CLINICAL STUDY

# Dengue fever in the Czech Republic

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**Abstract**

***Background:*** **Dengue fever has become, in Western Europe, the second most frequently imported disease after viral hepatitis A.**
**Objectives: Dengue fever was diagnosed at the Department of Infectious Disease, University Hospital in Brno, so the authors decided to make local physicians aware of the possibility of the disease being contracted by Czech travelers.**
**Methods*:* The first two cases of dengue fever, with the patients hospitalized at the Department of Infectious Disease, University Hospital in Brno, Czech Republic, are described.**
***Results:*** **A young couple contracted this infection in a region usually visited by tourists in Thailand. The disease broke out 12 hours after their return home. The clinical and laboratory pictures of the disease and the kinetics of serological responses are described in detail.**
***Conclusion:*** **The chief diagnostic clue with this disease, beside a visit to a high-risk area, can be considered a sudden onset of fever accompanied by marked fatigue, myalgia, and arthralgia. Laboratory tests showed characteristic thrombocytopenia, leukopenia, and pathological values of AST and ALT. The clinical picture is characterized by symptoms of persisting fatigue and exhaustion, even after the fever has subsided.** ***(Tab. 3, Ref. 23.)***
**Key words: dengue, dengue fever, dengue hemorrhagic fever.**

The explosion of travel and business has brought to the spectrum of the infectionists attention diseases we considered exotic a few years ago. Recently, dengue fever has become the second most frequently imported disease (after viral hepatitis A) in Western Europe, mainly as a result of serology-based diagnosis (2).

Dengue fever is caused by one of four serotypes of viruses belonging to arboviruses. The vector is a mosquito of the Aedes genus. In nature, the reservoir may be monkeys in some regions, however, the source of infection is primarily man developing viremia. Female mosquitoes may transmit the virus from day 8 after sucking the patients blood until the end of their lives (1—3 months). Dengue fever was first described in Batavia as early as 1740 (1) and, from 1800, there were repeated epidemics of the disease from the territory of the United States across the Caribbean and the Mediterranean region to Australia. A transient decline in 1980 was followed by its considerable spread so today dengue fever is endemic in more than 100 countries of the world (1), and one of the main risks in the tropical regions of Asia, Africa, and the Americas. Infected mosquitoes may also be imported, but the risk of further spread in the mild climatic zone is zero (1). After 1980, there have been repeated cases of importation by viremic travelers and spread of the disease to other individuals in Queensland, Australia (6, 15). Each year, some 80—100 million persons contract the disease, with several hundred thousand individuals developing the hemorrhagic form. Even in treated individuals, case fatality rate is as high as 5 % (5, 9). The cause of the spread of the disease in recent years has been multifactorialincreased resistance of mosquitoes to the insecticides used, importation of mosquitoes to yet unaffected regions; a role is also played by air transport and expansion of slums (1). The greenhouse effect with an increase in the average temperature by 2 °C could result in further spread of the disease into the moderate climatic zone (10). There have been several reports of mother-to-fetus transmission; during childbirth, the woman is mainly at risk of bleeding. Transmission of the disease to the healthcare personnel via a needle contaminated with the patients blood has also been described (21, 23).

The incubation period is 3—14, most often 10 days; this is followed by a sudden rise in fever up to 42 °C with intense, in some cases devastating headache, pain in muscles and the spine.

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**Tab. 1. Some of the haematologic and biochemical results — man.**

| Date | 30.9. | 3.10. | 5.10. | 7.10. |
|---|---|---|---|---|
| Leukocytes | 2.6 | 3.8 | 4.3 | – |
| Thrombocytes | 80 | 87 | 176 | – |
| ALT | 0.32 | 1.14 | 1.43 | 1.79 |
| AST | 0.50 | 1.38 | 0.89 | 1.38 |

**Tab. 2. Some of the haematologic a biochemical results — woman.**

| Date | 30.9. | 2.10. | 5.10. | 7.10. |
|---|---|---|---|---|
| Leukocytes | 1.7 | 2.6 | 3.8 | 4.5 |
| Thrombocytes | 124 | 76 | 219 | 290 |
| ALT | 2.40 | 3.59 | 3.02 | 1.75 |
| AST | 6.30 | 6.65 | 2.93 | 1.50 |

The patient also complains of extreme weakness and, occasionally, diarrhea has been reported as another manifestations of the disease (7). The features include facial erythema and reddening of the conjunctiva. The lymphatic nodes get enlarged. Exanthema manifestations occur in two forms (in 50—80 % of patients). The initial rash resembles a slightly dotted erythema involving principally the trunk and subsiding within 2 days. The first phase of the disease ends after 3—4 days with a sudden drop in temperature and relief. In 50 % of patients, fever recurs within 1—3 days with malaise lasting 2—3 days but not as intense as those at disease onset. At that time, the patient will typically develop rubeliform exanthema across the body except for face, and the exanthema is hyperemic. Convalescence is long-term, associated with considerable adynamia, dizziness and, occasionally, depression. Laboratory investigations may reveal leukopenia with relative lymphocytosis, thrombocytopenia and increases in transaminase levels, with the levels of AST usually being higher than those of ALT (14). Complications of the above clinical pattern include myocardial dysfunction, hepatomegaly or splenomegaly, with peripheral neuritides or cramps reported as neurological complications.

