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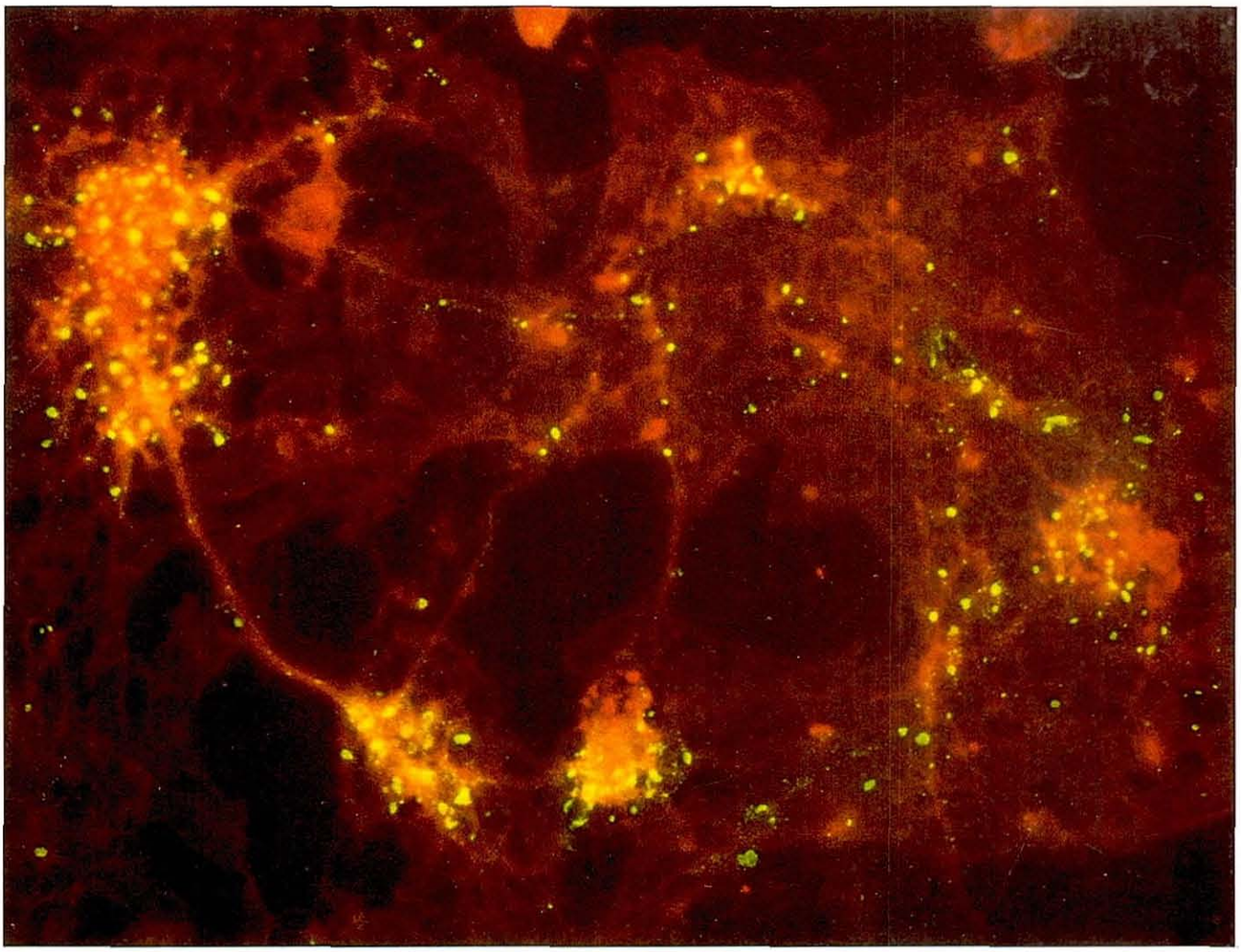

Fixed rabies virus-infected (CVS) primary rat cortical neurons in culture (see page 3).

