Rickettsia felis as Emergent Global Threat for Humans

Carlos E. Pérez-Osorio,* Jorge E. Zavala-Velázquez,* Juan José Arias León,* and Jorge E. Zavala-Castro*

Rickettsia felis is an emergent pathogen belonging to transitional group rickettsiae. First described in 1990, *R. felis* infections have been reported to occur worldwide in fleas, mammals, and humans. Because clinical signs of the illness are similar to those of murine typhus and other febrile illnesses such as dengue, the infection in humans is likely underestimated. *R. felis* has been found throughout the world in several types of ectoparasites; cat fleas appear to be the most common vectors. *R. felis* infection should be considered an emergent threat to human health.

Rickettsia felis is a member of the genus *Rickettsia*, which comprises intracellular pathogens that produce infections commonly called rickettsioses. Although the genus has no recognized subspecies, rickettsiae have traditionally been subdivided into 2 groups: the spotted fever group (SFG) and the typhus group. Infections produced by these 2 groups are clinically indistinguishable; however, groups can be differentiated by outer membrane protein OmpA (absent in the typhus group) and by vector. SFG members are transmitted by ticks; typhus group members, by fleas and lice (*1*,*2*). More recently, Gillespie et al. (*3*) added to this classification by designating the transitional group of rickettsiae and describing an ancestral group of rickettsiae.

In 1990, Adams et al. described a rickettsia-like organism, which resembled *R. typhi*, in the cytoplasm of midgut cells of a colony of cat fleas (*1*). The new rickettsia received the initial name of ELB agent after the company from which the fleas were obtained (El Labs, Soquel, CA, USA) (*4*). The first observations, such as reactivity with antibodies to *R. typhi* (*1*), the type of vector in which it was first discovered (*1*), and the apparent absence of OmpA (*5*), suggested that the new organism belonged to the typhus group of rickettsiae (*4*).

The molecular characterization of the organism described by Adams and reported by Bouyer et al. in 2001 provided sufficient evidence to support the designation of *R. felis* as a member of the SFG (*6*), and in 2002, La Scola et al. provided further characterization (*7*). One noticeable characteristic is the temperature-dependent growth of the bacterium, which requires incubation temperatures of 28°–32°C for optimal growth. However, the most striking characteristic of the novel rickettsia was the plasmid DNA in its genome (*8*).

World Distribution in Potential Host Vectors

Soon after the initial description of the typhus-like rickettsia, Williams et al. (*9*) reported that cat fleas collected from opossums in an urban setting in California were infected with the novel rickettsia, but no organism was detected in the tissues of the opossums. Since this report, this organism has been described in infected vectors from 20 countries on 5 continents (*9*). Not until 2002 did interest in *R. felis* increase, when the United States (*9*), Brazil (*10*), Mexico (*11*), and Spain (*12*) were among the first countries to describe cat fleas (*Ctenocephalides felis*) infected with *R. felis*. During the following 5 years, 28 additional reports appeared from all over the world (Table 1). These reports describe new potential vectors being infected with the emergent rickettsia, including the following: fleas, such as *C. canis* (*13*–*15*), *Anomiopsyllus nudata* (*16*), *Archaeopsylla erinacei* (*15*,*17*), *Ctenophthalmus* sp.

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Table 1. Potential vectors infected with *Rickettsia felis* reported worldwide, 1992–2007*

