Zeitschrift: Acta Tropica
Herausgeber: Schweizerisches Tropeninstitut (Basel)
Band: 35 (1978)
Heft: 1

Artikel: Progresses in ecology and epidemiology of rickettsioses : a review
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DOI: https://doi.org/10.5169/seals-312366

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Acta Tropica 35, 5–21 (1978)

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Progresses in ecology and epidemiology of rickettsioses

A review

F. WEYER

Summary

Despite the great successes in control, none of the rickettsioses pathogenic to man have been eradicated. Therefore, it is necessary to preserve the knowledge about these once devastating and important diseases, because the present situation could change suddenly. Under this aspect, a short review is presented with special reference to recent findings and actual problems in the ecology and epidemiology of rickettsioses.

Particular emphasis is given to louse-borne and tick-borne typhus fevers. Some foci of louse-borne typhus continue to exist in Africa (Rwanda, Burundi, Ethiopia), comprising several thousands of cases annually, and on a smaller scale in Central and South America. In Africa, the control is complicated by the increasing resistance of lice to insecticides. In Southern Europe, special interest is paid to the late relapses of typhus fever (Brill-Zinsser disease).

The constant and alarming increase of cases of Rocky Mountain spotted fever in the United States during the last years is of particular interest and is due to the more frequent contact of people with infected ticks. As to Old World tick-bite fever, research is mainly directed to the detection of causative agent reservoirs in animals and ticks. The disease is, as zoonosis, more widely spread than previously assumed. Strains of rickettsiae identical or closely related to the known rickettsial species were isolated, for instance, in Thailand, Pakistan, Armenia, Czechoslovakia, and more recently in Austria and Southern Germany.

Key words: Rickettsioses, ecology, epidemiology, epidemic typhus, Brill-Zinsser disease, tick-borne typhus fevers, review.

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Introduction

For a long time, few data about incidences of typhus fever and other rickettsioses have been published, so that many people believe that these diseases are no longer of any importance. We must not forget, however, that none of the rickettsioses transmissible to man have disappeared or have been eradicated by special control measures. The present situation can change unexpectedly. Therefore, authorities concerned with public health, including the World Health Organization (WHO), stress the fact that the experiences and knowledge in the field of rickettsioses, gained by difficult and arduous investigations, must be preserved in order to avoid dangers from these diseases [9, 109].

This has been emphasized repeatedly. In 1972, the WHO organized in Washington an International Symposium on the control of lice and the diseases transmitted by them at which some 30 papers were presented [66]. The themes dealt with new methods of lice control, resistance against insecticides, experiences in the control of lice and typhus fever in Yugoslavia, Hungary, South Africa and Bolivia, distribution and ecology of typhus fever in the world, and with questions of reservoirs and late relapses. In June 1976, the "IInd International Symposium on Rickettsiae and Rickettsial Diseases" was held in Smolenice (Czechoslovakia) and dealt, among other problems, with ultrastructure, biochemistry, metabolism, biological properties [107] and antigenic structure of rickettsiae [58], advances in research of diagnostic procedures and knowledge of immunity in rickettsial infections [41], along with a series of new contributions on ecology [67], various epidemiologic aspects (main results of observations 1968–1975) [97], and with the significance and control of rickettsioses. The "2nd International Colloquium on Natural Foci of Infectious Diseases in Central Europe" from 25.–28. 2. 1976 in Graz (Austria) also considered rickettsioses, and in the meeting of German-speaking societies of tropical medicine from 24.–26. 3. 1977 in Lindau (Federal Republic of Germany) rickettsioses were discussed in a special session.

Some of the observations and facts presented at these meetings are mentioned in this review including the most important progresses and some current problems in the field of rickettsioses, especially the incidence of diseases, properties of the causative agents, reservoirs and transmission, i.e. *ecology and epidemiology of rickettsioses* in its broadest meaning. Ultrastructure, metabolism of rickettsiae and related questions are not included in the present review.