Dengue hemorrhagic fever (DHF), occasionally with the shock syndrome, is associated with a decrease in body temperature: the patient feels unwell, develops tachycardia, a drop in blood pressure with the difference between systolic and diastolic being less than 20 mmHg, petechia, nosebleed, GI bleeding, or gynecological bleeding. Ultrasound may demonstrate ascites, rarely even pleural effusion has been described; hepatomegaly and splenomegaly occur frequently; spleen rupture has also been observed. The case fatality rate of patients in shock is 40—50 %. This form is explained by the immune response in the patient after a previous episode of dengue fever due to another disease caused by another type of the virus; this form occurs more often if preceded by infection with serotype 2 (4, 12, 16, 18).

The diagnosis is based on serology. Evidence of the presence of the virus can be obtained experimentally; the viremia correlates with the period of elevated temperature (22). The virus has been demonstrated in the serum, cerebrospinal fluid, and liver biopsy specimens (4). The diagnosis can be successfully established using PCR on days 2 to 5 of fever (8). Besides, evidence of the virus antigen in the serum and peripheral blood mononuclear cells can be obtained, with the antigens detectable on days 2 to 7 within the onset of the disease, peaking on day 4 (11). The following serological investigations are intended for routine primary care diagnosis: the hemagglutination inhibitory is instrumental in rapid diagnosis (IgM, IgG); however, the most often used tool for obtaining evidence of antibody is ELISA (IgM, IgG, and/or IgA) (17, 20).

Treatment of the disease is symptomatic only; in severe cases, it is advisable to provide sufficient infusion while it is not generally recommended to administer acetylsalicylic acid as an antipyretic.

No vaccine is currently available. The development of live attenuated vaccines against Japanese encephalitis and dengue fever paves the way to elimination of epidemics. However, there is the serious theoretic risk that the vaccinee could develop, when contracting the infection, the hemorrhagic forms of the disease. A theoretical consideration is whether or not vaccination against yellow fever could potentially afford protection also against dengue fever (1, 19).

## Case report

In late September 1998, two young people, a 24-year old man and a 22-year old woman were admitted to our department. They both had traveled from April 1998, first to Germany, the United States, New Zealand, spending the last three weeks before return in Thailand. While in Thailand, they drank only bottled water, had their meals in hotels; they spent some time in Bangkok and in Ko-Samui Island where they lived in a bungalow and swam in the sea. When staying in the tourist resort, they were repeatedly and heavily bitten by mosquitoes. They did not take antimalarics and had not been vaccinated before their trip.

They returned to their home country on 25 September in the morning and started to experience health problems in the evening. The young man complained of sudden, markedly progressing headache, followed by fever with chills and tremor, temperature of 39 °C, he had hallucinations, and described very vivid dreams. There was no recurrence of the tremor, his temperature decreased after antipyretics or poultice always for 2 hours only, and by a mere 1 °C, followed by an increase in the temperature. From 26 September, he complained of marked weakness, pain in joints and muscles, loss of appetite, nausea, and burning of the eyes. On 29 September, he was hospitalized to a catchment department of infectious disease to be transferred to our department on 30 September (her girl friend was admitted to our department on the same day).

The girl also developed problems in the evening of 25 September: temperature of 38.6 °C, headache, one diarrhea-like stool, developing nausea, orthostatic problems, feelings of weakness, pain of muscles all over her body, with persisting fever of 39 °C, loose stools once daily. A general practitioner administered oral cephadroxil, and the patient was admitted to our department on 30 September.

