

40. Bernabeu-Wittel M, del Toro MD, Nogueras MM, Munain MA, Cardenosa N, Marquez FJ, et al. Seroepidemiological study of *Rickettsia felis*, *Rickettsia typhi*, and *Rickettsia conorii* infection among the population of southern Spain. *Eur J Clin Microbiol Infect Dis*. 2006;25:375-81. DOI: 10.1007/s10096-006-0147-6

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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 8 月 4 日	新医薬品等の区分 該当なし	総合機構処理欄
一 般 的 名 称	別紙のとおり	研究報告の 公表状況	ProMED-mail, 20080728.2306	公表国 オランダ	
販 売 名 (企 業 名)	別紙のとおり				
研究報告の概要	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。 Coutinho 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。				使用上の注意記載状況・ その他参考事項等
					記載なし
報告企業の意見			今後の対応		
別紙のとおり			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。		

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人免疫グロブリン、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疫グロブリン*、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献血ベニコロンⅠ、⑦ベニコロン*、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*、㉑ノバクトF*、㉒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キシエラ・バーネッティ (<i>Coxiella burnetii</i>) による人畜共通感染症である。菌の大きさは$0.2\sim0.4\times1.0\mu\text{m}$で、球菌の$1/2\sim1/4$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$0.2\mu\text{m}$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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Published Date 28-JUL-2008

Subject PRO/AH/EDR> Q fever - Netherlands (02): (NBR)

Q FEVER - NETHERLANDS (02): (NBR) (02)

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

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]

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]

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. Respectably 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 Sport 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

[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

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PROMED-mail

Communicated by:

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

development of the policy is being continued. possible action to diminish the risk of further spread. The spread of Q fever. The measures are aimed at the earliest 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.

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

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.

Other measures and consultations

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.

Measures regarding manure

Designating Q fever as an infectious, reportable animal disease 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.

being tested in Denmark and France, considering its possible experimental application in the Netherlands as well.

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サングロボール ②サングロボール点滴静注用 2.5g (CSL ベーリング株式会社)				
研究報告の概要	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 とスクレイビ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 とスクレイビーは、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。 スクレイビー感染した血液を投与された 21 頭のうち、9 頭がスクレイビーの症状を発現し、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 やスクレイビ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 やスクレイビ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。				使用上の注意記載状況・ その他参考事項等
	報告企業の意見	今後企業の見解 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。					



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Press Releases

Variant of Mad Cow Disease May Be Transmitted by Blood Transfusions, According to Animal Study

(WASHINGTON, August 28, 2008) – Blood transfusions are a valuable treatment mechanism in modern medicine, but can come with the risk of donor disease transmission. Researchers are continually studying the biology of blood products to understand how certain diseases are transmitted in an effort to reduce this risk during blood transfusions. According to a study in sheep prepublished online in *Blood*, the official journal of the American Society of Hematology, the risk of transmitting bovine spongiform encephalopathy (BSE, commonly known as "mad cow disease") by blood transfusion is surprisingly high.

BSE is one of a group of rare neurodegenerative disorders called transmissible spongiform encephalopathies (TSEs), and there is no reliable non-invasive test for detecting infection before the onset of clinical disease. In addition to BSE, these diseases include scrapie, a closely related disease in sheep, and Creutzfeldt-Jakob disease (CJD) in humans, which causes neurological symptoms such as unsteadiness and involuntary movements that develop as the illness progresses, rendering late-stage sufferers completely immobile at the time of death.

A new variant of CJD (termed vCJD) was recognized in the United Kingdom in the mid-1990s, apparently as a result of the transmission of BSE to humans. Because the symptoms of this disease can take many years to appear, it was not known how many people might have been infected, and without a reliable test for identifying these individuals, clinicians were very concerned that the infection could be transmitted between people by blood transfusion or contaminated surgical and dental instruments. As a result, costly control measures were introduced as a precautionary measure to reduce the risk of disease transmission, although at the time it was unclear whether there really was a significant risk or whether the control measures would be effective. This sheep study sought to better understand how readily TSEs could be transmitted by blood transfusion in order to help develop more targeted controls.

"It is vitally important that we better understand the mechanisms of disease transmission during blood transfusions so we can develop the most effective control measures and minimize human-to-human infections," said Dr. Fiona Houston, now a Faculty of Veterinary Medicine, University of Glasgow, UK, and lead author of the study.

The nine-year study conducted at the University of Edinburgh compared rates of disease transmission by examining blood transfusions from sheep infected with BSE or scrapie; the BSE donors were experimentally infected, while the scrapie donors had naturally acquired the disease. While scrapie is not thought to transmit to humans, it was included as an infection acquired under field conditions, which could possibly give different results than those obtained from experimentally infected animals. Because of the similarity in size of sheep and humans, the team was able to collect and transfuse volumes of blood equivalent to those taken from human blood donors.

The outcome of the experiment showed that both BSE and scrapie could be effectively transmitted between sheep by blood transfusion. Importantly, the team noted that transmission could occur when blood was collected from donors before they developed signs of disease, but was more likely when they were in the later stages of infection. Of the 22 sheep who received infected blood from the BSE donor group, five showed signs of TSEs and three others showed evidence of infection without clinical signs, yielding an overall transmission rate of 36 percent. Of the 21 infected scrapie recipients, nine developed clinical scrapie, yielding an overall transmission rate of 43 percent.

Investigators noted that the results were consistent with what is known about the four recorded cases of vCJD acquired by blood transfusion in humans. In addition to the stage of infection in the donor, factors such as genetic variation in disease susceptibility and the blood component transfused may influence the transmission rate by transfusion in both sheep and humans.

"The study shows that, for sheep infected with BSE or scrapie, transmission rates via blood transfusion can be high, particularly when donors are in the later stages of infection. This suggests that blood transfusion represents an efficient route of transmission for these diseases," said Dr. Houston. "Since the results are consistent with what we know about human transmission, the work helps justify the control measures put in place to safeguard human

blood supplies. It also shows that blood from BSE- and scrapie-infected sheep could be used effectively in non-human experiments to answer important questions, such as which blood components are most heavily infected, and to develop much-needed diagnostic tests."

Reporters who wish to receive a copy of the study or arrange an interview with lead author, Dr. Houston, may contact Becka Livesay at 202-776-0544 or rlivesay@hematology.org.

The American Society of Hematology (www.hematology.org) is the world's largest professional society concerned with the causes and treatment of blood disorders. Its mission is to further the understanding, diagnosis, treatment, and prevention of disorders affecting blood, bone marrow, and the immunologic, hemostatic, and vascular systems, by promoting research, clinical care, education, training, and advocacy in hematology.

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