Epidemic (louse-borne) typhus

The classical, epidemic, louse-borne typhus, transmitted to man by lice, is still the rickettsiosis with the greatest significance to public health and it belongs to those diseases that have to be reported and are continuously checked by the WHO. Fortunately, the times of great typhus fever epidemics with their many thousands of victims are over. The decisive change came after the World War II through the introduction of antibiotics in therapy and application of effective insecticides, especially of DDT, against lice as vectors of epidemic typhus [111]. The disease has almost completely disappeared from those areas in Europe, Asia, South and North Africa, where it used to be widely distributed. At present, the most important remaining foci are found in Africa, mainly in Rwanda and Burundi [110]. Of the 10,548 officially reported cases in 1975 (148 deaths), 10,308 were in Africa and of these 9,000 in Burundi alone [113].

Ethiopia must be considered as another focus in Africa. It is true that no cases of typhus fever have been reported since 1971 – probably due to organizational difficulties – but until then 2,000–3,000 cases had been reported each year. It is unlikely that this situation has changed remarkably since that time.

During 1975, according to WHO [115] a total of 8,065 cases (106 deaths) occurred worldwide. 94.6% of these again came from Africa. In Burundi, the number of cases decreased to 7,022. In Uganda, however (at the border to Rwanda), 185 cases (6 deaths) have been registered for the first time.

Apart from Africa, there exist only some insignificant foci of epidemic typhus in Middle and South America (Mexico, Bolivia, Ecuador, Peru, Guatemala). In Peru, two small epidemics were reported in 1976, one in the springtime with 33 cases and the other near the end of the same year with 22 cases (8 deaths) [114]. In Bolivia, 150 cases and in Ecuador 16 cases were registered [115]. In Peru, 129 cases have already been reported during 1977 [116].

Although the real number of cases in the world may be greater than the number of reported cases, this fact is, in comparison with other diseases, of no practical importance. On the other hand, the question is justified, why this disease is still present and why despite favourable conditions, the elimination of the remaining foci of typhus fever cannot be achieved. The population at risk lives under very primitive conditions in widely scattered and barely accessible mountain villages. As a result, control would be very difficult and expensive. Besides, there is, especially in Africa, an increasing resistance of lice to insecticides. Insecticide resistant populations of lice have been known for a long time in several regions of the world, but this was not a serious obstacle to their control. The resistant populations were small and, moreover, it was a resistance in the first place to DDT. There were and are enough other effective insecticides at hand, although they have some disadvantages in comparison with DDT. It seems that particular difficulties appeared in Rwanda and Burundi in connection with the resistance of lice against several otherwise effective insecticides. From Ethiopia, a resistance of lice against malathion was reported [90].

The possibility to eradicate epidemic typhus is very promising because it is an anthropozoonosis involving no animal reservoirs in the normal life cycle of the agent. By contrast, all other rickettsioses (with exception of trench fever) are zoonoses, in which the man is merely an accidental host and does not represent an indispensable member in the biological cycle of the agent. The consensus that only man represents the warm-blooded reservoir of the agent of typhus fever, *Rickettsia prowazekii*, was shaken by the detection of the same agent in goats, sheep and some ixodid ticks infesting these domestic animals and zebus [71]. This discovery, made in Ethiopia, gave rise to the hypothesis that domestic animals and ticks may play a role as reservoirs of *R. prowazekii* and the disease caused by them. This stimulated a great deal of research.

The idea that domestic animals may be involved as reservoirs in the life cycle of the agent of epidemic typhus was at first supported by the identification of antibodies against *R. prowazekii* in these animals in regions where typhus fever still existed, for instance in Egypt, Mexico and Ecuador [62]. However, extensive serological investigations of domestic and wild animals, mainly in North Africa, along with attempts to infect experimentally domestic animals and ticks with *R. prowazekii*, could not confirm this suspicion [18, 24, 51a, 57]. It was not possible to detect any clinical symptoms or to isolate the rickettsiae from the blood of ewe-lambs after being inoculated with *R. prowazekii* and with the closely related species *R. canada* (see below) [85]. It seems that agglutinins against *R. prowazekii*, which can sometimes be found in the blood of domestic animals, are probably induced by other organisms [84]. In Serbia, complement fixing antibodies were found in the blood of cows and sheep not only in hyperendemic areas of typhus fever but also nearly in the same abundance (in sheep more than 30%) in places, where typhus fever has not existed for more than 20 years [61]. Occurrence and identification of such antibodies cannot be considered as a reliable evidence of an infection in the past.