Year	Source of DNA sample	Animal†	Country	Reference
1992	*Ctenocephalides felis*	Opossum	USA	(*9*)
2002	*C. felis*	Cats and dogs	Brazil	(*10*)
2002	*C. felis*	Dogs	Mexico	(*11*)
2002	*C.felis*	Cats and dogs	Spain	(*12*)
2003	*Haemophysalis flava, H. kitaokai,* and *Ixodes ovatus*	Unknown (flagging)	Japan	(*19*)
2003	*C. felis*	Cats	France	(*22*)
2003	*C. felis*	Cats and dogs	UK	(*23*)
2004	*C. felis*	Dogs	Peru	(*24*)
2005	*Anomiopsyllus nudata*	Wild rodents	USA	(*16*)
2005	*C. felis*	Cats and dogs	New Zealand	(*25*)
2005	*C. felis*	Monkey	Gabon	(*26*)
2006	*C. felis* and *C. canis*	Dogs	Brazil	(*13*)
2006	*C. felis* and *C. canis*	Cats and dogs	Uruguay	(*14*)
2006	*Archaeopsylla erinacei* and *C. canis*	Hedgehog and rodents	Algeria	(*15*)
2006	*A. erinacei* and *Ctenophtalmus sp.*	Rodents and hedgehog	Portugal	(*17*)
2006	*Xenopsylla cheopis*	Rodents‡	Indonesia	(*18*)
2006	*C. felis, Rhipicephalus sanguineus,* and *Amblyommma cajennense*	Dogs and horse	Brazil	(*20*)
2006	Unknown flea	Gerbil	Afghanistan	(*27*)
2006	*C. felis*	Cats and dogs	Australia	(*28*)
2006	*C. felis*	Cats	Israel	(*29*)
2006	*C. felis*	Rodents	Cyprus	(*30*)
2007	Mites	Wild rodents	South Korea	(*21*)
2007	*C. felis*	Cats	USA	(*31*)
2007	*C. felis*	Cats	Chile	(*32*)

*PCR was used to detect *R. felis* infection with 1 noted exception.
†Animal host of potential vectors.
‡Quantitative PCR.

(*17*), and *Xenopsylla cheopis* (*18*); ticks, *Haemaphysalis flava* (*19*), *Rhipicephalus sanguineus* (*20*), and *Ixodes ovatus* (*19*); and mites from South Korea (*21*) (Table 1). Despite the large number of potential vectors reported, the only vector currently recognized is *C. felis* because it has been demonstrated that this flea is able to maintain a stable infected progeny through transovarial transmission (*4*). In addition, production of antibody to *R. felis* has been noted in animals after they have been exposed to infected cat fleas (*9*). Other evidence to be considered is the fact that 68.8% of the reports state that the cat flea is the most recurrent vector in which *R. felis* has been detected. These data further support the wide distribution of rickettsiae because they correlate with the worldwide distribution of *C. felis;* this distribution represents a threat to the human population because of lack of host specificity of the cat flea.

R. felis infection is diagnosed by PCR amplification of targeted genes. The genes most commonly amplified by researchers are *gltA* and *ompB*; followed by the 17-kDa gene. Also, 25% of published articles report that *R. felis* was detected by amplifying >2 genes, and all report that amplicons were confirmed as *R. felis* by sequencing. The animal hosts from which the infected ectoparasites were recovered represent a diversity of mammals (Table 1), which included 9 different naturally infested animal species. However, in 16 of 33 articles, ectoparasites were recovered from dogs. Other hosts for ectoparasites were cats (in 13 of 33 reports); rodents (5 of 33 reports); opossums and hedgehogs (2 reports each); and horses, sheep, goats, gerbils, and monkeys (1 report for each animal species).

In summary, the presence of *R. felis* in a diverse range of invertebrate and mammalian hosts represents a high potential risk for public health and the need for further studies to establish the role of ectoparasites other than *C. felis* as potential vectors. To date, whether any vertebrate may serve as the reservoir of this emergent pathogen has not been determined. However, preliminary data from our laboratory suggest that opossums are the most likely candidates.

World Distribution of Human Cases

In 1994, the first human case of infection with the new cat flea rickettsia was reported in the United States (*2*). This became the first evidence of *R. felis'* potential as a human pathogen. *R. felis* infection had a similar clinical manifestation as murine typhus (including high fever [39°–40°C], myalgia, and rash). Although the initial idea was that the murine typhus–like rickettsia had a transmission cycle involving cat fleas and opossums (*2,5,9*), no viable *R. felis* has yet been isolated from a vertebrate host.

Three more cases of *R. felis* infection were reported from southeastern Mexico in 2000. The patients had had contact with fleas or animals known to carry fleas. The clinical manifestations were those of a typical rickettsiosis: all patients had fever and myalgia; but the skin lesions, instead of a rash, were similar to those described for rickettsialpox. In addition, for 3 patients, central nervous system involvement developed, manifested as photophobia, hearing loss, and signs of meningitis (*33*).