On admission, the young man was described to have petechia on the chest skin; red sclera; tiny nodes could be felt on

**Tab. 3. Results of the serologic examinations – antibodies anti-dengue virus. The values 1:200 and more are considered as positive.**

| Man | 29.9. | 2.10. | 19.1. |
|---|---|---|---|
| Anti-dengue virus IgM ELISA | negative | 1:502 | 1:227 |
| Anti-dengue virus IgG ELISA | negative | negative | 1:700 |
| Woman | 1.10 | 27.10. | 18.12. |
| Anti-dengue virus IgM ELISA | 1:307 | 1:316 | 1:200 |
| Anti-dengue virus IgG ELISA | negative | 1:648 | 1:604 |

palpation below the mandible and in the groins, the liver was enlarged; otherwise, the finding was physiological. As regards the ensuing course, both patients were afebrile beginning 1 October, the man reported transient itching in his gums, the girl had reddening of her palms and face. The clinical course was otherwise uneventful; both complained only of considerable fatigue, still, they insisted on being discharged which they were on 7 October.

The abnormal laboratory findings and their dynamics are illustrated in Tables 1 and 2 (values given in SI units). Both patients had normal erythrocyte sedimentation rates, C-reactive protein, bilirubin, and erythrocyte counts. High lymphocytosis (72 %) was present in the girl.

Microbiological findings: both young people had negative serology to influenza A and B, RS virus, adenovirus, viral hepatitis A, and Mycoplasma pneumoniae. The results of stool bacteriology and blood culture, blood smears and serology to malaria, serology to dysentery were all negative. In addition, the girl had negative throat and nose smears; the man had negative urine culture. The patients were discharged with the diagnosis of dengue fever, which was confirmed in both by serology (Table 3), suggesting further dynamics of serological tests. The feeling of fatigue progressively subsided and the biochemical finding normalized within about a month.

## Discussion

Dengue fever as an infection imported upon return from the tropics is diagnosed as the cause of fever surprisingly often, if considered at all. For instance, about 500 cases are imported to Germany each year (1), a Spanish report described a positive result in 37.4 % of febrile travelers returning from high-risk regions (13), and a Swiss paper reported 8 % (5).

Our two patients had a fully typical clinical and laboratory course of benign dengue fever. They were the first two cases of this disease hospitalized in our department. At the Department of Infectious Disease of Pragues Bulovka Hospital, the first case of dengue fever imported from Taiwan (caused by serotype 2) was diagnosed as early as 1991. In the ensuing years, a total of 8 patients with this imported infection were treated at the above department. The serological tests of our patients were performed at the Department of Virology of the Regional Hygienic Center in Ostrava.

Against the background of the current explosion of international travel, we have to be aware of the possibility of importation of infectious disease we virtually never encountered in the past. Dengue fever must have been imported before; however, these cases remained undetected and were all referred to as a "virosis upon return from a trip." No doubt, our diagnostic potential has been expended by the availability of serological evidence of the disease.

The chief diagnostic clue with this disease, beside a visit to a high-risk area, can be considered a sudden onset of fever accompanied by marked fatigue, myalgia, and arthralgia. Laboratory tests show characteristic thombocytopenia, leukopenia, and pathological values of AST and ALT. Other features instrumental in establishing late diagnosis include persisting fatigue and exhaustion, even after the fever has subsided.

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## NEW BOOKS

**Buc M.:** Immunológia. (In Slovak). Bratislava, Veda 2001, pp. 464, Fig. 200, Tab. 66.

The Slovak medical community and those who are interested in natural sciences, but especially in immunology, will be certainly delighted to read this highly interesting book.

It contains updated information, which, otherwise, is difficult to obtain. In addition, it brings many comprehensive Tables and a plethora of illustrations which well supplement the written word. Being aware that several textbooks on immunology appeared also on domestic market, the author has successfully avoided undesired redundancies mainly devoting his attention to the description of most recent developments describing the molecular basis of antigen recognition and immune signalling.

The book begins with a chapter on General Principles of Immune System functions, followed by chapters describing the B and T lymphocyte receptors at antigen presentation and recognition. Especially valuable are descriptions dealing with generation of diversity at antibody production, the comments to intracellular and extracellular immune cell signalling at antigen presentation, the reviews on T cell receptor activation and the chapter on cytokine production and action. Many new data are related of the function and activation of immune cell differentiation antigens (a Table listing over 150 CD antigens is included). The HLA antigens, their function at antigen recognition and during the cytotoxic T cell response are comprehensively described; this is accompanied by the map of corresponding genes and the description of relevant glycoproteins. Finally, the author presents a nice overview of the molecular basis of complement activation, of the recruitment of inflammatory cells, of leukocyte migration and of the adhesive behaviour of endothelium cells.

The book is written in a clear language highlighting the author's ability to select the most important information and group it in a manner providing new valuable data in combination with classical knowledge for beginners. I recommend Buc's Immunology not only to immunologists, microbiologists, virologists and immunologists, but to any specialist in natural sciences, who wishes to explore the fascinating world of molecular interactions underlying well known immunological phenomena. In this sense I believe that this book will fulfil the goal to become an unevitable title in each medical library.

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