Therefore, there is no doubt that domestic animals may play only a temporary and locally limited role in the epidemiology of epidemic typhus, without any influence on the possibility of eradication of the disease. Domestic animals and ticks were not involved in the great epidemics of the past, chiefly those in Europe and Asia.

Nevertheless, the observations made in Ethiopia remain important and interesting. The same is true for the recent detection of rickettsiae in the eastern flying squirrel (*Glaucomys volans volans*) in Florida and Virgina [7, 8]. Here, 13 strains of rickettsiae – 3 of them from fleas and lice parasitizing on the squirrels – were isolated and tested in detail. Considering all known facts, these rickettsiae cannot be distinguished from *R. prowazekii* or are identical with this species. Although this finding may be sensational for all rickettsiologists, it will not allow the conclusion that flying squirrels represent a reservoir for *R. prowazekii*. But we may remember that it was also a great surprise, when the rabbit tick, *Haemaphysalis leporis palustris*, in Canada was found to contain a rickettsia, which showed close relationship to *R. prowazekii* and *R. mooseri* in their antigenic structure and which, therefore, was systematically included in the typhus group of rickettsiae.

This species named *R. canada* has been the subject of a great number of investigations. At first, its behaviour was studied in ticks and in several warm-blooded animals [13]. Later on, an intranuclear propagation and a transovarial transmission (like in members of the spotted fever group) could be demonstrated in *Dermacentor andersoni*. The rickettsia also multiplied in body lice, though its behaviour was clearly different from that of *R. prowazekii* and *R. mooseri* [112]. Transmission experiments showed a good adaptation to soft and hard ticks [38]. The rickettsia could be demonstrated in *Ornithodoros papillipes* and *O. moubata* up to 735 and 588 days after inoculation. The ticks were also infected after feeding on guinea pigs. In *O. papillipes* and *Hyalomma dromedarii*, a transovarial transmission was seen, but not a transmission by feeding infected ticks on guinea pigs. However, the results of all these interesting and comprehensive investigations cannot explain the close relationship of the species to *R. prowazekii* and *R. mooseri* and cannot answer the question whether *R. canada* phylogenetically belongs to the Rocky Mountain spotted fever group or to the typhus group. It is not certain, whether *R. canada* is pathogenic to man, although there is serologic evidence according to observations made in the USA [6].

Thus, we can still start from the fact that among warm-blooded organisms humans are the only reservoirs for the typhus agent *R. prowazekii*. Through careful evaluation of many case histories and by experiments it has been proved that some persons keep their rickettsiae without any symptoms after reconvalescence from typhus fever. Sometimes, these persons are affected by a *late relapse*, well known as Brill-Zinsser disease, after years or even decades. The reasons for the persistence of rickettsiae and for the origin of such a relapse are unknown. Certain criteria show, however, that a diminished resistance through other diseases may provocate relapses. In their case history, some patients had mentioned paratyphoid fever, leptospirosis, influenza and shigellosis [52]. In any case, there is no doubt that lice can infect themselves on patients with Brill-Zinsser disease, in spite of its relatively mild clinical course. This phenomenon has been known for a long time, and has been re-confirmed by new experiments [28]. In a lice-infested population, cases of Brill-Zinsser disease can become the source of new cases of epidemic typhus [28, 53], thus confirming that epidemic typhus in this way can survive interepidemic phases. Incidentally, late relapses are known in trench fever, whose agent, *Rochalimea quintana*, is also transmitted by lice. The longest observed interval lasted about 32 years [54].