As occurred with the fast-growing reports of the worldwide detection of *R. felis* in arthropod hosts, the reports of human cases of *R. felis* infection increased rapidly in the following years (Table 2). But, in contrast, only 11 articles reported human infection by *R. felis* compared with 32 that reported ectoparasite infection with the new rickettsia. Nevertheless, these findings indicate that an effective surveillance system is urgently needed to distinguish *R. felis* rickettsiosis from other rickettsial infections such as murine typhus and Rocky Mountain spotted fever, and from other febrile illnesses such as dengue. Although PCR is still a method of choice for many laboratories, its high cost prevents many from using the technique, particularly in developing countries. Important advances have been achieved in diagnostics, such as the recent establishment of a stable culture of *R. felis* in cell lines that allows its use as antigen in serologic assays differentiating the cat flea rickettsia from others. Use of this culture in the immunofluorecent assay has enabled detection of additional human cases (*38*).

The first autochthonous human case in Europe was reported in 2002, which demonstrated that *R. felis* has a potential widespread distribution and is not confined to the Americas. It also confirmed the risk for human disease anywhere in the world. After the first report in Europe of a human infection of *R. felis*, other human cases have appeared in other countries around the world, including Thailand (*36*), Tunisia (*38*), Laos (*39*), and Spain (*40*); additional cases have been reported in Mexico and Brazil (*34*). All the data support the conclusion that the incidence of *R. felis* rickettsiosis and the simultaneous worldwide distribution of the flea vector plausibly explain its endemicity.

At present, the involvement of domestic animals (e.g., dogs and cats) or wild animals coexisting in urban areas (e.g., opossums) maintains *R. felis* infection in nature. *C. felis* fleas serve as the main reservoir and likely have a central role in transmission of human illness.

Conclusions

R. felis is an emergent rickettsial pathogen with a worldwide distribution in mammals, humans, and ectoparasites. The clinical manifestations of *R. felis* infections resemble those of murine typhus and dengue, which makes them difficult to diagnose without an appropriate laboratory test. For this reason, infections due to this emergent pathogen are likely underestimated and misdiagnosed. Although *R. felis* may require only fleas for its maintenance in nature, we still do not know the role of animals in the life cycle of flea-borne spotted fever rickettsia. In addition, flea-borne spotted fever should be considered in the differential diagnosis of infectious diseases. Further research should be conducted to determine the actual incidence of *R. felis* infection in humans, the spectrum of clinical signs and symptoms, and the severity of this infection and also to assess the impact on public health.

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Mr. Perez-Osorio is currently professor of microbiology at the Autonomous University of Yucatan. His research interests focus on rickettsial diseases.

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Table 2. Human cases of *Rickettsis felis* infection reported worldwide, 1994–2006*

Year	No. cases	Method	Country	Reference
1994	1	PCR	USA	(*2*)
2000, 2006	5	PCR	Mexico	(*33*)
2001, 2006	3	PCR	Brazil	(*34*)
2002	2	PCR/serology	Germany	(*35*)
2003	1	Serology (seroconversion)	Thailand	(*36*)
2005	3	Serology (Western blot)	South Korea	(*37*)
2006	8	Serology (IFAT/Western blot)	Tunisia	(*38*)
2006	1	Serology (seroconversion)	Laos	(*39*)
2006	33	Serology (IFAT)	Spain	(*40*)
Total	68			

*IFAT, indirect fluorescent antibody test.

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別紙様式第 2－1

医薬品　研究報告　調査報告書

<table>
<tr><td>識別番号・報告回数</td><td></td><td></td><td>報告日</td><td>第一報入手日
2008 年 8 月 4 日</td><td colspan="2">新医薬品等の区分
該当なし</td><td rowspan="3">総合機構処理欄</td></tr>
<tr><td>一般的名称</td><td colspan="2">別紙のとおり</td><td rowspan="2">研究報告の
公表状況</td><td rowspan="2" colspan="2">ProMED-mail, 20080728.2306</td><td rowspan="2">公表国
オランダ</td></tr>
<tr><td>販売名(企業名)</td><td colspan="2">別紙のとおり</td></tr>
<tr><td>研究報告の概要</td><td colspan="6">問題点：オランダにおける調査において、2008 年 7 月の時点で Q 熱症例報告数が急激に増加している。