Current Concepts in Rabies

Henri Tsiang,
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Newly designed vaccines are now being developed to improve efficacy and decrease the risk of side-effects.

Puerperal Fever: iatrogenic epidemics of the 18th/19th centuries

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A history of lessons learnt too late for too many mothers.

Current Concepts in Rabies

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Introduction

As one of the diseases identified in ancient times, rabies has provoked fear throughout the centuries. This disease has been the subject of special attention despite the relatively low number of registered human cases. Before rabies treatment by vaccination was applied by Louis Pasteur,[1] the number of patients dying from rabies in France was estimated to be only 27 per year. Yet the World Health Organization (WHO), in a worldwide survey in 1992,[2] reported 35,000 human rabies cases of which 97% were diagnosed in Asia. The real figures may be much higher due to unreported cases.

Biology of rabies

Rabies is caused by a neurotropic virus which belongs to the lyssavirus genus of the rhabdoviridae family. Its genome consists of a negative, non-segmented and single-stranded RNA associated with three proteins (transcriptase, nucleoprotein and phosphoprotein). The resulting nucleocapsid forms a helix surrounded by the matrix membrane protein and a lipid bilayer envelope. On the outer layer of the membrane, 'spikes' consisting of glycoprotein protrude from the virus surface. Electron microscopy shows the virion to be morphologically similar to a bullet (**Figure 1**).

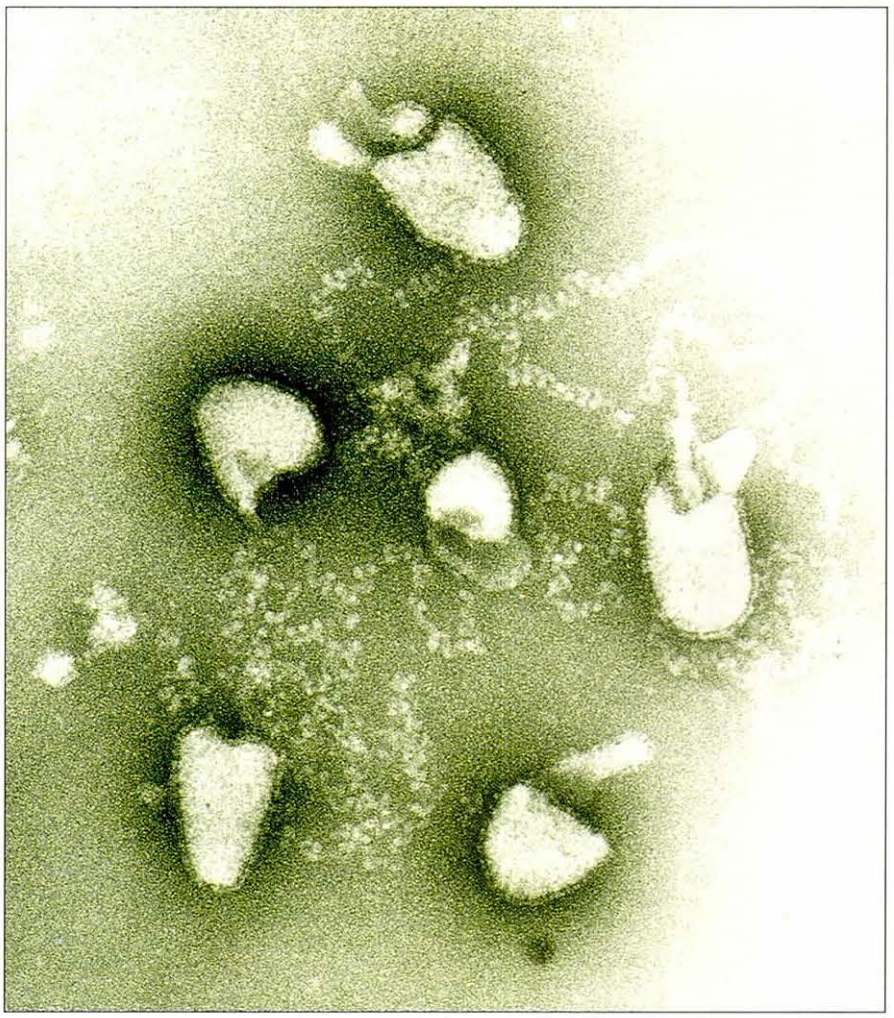

Figure 1: Electron microscopy of purified bullet-shaped fixed rabies virions (ERA strain) showing nucleocapsids containing the virus genome. (Photo by C Dauguet and H Tsiang.)