Interesting data were collected in Yugoslavia and Czechoslovakia about cases of Brill-Zinsser disease registered during the last years, and about some questions connected with this phenomenon. In Yugoslavia, 651 first attacks of epidemic typhus occurred between 1961 and 1971 [28]. Since 1964, Brill-Zinsser disease were officially registered there. 803 cases were observed between 1964 and 1975, 623 of them in Bosnia alone. In Serbia at the same time 107 cases were investigated [60]. In more than 26% of the cases there was an interval of 30–39 years between the first attack and the relapse. In the southern part of East Slovakia, 37 cases were registered between 1956 and 1971 [53]. Further observations were made in Romania [19]. Here most of the relapses appeared 10–20 years after the first attack. 54% of the persons who had had epidemic typhus showed antibodies in their serum, some of them for up to 50 years after the affection. Similar findings were made in a group of the population of western Bosnia that suffered from a severe epidemic of typhus fever during World War II [5]. This population was resettled after the war in a region without lice and typhus fever, thus giving us an opportunity to study Brill-Zinsser disease.

In the program to eradicate typhus fever in Serbia, which has been going on for many years, the detection of cases of Brill-Zinsser disease plays an important role [4]. A correct diagnosis is absolutely essential. An improvement in diagnostic methods is also of interest [63]. When comparing different serological procedures, the indirect micro-immunofluorescence test is considered to be the most sensitive one [64]. This method can be used in the differentiation between first attack and relapse [59].

Cases of late relapses which can occur in all regions where persons are living with a history of typhus fever, are at present quite problematic, particularly because lice can get infected on such cases, this depending on the density of infestation with lice [28]. The control of lice should not be neglected. In this context, we have to remember that the number of persons infested with lice has been steadily increasing for more than 10 years, especially in "highly developed" countries [32, 93, 94, 110] (the cited publications are only hints as regards the situation). Although these "lice of affluence" chiefly involve head lice, we have to bear in mind that head lice are also able to become infected with, and transmit *R. prowazekii* (*Borrelia recurrentis*, the agent of relapsing fever, as well), a fact, that was recently re-confirmed experimentally [56]. Likewise, rickettsiae can develop in crab lice [108].

Murine (flea-borne) typhus

Murine typhus, which is closely related to classical typhus and transmitted by rat fleas, mainly by *Xenopsylla cheopis*, presents no actual problems. The causative agent, *R. mooseri*, and its behaviour in the plague flea, were investigated by means of electron microscopy. This led to quite impressive pictures [39]. The successful control of rats and rat fleas has considerably reduced the number of human cases, especially in the USA, but this rickettsiosis has also not yet been extinguished. During the last years, cases were reported from Vietnam, Thailand, Mexico, Guatemala, Costa Rica and also from the Mediterranean area [for references see 110]. Recent data about murine typhus came from Malaysia and Israel. In a village in Malaysia, 45% of the inhabitants and 35% of the examined rats showed antibodies to *R. mooseri* [12]. There, human cases of murine typhus have also been observed. Between 1969 and 1972, more than 100 patients treated in hospitals, some with severe symptoms, have been reported in

Israel [79]. The number of cases decreased distinctly since 1948/49, but increased again since 1972. Murine typhus is primarily a rodent disease, mainly of rats. Attempts to eradicate this disease are therefore limited.

Tick-borne typhus fevers of the Old World

The tick-borne rickettsioses, tick-borne typhus fevers in a comprehensive sense, occur chiefly in warm countries. They are found on all continents, but mainly as sporadic cases. In the Old World, they have a relatively mild clinical pattern. The Asian tick typhus has gained public health significance because of the great number of cases and their wide geographical distribution. It is found from Central Asia to Siberia, on the islands in the Japanese Sea and on the west coast of the Pacific Ocean. Foci of the disease also exist in Northern Asia (Tula region) [119].

Wild animals, chiefly rodents and, furthermore, ixodid ticks are the natural reservoirs for tick-borne typhus fevers, because rickettsiae in ticks are passed not only transstadially but also transovarially to the following generations. This transovarial transmission was verified with *R. rickettsii*, the agent of Rocky Mountain spotted fever, in the laboratory and followed up to the 11th generation [17]. Even after such a long time, 100% of the offspring of ticks may still be infected. Thus, ticks and their relationship to rickettsiae have gained an increasing interest for quite some time [29, 30, 33, 48, 51].