ブラバント州の公衆衛生局が行った調査では、2008 年 7 月 21 日付けで 491 症例が報告されている。オランダ保健省によると、これはブランバント居住者 5,000 名が感染したことになる。Q 熱は、ノールトブラバント州で急速に広がり、ナイメーヘン地域でもある程度広がった。感染症管理センター長である Roel Coutinho によると、実際の感染者数は報告された症例数の 5 倍というより 10 倍であると思われる。
労働党のブラバント州事務所は、この問題を評議会にかけた。評議会メンバーの Nora Kasrioui によると、理事会がどう対処する予定かわからない。Kasrioui は、「Q 熱は重篤な疾患であり、地域住民にとって、ますます大きな問題となっていて、政治的な働きかけが必要だと思います。」と述べた。Q 熱には不明な点が多く、方針を打ち出し難いと認識しており、「団体は、違和感のある無しにかかわらず、いつでも経済的な援助やそれ以外の援助を受けることができます。」とも述べた。
Countinho によると、Q 熱を根絶することは不可能である。Q 熱はヒツジの出産シーズン中からそれ以降に再発することが一般的であり、今のところ、ヤギが主な感染源であると考えられている。RIVM（国立衛生環境研究所）は、獣医学の専門家と共に、どのようにして Q 熱が動物から人に感染するのかを検討中であり、その後、詳細な予防対策が決定される。ちなみに、2007 年までオランダに Q 熱は存在しないも同然であった。</td><td>使用上の注意記載状況・
その他参考事項等

記載なし</td></tr>
<tr><td colspan="4">報告企業の意見</td><td colspan="3">今後の対応</td><td rowspan="2"></td></tr>
<tr><td colspan="4">別紙のとおり</td><td colspan="3">今後とも関連情報の収集に努め、本剤の安全性の確保を図っていきたい。</td></tr>
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MedDRA/J ver.11.0

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別紙

一般的名称	①人血清アルブミン、②人血清アルブミン、③人血清アルブミン*、④人免役グロブリン、⑤乾燥ペプシン処理人免疫グロブリン、⑥乾燥スルホ化人免疫グロブリン、⑦乾燥スルホ化人免疫グロブリン*、⑧乾燥濃縮人活性化プロテインC、⑨乾燥濃縮人血液凝固第Ⅷ因子、⑩乾燥濃縮人血液凝固第Ⅸ因子、⑪乾燥抗破傷風人免疫グロブリン、⑫抗 HBs 人免疫グロブリン、⑬トロンビン、⑭フィブリノゲン加第XⅢ因子、⑮乾燥濃縮人アンチトロンビンⅢ、⑯ヒスタミン加人免疫グロブリン製剤、⑰人血清アルブミン*、⑱人血清アルブミン*、⑲乾燥ペプシン処理人免役グロブリン*、⑳乾燥人血液凝固第Ⅸ因子複合体*、㉑乾燥濃縮人アンチトロンビンⅢ
販売名(企業名)	①献血アルブミン20"化血研"、②献血アルブミン25"化血研"、③人血清アルブミン"化血研"*、④"化血研"ガンマーグロブリン、⑤献血静注グロブリン"化血研"、⑥献血ベニロン-I、⑦ベニロン*、⑧注射用アナクトC2,500単位、⑨コンファクトF、⑩ノバクトM、⑪テタノセーラ、⑫ヘパトセーラ、⑬トロンビン"化血研"、⑭ボルヒール、⑮アンスロビンP、⑯ヒスタグロビン、⑰アルブミン20%化血研*、⑱アルブミン5%化血研*、⑲静注グロブリン*、⑳ノバクトF*、㉑アンスロビンP1500注射用
報告企業の意見	Q熱はリケッチアの一種コクシエラ・バーネッティ(*Coxiella burnetii*)による人畜共通感染症である。菌の大きさは0.2～0.4×1.0μmで、球菌の1/2～1/4である。感染源はおもに家畜や愛玩動物であるが、自然界では多くの動物やダニが保菌しており感染源となりうる。菌は感染動物の尿、糞、乳汁などに排泄され、環境を汚染する。ヒトは主にこの汚染された環境中の粉塵やエアロゾールを吸入し感染する。ヒトからヒトへの感染はほとんどおこらない。Q熱の患者は世界中で報告されている。日本では1999年4月から感染症法による届出が始まり、最近では2004年に7人、2005年に8人、2006年に2人の患者が報告されている。 Q熱の潜伏期は一般的には2～3週間で、感染量が多いと短くなる。発熱、頭痛、筋肉痛、全身倦怠感、呼吸器症状といったインフルエンザ様症状を示すが、主症状が肺炎、肝炎、あるいはその他の症状であったりと、その臨床像は多彩でQ熱に特徴的な症状や所見はない。また、患者の2～10%は心内膜炎を主徴とする慢性型に移行するといわれており、適切な治療をしないと致死率も高くなる。 本剤を含む当所で製造している全ての血漿分画製剤の製造工程には、約0.2μmの「無菌ろ過工程」および、本菌よりも小さいウイルスの除去を目的とした平均孔径19nm以下の「ウイルス除去膜ろ過工程」が導入されているので、仮に製造原料に本菌が混入していたとしても、これらの工程により除去されるものと考えられる。更に、これまでに本剤によるQ熱感染の報告例は無い。 以上の点から、本剤はQ熱感染に対して一定の安全性を確保していると考える。