Pathogenesis

The pathogenesis of rabies has been extensively described in reviews and books. A remarkable feature of rabies virus infection is that it infects and replicates preferentially in neural cells (**Figure 2**). The main route of virus spread is not the bloodstream but the intra-axonal transport of rabies virions in neurons. Trans-synaptic virus transport is also a mode of virus spread from the site of peripheral virus inoculation to the final neuronal target in the brain.[3]

It has now been shown that rabies virus impairs brain function. Electrophysiological studies demonstrate impairment of brain function and regulatory capacities during rabies. Neuropharmacological studies also point to involvement of neurotransmitter metabolism alterations at the level of their uptake and evoked-release by nervous tissues and their receptors.[3] The involvement of inducible nitric oxide in rabies-infected brain may also be an element of the pathogenic mechanism of the disease.[4]

Clinical features of rabies encephalitis

The early clinical symptoms of rabies are difficult to differentiate from other encephalitides. The onset of the disease is usually accompanied by fever which decreases as the disease progresses. A wide variety of clinical manifestations can be found ranging from 'furious' (or encephalitic form) to a paralytic rabies. A Guillain-Barré paralysis syndrome is observed in some cases. Periods of severe agitation alternate with periods of depression. Fluctuations of consciousness range from sudden confusion to periods of mental lucidity evolving toward coma and death. Hydrophobia and aerophobia are usually present in furious forms of rabies, as well as hypersalivation and other autonomic disorders. During the paralytic form, the patient is usually conscious but progressive weakness at the site of the bite develops involving the pharynx and respiratory tract. In most cases, death occurs after quadriplegia and a short period of coma.

Epidemiology

Animals

Rabies is primarily a veterinary disease affecting domestic carnivores and wildlife. However, the epidemiology of rabies offers a great variety of situations. For instance, the dog is certainly the main reservoir and vector for human rabies in Africa, most regions of Latin America, Asia and the Middle East. In Western European countries, despite the fact that the main reservoir and vector is the red fox, most human patients treated for rabies have been bitten by a dog. Among the wildlife vectors, jackals and mongoose are frequent vectors in Africa, whereas the fox is by far the main vector in Europe. Interestingly, a racoon epizootic began in the US after the animals were transported by hunting associations to the border between Virginia and West Virginia.[5] Bats are also becoming an important vector in North America, with a spectacular involvement of vampire bats in Latin America.[6] Although less common, the wolf is a feared vector in Eastern and Middle-eastern Europe because of the severity of the wounds inflicted.