Depending on the geographical distribution, we can differentiate between fièvre boutonneuse, African, Indian, Asian, Siberian and North Queensland tick-borne typhus fevers and at last three more or less related species of agents: *R. conorii*, *R. sibirica* and *R. australis*. During the last years, investigations primarily concerned the search for rickettsial strains in ticks and wild animals, and serological surveys. It was found that these rickettsioses, at least in the form of zoonoses, are remarkedly wider distributed than had been previously suspected. Strains of rickettsiae, identical with or closely related to the known species *R. conorii* and *R. sibirica*, were isolated from ticks in West Pakistan, Thailand [74, 75], Israel [31] and Armenia, (USSR) [98, 99]. Three species of ixodid ticks were collected in 7 districts of Armenia. In 105 of them rickettsiae belonging to the spotted fever group were found. Thirty-seven strains of this group were isolated from *Dermacentor marginatus* and 2 strains from *D. reticulatus*. Furthermore, antibodies against antigens of this group were detected in man, cows, sheep and mice. The isolated strains were tested in detail [1]. Thirteen infections of man, some of them rather severe, were observed on the coast of Israel [34]. Additional 11 cases from another region were studied between 1969 and 1972 [79]. The agent involved was probably *R. conorii* though the clinical pattern resembled Rocky Mountain spotted fever.

Some years ago, strains of rickettsiae belonging to the spotted fever group were also detected in ticks in Czechoslovakia [68, 69]. It was possible to isolate

24 strains from *D. marginatus*. They were later studied more intensively [118]. Antibodies to the agents of this group were seen in 66 animal sera, including 10 from 114 cows. A species isolated in Central Slovakia was carefully investigated and appears to be a new one. The name *R. slovaka* is proposed for this species as a new member of spotted fever rickettsiae [104]. Spotted fever group rickettsiae were detected in *Ixodes ricinus* in South Bohemia [70a]. Antibodies to rickettsiae of the Rocky Mountain spotted fever group were found in wild animals in Italy, Yugoslavia and Austria [92]. Rickettsiae of the same group could be isolated from *D. marginatus* in Southern Germany [70] and in Tyrol [2]. The rickettsiae isolated in Tyrol and Southern Germany are very similar to or identical with *R. slovaka*. A new spotted fever group rickettsia was isolated from the brown dog tick, *Rhipicephalus sanguineus*, in USA, investigated in detail and named *R. rhipicephali* [17a, 18a]. In Oregon (USA) a rickettsial strain related to the spotted fever group was found in *Ixodes pacificus* [37]. After many years of investigations in Queensland, *R. australis*, the causative agent of Queensland tick-borne typhus, was detected in *Ixodes holocyclus* and *I. tasmani* [21].

It is noteworthy that the tick-borne typhus fever of Africa and of the Mediterranean region, fièvre boutonneuse, with *R. conorii* as its agent, has gained some importance with regard to tourism, because many attractive places exist in these areas. The tendency to stay in the open air longer, for instance when camping, visiting safari parks and the like has enhanced the danger of contact with infected ticks. Tick-borne typhus fever has already been brought into the Netherlands, Germany and Switzerland by returning tourists [110].

Fièvre boutonneuse can be differentiated into a field- and a domestic-form [2]. The difference between the two forms is based only on the species of ticks acting as a vector. Quite a number of not recognized or incorrectly diagnosed cases such as those reported from Italy [22], should be added to the few human cases that have become known.

Rocky Mountain spotted fever

The current situation of Rocky Mountain spotted fever in the USA is of special interest. From the clinical point of view, this is the most severe rickettsiosis. Formerly, a fatality rate of about 90% was recorded in some places. Until 1949, an annual average of 500 cases was counted. This number decreased to less than 200 within the next 10 years. Despite an improved diagnostic technique, an effective therapy and sufficient knowledge of the ecology of the disease, especially of the reservoirs and the distribution of the vectors, the disease incidence then surprisingly and significantly increased from year to year [14–16, 35, 36, 87]. Between 1970 and 1975, a total of 3601 cases were registered with a yearly incidence of 380, 432, 523, 668, 754 and 844 cases, respectively. In 1976 the number of cases climbed to 892, the highest number of cases ever recorded [15].