*現在製造を行っていない

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Q FEVER - NETHERLANDS (02): (NBR) (02)
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A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases
<http://www.isid.org>

[1]
Date: Fri 25 Jul 2008
Source: Agrarisch Dagblad [trans. from Dutch by Mod.AS, edited].
<http://www.agd.nl/1057422/Nieuws/Artikel/Forse-toename-meldingen-Q-koorts.htm

A substantial increase in the number of reported Q-fever cases
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The number of reported cases of Q fever has risen sharply in recent weeks again [For the officially available data, indicating that the 2008 epidemic seems to have peaked by now, see the commentary. - Mod.AS]

The Public Health Service for Brabant had, in their last census on 21 Jul 2008, 491 known cases. That means that 5000 Brabanders have been actually infected, says the Ministry of Health. The disease spread rapidly in Noord-Brabant and, to a lesser extent, in the Nijmegen region. According to Roel Coutinho, head of the Centre for Infectious Disease Control, the actual number of victims is not 5-fold the number of reported cases but rather 10-fold.

The state branch of the Labour Party in Brabant has raised questions about the matter to the Executive Council. According to council member Nora Kasrioui, it is unclear what the directorate intends to do. "The disease is really a serious and growing problem for the population. We believe that the politics should go into action." Kasrioui acknowledges that it is difficult to make policies aimed at Q fever because much remains unclear about the disease. "Uncomfortable or not, organizations can always use help, financial or otherwise." [For the official government policy and background, see item 2].

According to Coutinho, the disease can never be fully eradicated. Normally it reappears during and following the lambing season. At present, goats are seen as the main source of infection. The RIVM (National Institute of Health and Environment), along with veterinary experts, is considering how the transfer from animal to man is established. Thereafter, a decision on further measures for disease prevention will be taken. Until last year [2007], Q fever was almost non-existent in the Netherlands.

[Byline: Jan Cees]

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Communicated by:
ProMED-mail
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[2]
Date: 10 Jun 2008
Source: Dutch government official document No VD. 2008/1191, "Measures for Q fever" [Trans. from Dutch by Mod.AS, edited]

<http://www.minlnv.nl/cdlpub/servlet/CDLServlet?p_file_id=28304>

A letter from the Ministers of Agriculture and of Health to the Parliament

Introduction

During the recent weeks, a significant increase in the number of Q-fever infections in humans has been observed again in the north-eastern region of the province Noord (north) Brabant. This has led to unrest among local people. With this letter we will bring you up to date with additional precautionary measures that we will undertake to prevent the spread of Q-fever as much as possible.

Q-fever

Q fever is a disease caused by the bacterium _Coxiella burnetii_. It is a zoonotic disease, which means that spread from animals to humans can take place. Q fever is traditionally present around the world and may affect many species -- not only farm animals but also species such as birds, dogs, cats, rats and wild animals. Ticks can be a vector in the transmission of Q fever between animals.