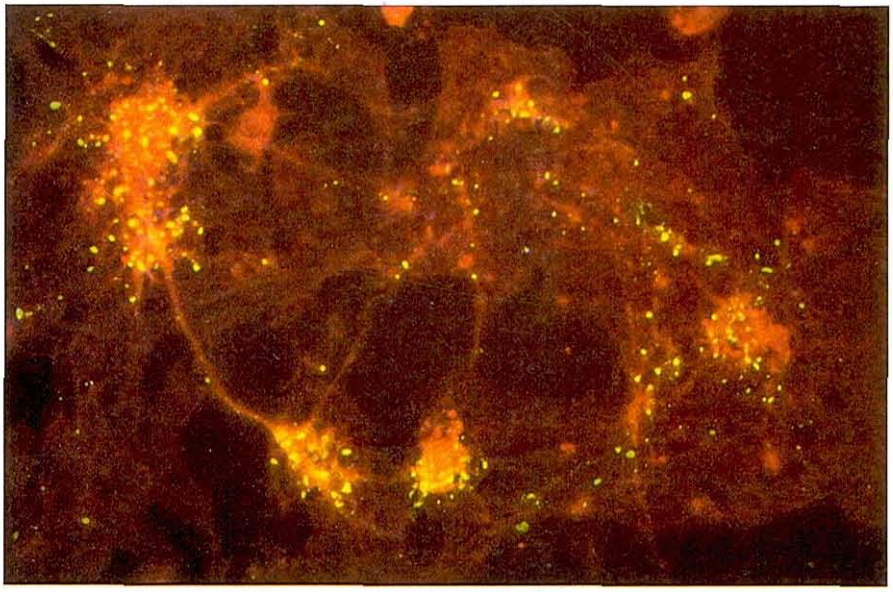

Figure 2: Fixed rabies virus-infected (CVS) primary rat cortical neurons in culture. The viral inclusions are visualised as green to yellow-coloured spots after staining with antirabies nucleoprotein fluorescent conjugate.

In Latin America, an increase in the amount of vampire bat (mainly *Desmodus rotundus rotundus*) rabies has been observed,[7] with a concomitant increase in the number of domestic animals infected by vampire bats. As a consequence, the number of human deaths due to vampire bat bites or of rabies treatment after a vampire bat bite are increasing. Thus, there seems to be emergence of a new epidemiological situation with a shift from dog rabies to vampire rabies.

Humans

Human rabies occurs predominantly in Asian countries such as India and China, as well as in Africa and Latin America. The main mode of rabies transmission is animal bites, whilst contamination by scratches, abrasion or licking of open wounds is rare. Contact with urine, faeces or even blood from a rabid animal is not usually a cause of transmission, provided there is no skin trauma or lesions. Contamination by highly concentrated virus aerosols produced by rabid bats in humidity-saturated caves in southern Texas has been described,[8] although accidental inhalation of highly concentrated virus aerosols by research scientists has also occurred. Several cases of rabies following corneal transplant from donors with undiagnosed rabies have occurred first in the United States, then in France and Thailand.[9] Two cases of rabies after corneal transplantation have also been recorded in 1994 in Tehran.[10] Thus corneal transplant may be a major risk in cases of undiagnosed brain pathologies. A peculiar mode of contamination was reported following the preparation of rabid dog carcasses for consumption whereby the cook died from rabies and the consumers were unaffected.[11]

Control of rabies

Prevention from animals

For several decades, prevention of animal rabies has been based on the control of stray dogs and the vaccination of domestic animals. This was sufficient to control dog rabies in the United States and in Western Europe in the first half of the 20th century. However, an epidemic of fox rabies has swept into Europe from Poland to France, recently reaching the suburbs of Paris.[12] Similarly, wildlife rabies has been prominent in the recent spread of the disease in the United States.[13]

In most developing countries where rabies is endemic, preventative measures have only limited the spread of the disease. However, in Latin America, a global vaccination campaign in dogs has succeeded in greatly decreasing urban rabies.[14]

Control of wildlife rabies has been more difficult to manage. Epizootics of rabies can occur almost anywhere with little possibility of intervention. For instance, epizootic rabies is occurring in south Texas in the United States, involving an increasing number of rabid coyotes during the last few years.[13]

In Europe, killing foxes by poisoning and hunting has not been successful in reducing the incidence of rabies. Oral vaccines were developed in Switzerland in 1977 and in the United States. After several developments, modified live vaccines and vaccinia recombinant rabies glycoproteins have been successfully used in baits.[15] Oral vaccines are distributed by aeroplane or far more efficiently by helicopter in the areas to be treated. In 1994, a large-scale vaccination programme involved Austria, Belgium, France, Germany, Italy, Slovakia, Slovenia, The Czech Republic and Switzerland, and was highly successful and the number of rabid foxes has significantly decreased in several Western European countries. In France, the oral vaccination of foxes has been very effective (**Table 1**). It is conceivable that rabies could disappear from several European countries in the next decade.