Of 2,757 cases reported between 1970 and 1974 it was possible to analyze 1,522 (55%) cases clinically and epidemiologically [36]. Accordingly, 58% of the patients mentioned that they had been bitten by ticks. The patients were exposed to 456 dogs. 43% of these dogs were infested by ticks and only 19% were believed to be free of ticks. The average mortality reached 6.8%, in black people 13.9%, in white people 5.8%, in males 8.2%, in females 4.5%, in patients over 30 years 13.9% and in patients of less than 30 years of age 5.4%. Normally, only those cases ended in death which were not recognized or were diagnosed too late [55]. Recovery is possible, if treatment (with antibiotics) starts not later than on the 6th day after the onset of the disease. The correct and efficient diagnosis is a life-saving problem. Therefore, the typical symptoms, clinical features, and the diagnostical and therapeutical possibilities should be emphasized continuously. One out of 4 patients will die, if diagnosis or treatment are wrong. For a quick diagnosis and prompt confirmation, an identification by immunofluorescence of the rickettsial agent in skin biopsies has been recommended [117].

Although the disease occurs throughout the USA, more than 90% of the yearly reported cases are from areas east of the Mississippi river. Most of the patients came from the five states of the Atlantic coast: Maryland, Virginia, North and South Carolina and Georgia. The disease does not occur in Vermont, Maine, Hawaii and Alaska. More than ⅔ of the patients were children under 15 years of age.

There are evident reasons for this unexpected development which is caused by more frequent and more intensive contact of the population with infected ticks through an increase in working in forestry and the use of forest for hunting, tourism, including spending the night in the open, residential shifting from cities to suburbs, increased keeping of dogs and finally the changing of farmland into forest, thus giving origin to new biotops of ticks [15, 16]. Ticks are active from early spring through fall. Prerequisite for this development is the fact that Rocky Mountain spotted fever is also a zoonosis, for which numerous not yet completely known warm-blooded reservoirs exist [15]. Moreover, because of transovarial infection ticks have an important function in maintaining *R. rickettsii* [17]. Therefore, measures of control and prevention must first of all be based on an educational program for the public, beginning in the schools with information about the disease and the importance of ticks as vectors [16]. The role of dogs in the epidemiology of the disease is not yet fully understood. Probably they are, like man, only accidental hosts of rickettsiae. They may obtain their greatest significance as blood-donors and carriers of infected ticks. Even cats may play a certain role [15]. Dogs and cats can bring ticks into homes and human surroundings.

In Mississippi, 46% of 116 dog sera represented complement fixing antibodies against spotted fever antigens. *R. rickettsii* was found only in one of 129 *Dermacentor variabilis*, but quite unexpectedly 165 (19.9%) of 884 *Rhipicephalus sanguineus*, taken from these dogs, harboured an agent related to but distinct from *R. rickettsii* [18a, 88]. It is interesting that dogs can easily be infected experimentally with Rocky Mountain spotted fever and that the pathogenesis in dogs is similar to that in man [42]. The rickettsemia lasted 10–14 days. Some infections ended fatally. With respect to prophylaxis of man it is of importance that a transmission of rickettsiae by tick saliva normally does not occur earlier than 4–6 [55] or even 10 h after tick attachment [15].

Mite-borne typhus

The mite-borne typhus (chigger-borne rickettsiosis, Tsutsugamushi fever, scrub typhus), distributed in East Asia and in the Pacific region, poses no special actual problems. The ecology of the disease in South East Asia was the object of intensive research work [101]. After the World War II, new and large territories of distribution of the disease were discovered in the Soviet Far East, on the Pacific coast and on the adjacent islands. In some regions, the distribution coincides with that of Asian tick-borne typhus fever. The study of the ecology of mite-borne typhus, especially of the natural reservoirs and the great number of mites of the family of *Trombiculidae*, which can act as vectors, represents a great part of the special scientific literature in the USSR during the last years [45, 95, 96].