In particular, small ruminants are regarded as a major source of infection for humans. After excretion, the bacterium can survive a long time in the air and sometimes spread over long distances. People can be infected through various routes, including the inhalation of infectious, airborne particles. Human infection is often manifested by mild symptoms but a more serious course may occur.

The main clinical sign of Q fever in ruminants is abortion in pregnant animals, caused by the bacterium. During and after the abortion the animals excrete large quantities of the bacteria in their manure.

Small ruminants intended for milk production are held mainly in so-called pen barns. A pen barn is a shed where the manure is covered on a regular basis with a new layer of straw. When the mixture of manure and straw reaches a certain height, the shed is emptied. Especially during the manure removal process, bacteria are shed into the air with the consequent risk for both the public and animal health. Possibly, the spreading of manure on land is also a risk factor, but this procedure seems to be of less significance than the removal process of manure from the pen barns. This difference became apparent since manure from Noord Brabant farms has been used as fertilizer in other provinces without harmful results in humans.

Initiatives undertaken

Following the 2007 Q-fever outbreak in Herpen, Noord-Brabant, some steps were agreed between the Ministry of Health, Welfare and Sport (VWS) and the Ministry of Agriculture, Nature and Food Quality (LNV) to obtain better insight regarding the Q-fever problem and to prevent, as far as possible, its spread to man. In this framework, advisory information on the hygiene measures to be applied in small-ruminant farms has been prepared and published on the sites of the Health, Welfare and Sports Ministry, the Agriculture Ministry, and the Animal Health Service (GD).

Research by the Health Services has been undertaken in both large and small ruminant sectors to obtain better understanding of the extent of the problem. This research is funded by both sectors and by the government. There is also research under way into the risk factors for the spread of Q-fever.

The relevant research institutes, namely the National Institute of Health and Environment (RIVM), the Central Veterinary Research Institute (CVI) and the Health Service (GD) are also in the process of development and validation of testing methods suitable for the detection and identification of the bacterium.

Finally, a research initiative is ongoing regarding intervention strategies. Special attention is paid to a vaccine which is currently being tested in Denmark and France, considering its possible experimental application in the Netherlands as well.

Designating Q fever as an infectious, reportable animal disease
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In order to be able to apply preventive and control measures on animal holdings, Q fever should be designated a reportable infectious animal disease. Indeed, this has been carried out by the Minister of Agriculture, adding Q fever to the list of animal diseases (including zoonoses) for which compulsory prevention, control and monitoring are regulated. Holders of small ruminants kept in pen barns are required to report signs which may indicate Q fever. This requirement obliges the veterinarians as well.

Measures regarding manure

Experts agree that manure probably plays an important role in the dissemination of the Q-fever agent in the province of Noord Brabant.

As a meaningful, provisional measure based on the precautionary principle, we plan to ban, for the duration of 3 months, the use of manure from small ruminant holdings in pen barns where serious infection has been established. A period of 3 months is regarded sufficient for a significant reduction of the infection load in the manure. Since the removal of manure from the pen barns is unavoidable as soon as the installation runs full, a practical solution is to be sought and finalized soon.

Other measures and consultations

In addition to the specific measures for the treatment of manure on infected holdings, further sector-related advice will be given in order to prevent future spread of Q fever. One of the ideas is to prescribe an advanced timetable for an earlier-in-season spreading of manure in the fields, preceding the lambing season. The aim is to prevent the utilization of the manure until at least 3 months after the lambing season, allowing significant reduction of its infection load.

Holdings with small ruminants are often frequented by recreation visitors and others interested. Contacts of people with infected premises are also undesirable. Temporarily preventing visits to such holdings seems to us advisable.

There are also a certain number of sheep and goat farms which produce their own cheese. This is often made with raw milk. The consumption of raw products from infected farms is discouraged by the RIVM (National Institute for Healthcare and the Environment). It seems therefore primarily useful to prescribe pasteurization in certain cases. The Minister for Health, Welfare and Sport will take these measures in consultation with RIVM.

With the above mentioned steps we try to limit, as far as possible, the spread of Q fever. The measures are aimed at the earliest possible action to diminish the risk of further spread. The development of the policy is being continued.