As a consequence of the decrease in the number of rabid foxes in Europe, the risk that rabies virus may contaminate Great Britain through wildlife is fading. The European coast facing the British mainland has been virtually free from fox rabies since 1994. However, absence of rabies from the coast must be monitored for a sufficiently long period to ensure that there is no risk of a rabies focus being reactivated. Thus the main possibility for the introduction of rabies into Great Britain would be quarantine failure.

However, it must be remembered that besides this optimistic point of view, potential transfer of rabies virus from the fox vector to a yet unknown wildlife reservoir cannot be excluded in future. This has happened several times in the Americas and in Europe. There are recent observations that rabies-related rhabdovirus serotypes found in a European bat population may be the source of a limited epizootic burst in Europe (mainly in the Netherlands).[16] This is a warning that infectious diseases under preventative control have the capacity to emerge in new forms when epidemiological conditions favour the establishment of viruses in a new ecological niche.

Prevention in humans

Human rabies vaccination is the only effective treatment following the infection occurring usually after a dog bite. It is thus important to assess the risk that the animal was rabid in order to decide whether vaccination is indicated. This decision must take into account several factors such as the sanitary status of the dog, quarantine conditions and the geographical and epidemiological status of the region from which the dog or wildlife came from.

Vaccines

Prevention of rabies in humans is based on the Pasteur concept of vaccination and subsequent serotherapy. Pasteur developed the concept that the immune response toward an unknown filter-passing pathogenic agent can protect against this pathogen. Although qualitative improvements have greatly enhanced the effectiveness and safety of Pasteur's original vaccines which used rabid rabbit spinal cords, the rationale of the treatment is the same: induce a specific immune defence mechanism against the viral pathogen.

Table 1: Decrease in rabies cases in France.

	1990	1991	1992	1993	1994
Rabies cases	2984	2165	1149	261	99
Percentage reduction		28%	47%	83%	62%

The efficacy of oral vaccination of foxes is shown by the 97% reduction of the cases in 1994 compared with 1990.

Rabid European fox. (Photo from CNEVA.)

After Pasteur developed the concept of rabies immunisation, improvements of brain tissue vaccines mainly consisted of two aspects. First, the use of new-born animals lacking the presence of myelin in the brain resulted in decreasing the risk of side-effects during immunisation. Second, total inactivation of the vaccine resulted in the elimination of the accidental emergence of vaccine-induced rabies. The use of chicken and duck embryo vaccines has also proved to be useful. The main breakthrough was based on the use of tissue culture vaccines. These mainly consisted of primary kidney cells from various species (hamster, bovine, porcine). Subsequently, human diploid cells and monkey kidney-derived cells (VERO) have been used for the production of concentrated and purified rabies vaccines.[17]

The development of rabies vaccines for veterinary use followed the same principle except that cell lines such as BHK cells were used. The development of oral vaccination of wildlife has impeded the production of recombinant vaccinia virus expressing the G protein. Yet, recombinant viruses expressing the G protein have been extensively investigated and shown to have a protective effect.[18] Studies also suggest a protective role for the N protein.[19] However, vaccinia virus recombinant expressing the rabies nucleoprotein was ineffective in conferring protection.[20] On the other hand, the rabies nucleocapsid has been shown to have superantigen properties. The capacity of the rabies nucleocapsid to modulate the immunological response is the consequence of an association of the viral protein to the human MHC class II molecules.[21]

An infectious rabies virus has been successfully obtained from cloned cDNA.[22] The intracellular expression of full-length viral antigenome-like T7 RNA polymerase transcripts and viral proteins (N, P, L) from transfected plasmids resulted in the formation of transcriptionally active nucleocapsids. These data offer the possibility of newly designed vaccines in the future.

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Erratum

In the article by J Holton entitled 'Recent Advances in Helicobacteriology' on page 6 of *Culture* 16.1, '(requiring 15–17% oxygen and 6–10% carbon dioxide)' should read '(requiring 5–7% oxygen and 6–10% carbon dioxide)'.