Numerous strains of the agent *R. tsutsugamushi* from different geographical regions have been isolated and examined. Most of them cause a mild course of illness in man. In recent years, attacks of scrub typhus or isolations of the agent (mainly from rodents and mites from different habitats) were reported, for instance from Vietnam [47], Thailand [103], West Pakistan [89], Taiwan [27], the Pescadores Islands [26], Kurilian Islands [95], the eastern coast of Kamchatka [120] and Sachalin [91]. In the Pescadores Islands, military personnel from Taiwan had the highest incidence of infection with *R. tsutsugamushi* in 1976 [56a]. In some places in Malaysia, the disease has a mild character and often is unnoticed. In an oil plantation in Malaysia, for instance, 400 workers became ill annually with a disease identified as scrub typhus by serological survey [11].

The physiologic properties of certain strains of *R. tsutsugamushi*, especially their virulence, are still under investigation [25, 43, 77]. Chickens have proved useful for collecting vector mites, since the agent of scrub typhus can survive sometime in chickens [44]. The ingestion of rickettsiae by feeding mites, their development in the life stages of mites and the transovarial passage to the next generation has been the aim of several experimental investigations [102, 106]. Transovarial transmission was demonstrated in different species of *Leptotrombidium*. In Malaysia, *L. fletcheri* and *L. arenicola* play a role as vectors. In laboratory colonies of both species transovarial transmission of the rickettsiae could be shown [72, 73]. In connection with investigations on scrub typhus the technique of microimmunofluorescence has also proved to be very useful [76].

Q-fever

Q-fever will be mentioned only briefly here. In this disease, the zoonosis character is much more pronounced than in the other rickettsioses. Its distribution is world-wide [100] and it is primarily a disease of domestic animals, mainly of cows, sheep and goats. Therefore, Q-fever is chiefly distributed in areas with dairy and cattle-breeding industry. In some countries, Q-fever is at present the most frequent and most important rickettsiosis with respect to domestic animals. This is the case, for instance, in the USSR, Czechoslovakia and South Africa [46, 86]. Accordingly, more attention has been directed to the role of ticks in the biological cycle of the agent and as vectors of the causative agent to domestic animals, particularly in Germany and Switzerland [10]. In South Germany, *Coxiella burnetii* was found in the hard tick *Dermacentor marginatus* [48–51]. Evidently, natural foci of Q-fever exist in these places where the ticks in great numbers are parasitizing sheep. A review of the Q-fever situation in Germany from 1947 till 1973 (number of human cases and the most important epidemics) has been compiled [50]. New reports of cases of Q-fever come, for instance, from East Slovakia [65], Italy [78], Iran [80], Kenya [105] and South Africa [86].

Coxiella burnetii or antibodies to it are repeatedly found, for instance in Tyrol (Austria), Switzerland, Yugoslavia and Italy [40, 92]. The host range of this agent seems to be inexhaustible. Under such conditions and considering the unusual resistance of the agent, which is capable of surviving under humid and dry conditions and of remaining infectious for months, it is still puzzling why the disease does not appear more frequently in man.

The ultimate goal of longtime studies is to develop an effective and well tolerable vaccine for protecting especially endangered persons, such as shepherds, veterinarians and workers in dairies and slaughter-houses or for the vaccination of cattle. These investigations are still in progress. Some successful results have already been reported [3, 23, 81–83].

Conclusions

During the last years, a number of new and interesting facts have been discovered in the field of rickettsioses. They underline the fact that even here, new and promising areas of research can be explored. As far as public health is concerned, the present situation is not alarming because of the low incidence of human cases. Epidemic (louse-borne) typhus and Rocky Mountain spotted fever are still the most dangerous rickettsioses for man. Epidemic typhus is restricted to relatively small foci of more local significance. The incidence of Rocky Mountain spotted fever in USA increased significantly during the last years.

Knowledge and better understanding of this disease complex should not be neglected by physicians and the young generation of scientists because the present situation could change unexpectedly.

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