[Byline:
G. Verburg, Minister of Agriculture, Nature and Food Quality, and
Dr. A. Klink, Minister of Health, Leisure and Sport]

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Communicated by:
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[The above ministerial letter, addressed to the Dutch parliament, provides interesting and useful information on the epidemiology of the disease in the Netherlands and the preventive and control measures undertaken. It is also useful for those engaged in any handling of emergency situations related to zoonotic diseases. Hopefully, action plans and contemplated research will be accomplished according to plan.

In our previous posting (see ProMED archive below), data on the disease incidence from different media sources were inconsistent; we are grateful to Naomi Bryant, National Travel Health Network and

Centre (NaTHNaC), for drawing our attention to that. Official Q fever data for the first 28 weeks of 2008 (1 Jan - 23 Jul 2008) are available on the official website of the Public Health Service for Brabant (GGD Hart voor Brabant). The total number of reported human cases during the said period was 538. The 1st cases appeared during week 3, remaining under 10/week until the 15th week, when it began to rise, peaking during week 22 (72 cases). During the weeks 27-28, the number is again below 10; the outbreak seems to be dying out. The said data can be found (in Dutch) at <http://www.rivm.nl/cib/infectieziekten-A-Z/infectieziekten/Q_koorts/FAQ_Q-koor

According to the said website, prior to 2007 the mean annual number of human Q fever cases, on national level, was 15. Since the disease in animals was not reportable, there is no information on its incidence in animals during the said years. The source indicates that the main animal species responsible for the current outbreak are goats, followed by sheep. - Mod.AS]

[see also:
Q fever - Netherlands: (NBR) 20080725.2267]
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医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日 2008年9月9日	新医薬品等の区分 該当なし	厚生労働省処理欄
一般的名称	乾燥 pH4 処理人免疫グロブリン		研究報告の公表状況	Variant of Mad Cow Disease May Be Transmitted by Blood Transfusions, According to Animal Study http://www.hematology.org/media/08282008.cfm	公表国 英国	
販売名（企業名）	①サングロポール ②サングロポール点滴静注用 2.5g （CSL ベーリング株式会社）					

研究報告の概要	使用上の注意記載状況・その他参考事項等
問題点（動物実験で輸血により vCJD が感染することが報告） Blood Online の"Press Releases"に本研究の概要が報告された。しかし概要のため実験系の情報が少ないが、今回報告する。 英国グラスゴー大学獣医学部のヒューストン教授は、BSE とスクレイピーに感染したヒツジの輸血による感染について9年間研究している。その結果、ヒツジ間において BSE とスクレイピーは、輸血により効率的に感染することが示された。特に、疾患の兆候が発現する前のドナーから採取された血液でも感染が伝播し、感染の後期ではより感染していた。 BSE ドナー群の感染した血液を投与されたヒツジ 22 頭のうち、5 頭が TSE の兆候を示し、3 頭は臨床症状の発現なしで、感染のエビデンスを示し、全体で 36%の感染率であった。 スクレイピー感染した血液を投与された 21 頭のうち、9 頭がスクレイピーの症状を発現し、全体で 43%の感染率であった。 これらの結果は、ヒトの輸血により vCJD に感染した 4 症例と一致している。 ドナーの感染期に加え、疾病感受性の遺伝的多様性や輸血成分などの要因が、ヒツジやヒトでの輸血による感染率に影響する。 BSE やスクレイピー感染したヒツジで、輸血による感染率は高い、特にドナーが感染後期の場合は高い。 以上の結果がヒトでの感染と一致していることから、輸血はこれらの疾患が効率的に感染する経路の代表であることが示された。 また、どの血液成分が重篤に感染するかを解明したり、切望されている診断試験を開発するために、BSE やスクレイピーに感染したヒツジの血液は効率的に利用されるであろうことが示された。	

報告企業の意見	今後の対応
これまで血漿分画製剤によって vCJD が伝播した報告はない。製造工程において異常プリオンを低減し得るとの報告があるものの、理論的な vCJD 等の伝播のリスクを完全には排除できないので、投与の際には患者への説明を十分行い、治療上の必要性を十分検討の上投与することを添付文書に記載し、注意喚起している。	今後とも新しい感染症に関する情報収集に努める所存である。