* were detected (Table 1), and *P. falciparum* infections occurred on two different floors.

The areas of highest risk for importation of infected mosquitoes are Central and West Africa and the islands in the Indian Ocean.(15) Given the colonial past of Belgium, the Brussels airport developed an intense traffic with sub-Saharan Africa.

All patients worked at, or visited the airport in August 95, an exceptionally hot month with a minimal temperature above 19°C during more than 10 days. In such hot conditions an Anopheles can live up to one month, and the sporogonic cycle of *P. falciparum* takes 3 weeks, in contrast with the 6 to 7 weeks under normal Belgian climatological circumstances.(16) Nevertheless the 10 days period is not sufficient for a sporogonic cycle, hence the infection was transmitted through elsewhere infected mosquitoes. It has been suggested that European Anopheles species could infect themselves by feeding on passengers with malaria and transmit the parasite afterwards.(17) This hypothesis is rejected because autochthonous *Anopheles* have almost completely disappeared and their ability to transmit *P. falciparum* has never been proved: never *P. falciparum* positive *Anopheles* were found, nor successful experimental transmission obtained (18,19). The last reported case of malaria at European latitude occurred in 1958 in the Netherlands, where *An. atroparvus* transmitted *P. vivax*.(16)

The risk of airport malaria is highest in summer, not only because local weather conditions are favourable, but also because this period corresponds to the

period of high transmission in many endemic areas due to the increase in vector population. Nonetheless, in most countries the infection prevalence in mosquitoes is lower than 1 %, hence we suspect that actually many more than 100 mosquitoes have been imported, following our deduction that at least 3 different infected mosquitoes were involved. It seems highly unlikely that such an important number could have been imported by one single flight, suggesting that antimosquito measures were at least deficient.

Prevention

In passengers' flights, the possible sources of infected *Anopheles* are the cabin, the flight deck, the hand luggage, the cargo hold and the animal compartment.

The WHO recommends the use of manual aerosol application of a standard reference aerosol containing pyrethrum extract and DDT or permethrin to the passengers' cabin and all other accessible interior spaces of the aircraft after embarkation of passengers and closure of the doors, but before take-off.(20) Empty aerosol cans must be shown on arrival as evidence of disinsectisation.(14,20) Because of the perceived risk of the entry of mosquitoes into the airport buildings, spraying with the residual insecticide dieldrin of the tunnels which convey baggage containers by remote control into the baggage halls, and of the closed passageways for passengers, has been applied at Charles de Gaulle airport of Paris.(21) Since the introduction of this measure no cases of airport malaria occurred in France during 14 years until 1994, when again 6 cases were reported at the airport of Roissy.(22) Different authorities share responsibilities: airlines are responsible for vector control on the aircraft, but the airport health authority must keep the area within the airport perimeter free of the vectors of diseases of epidemiological significance to international health, and must prevent disease vectors from gaining access to aircraft.

The aerosol disinsectisation procedure is not always satisfactory. The use of insecticidal aerosol is 100 % efficient for the killing of mosquitoes that are present in the cabin, however efficacy is only 80% for mosquitoes that are within the hand luggage rack. The mosquitoes in the luggage hold are efficiently killed, but 15 % of those staying in relatively closed containers survive.(15) In an experiment with a Boeing 747B aircraft Russell found that mosquitoes survive for more than 7 flight hours in the wheelbays.(23) Moreover, previous studies in other airports have shown considerable neglect in the application of recommendations of disinsectisation of aircraft.(15)

CONCLUSION

In a case of fever of unknown origin, airport malaria should be considered in the differential diagnosis, especially during hot summer months. Besides the travel history, the clinician should question the patient if he or she lives near, works at or has visited an airport recently. Whenever thrombocytopenia is encountered in a patient with unexplained fever, the blood film should be examined for malaria trophozoites.

Although vector control measures may cause inconvenience to passengers and additional work to an already busy aircrew, it is important to adhere strictly to the recommendations of the WHO concerning disinsectisation of aircraft. Moreover, procedures should be reinforced in hot summer months. The walls of the compartment of live animals should be treated with residual insecticides and the walls of the cages with an insect repellent during embarkation. In addition to the cabins and the cargo hold, disinsectisation of wheel bays could be considered.(23) The personnel involved in checking the luggage should be equipped with insecticidal aerosols and protected by an insect repellent. All working areas that receive incoming luggage should be isolated from the luggage access ways by plastic flaps impregnated with residual insecticides.

Special attention should be given to cargo flights. All containers and packings should be sprayed before closure in the country of origin. The walls of the space where these containers are unloaded should be treated with residual insecticides and the employees involved should use insect repellent.

SAMENVATTING

Tussen 1969 en 1996 werden in Europa 64 gevallen van luchthavenmalaria geregistreerd, overwegend in Frankrijk, Zwitserland en België.

In de zomer van 1995 werden zes patiënten besmet op de luchthaven van Zaventem, drie bedienden en drie bezoekers. Bij één patiënt werd de diagnose pas postmortem vermoed, en finaal gesteld op de stoffelijke resten, via PCR en DNA sequencing.

De infecties waren te wijten aan twee verschillende *Plasmodium* species, en vonden plaats op ten minste twee verschillende locaties van de luchthaven. Bij bevraging blijkt dat de passagiersruimte correct met insecticide wordt behandeld volgens WGO normen, maar dat de inhoud van de handbagage, de bagageruimte, de dierenkooien, de opbergruimte voor het landingsgestel, en containervluchten in het algemeen nog mogelijke schuilplaatsen bieden aan geïnfecteerde muggen.

Bij koorts van onbekende oorsprong moet aan luchthavenmalaria gedacht worden tijdens warme zomers, en bij

trombopenie. Bijkomende muggenbestrijding is aangewezen, met aandacht voor bepaalde categorieën van het personeel, voor de containerinhoud en -terminal, de dierenkooien, de opbergruimten voor het landingsgestel, en de overgang tussen bagagesortering en -ophaling.

RÉSUMÉ

En Europe, 64 cas de malaria contractés dans les aéroports ont été enregistrés entre 1969 et 1996, la plupart en France, en Suisse et en Belgique.

Durant l'été 1995 six cas de malaria se sont déclarés à l'aéroport international de Bruxelles, Belgique. Parmi les six patients, trois étaient des employés de l'aéroport, les trois autres des visiteurs occasionnels. Un des patients décéda, le diagnostic ayant été établi postmortem par amplification PCR et séquençage d'ADN après exhumation.

Deux espèces distinctes de *Plasmodium* ont été détectées et les infections ont été contractées au moins à deux étages différents. D'après les informations reçues, la cabine des avions semble avoir été correctement traitée aux insecticides selon les recommandations de l'OMS, mais le contenu des bagages à main, la soute à bagages, la soute pour animaux, l'enchâssement des trains d'atterrissage et les vols à containers ont été identifiés comme abris possibles pour des moustiques infectés.

Lors d'un cas de fièvre d'origine inconnue, une malaria contractée à l'aéroport doit être prise en considération dans le diagnostic différentiel, spécialement durant les étés chauds, et lorsque qu'il y a thrombocytopénie. Des mesures antimoustiques complémentaires devraient être généralisées, en particulier pour certaines catégories du personnel, les containers et leur terminal, les cages d'animaux, l'enchâssement des trains d'atterrissage et le passage entre le triage des bagages et leur réception.

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