Puerperal Fever — iatrogenic epidemics of the eighteenth/ nineteenth centuries

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Introduction

Historians have the gift of perfect hindsight and it could be said that this paper is evidence of yet another example. However, although the period to be described (1772–1848) was prior to the confirmation of microbial disease, the evidence that simple hygienic measures could be taken to prevent these epidemics, appeared in 1772, only 20 years after the establishment of Lying-in hospitals, the principal foci of mortality from puerperal fever.

Puerperal fever

Childbirth (puerperal) fever has ancient origins. Hippocrates of Kos (469–399 BC) first commented on the disease, which had to be separated from less-virulent childbed fevers. Early reports were of sporadic cases only but by the middle of the 17th century 'clusters' of cases of puerperal fever were being reported.[1] By the middle of the 18th century, soon after Lying-in hospitals were created, epidemics of puerperal fever could be recognised. **Figure 1** describes the 18/19th century theories of epidemic disease. The word 'epidemic' described diseases which could be spread

GALENIC —	caused by natural cosmo-telluric phenomena, eclipses, comets, earthquakes
MIASMIC —	caused by noxious vapours and smells
LIEBIGIAN —	conveyed by non-living, decomposed animal-organic substances introduced into new hosts

Figure 1: Theories of epidemic disease.

in various ways and contagion was not implied. Galenic and Miasmic theories were held by most physicians but the non-contagionist chemical theory of Justus von Liebig (1803–1873) became popular in the middle of the 19th century. Progress in controlling epidemic disease depended on empirical hygiene until Pasteur (1822–1895) and Koch (1843–1910) had established the microbial cause of infectious diseases.

The 18th century physicians

The following 18th century English medical men made the earliest suggestions that puerperal fever was contagious and demonstrated how the spread of this disease could

Charles White.

be controlled. John Leake (1772), Nathanial Hulme (1772), Charles White (1773) and Alexander Gordon (1795) published their reports in the years shown in parentheses.[2] Charles White gave advice to the founders of the Vienna Lying-in hospital (where much later Semmelweis practised) and was well known for his work on hospital hygiene. His recommended prophylactic regimen included copious fresh air and clean surroundings but he did not specify the cleanliness of the medical and nursing attendants — an unfortunate omission in view of his report of two physicians practising in the same town "...one loses several patients every year of puerperal fever and the other never so much as meets with the disorder."[3]

Joseph Clarke (1790) disagreed with the miasmic theory and suggested that this fever had its origin in some local contagion. He based his conclusion on experience with puerperal fever deaths in a Dublin hospital where one ward remained entirely free from the disease. He recommended *isolation of infected patients, washing all* bedding and thoroughly cleaning walls and ceilings.[4]

Alexander Gordon (1752–1799) was the first physician to clearly and systematically demonstrate the contagious and transmissable nature of puerperal sepsis, carried on the hands of the doctor or midwife.[5,6] Gordon kept meticulous records of an epidemic which started in the Aberdeen area in 1789 and continued until 1792. His table of dates, names, addresses, cured, dead and by whom delivered, revealed that of 77 patients listed, 29 died from puerperal fever (38%). He was finally able to predict the fatal outcome of a delivery by noting which nurse or midwife attended the confinement. He admitted, in sorrow, that he must have carried this infection to a number of women. Using data from the Aberdeen Dispensary, Gordon recognised the connection between epidemic erysipelas and epidemic puerperal fever. He thought they were concomitant diseases. In Aberdeen both diseases began at the same time (**Table 1**). He noticed that erysipelas was closely associated with accidental or surgical wounds and drew the conclusion that only after the delivery was the mother vulnerable to this infection.

Holmes and Semmelweis

Oliver Wendell Holmes (1809–1894) and Ignaz Philipp Semmelweis (1818–1865) are the two names most closely associated with puerperal fever. Holmes gave credit to the earlier workers but Semmelweis had to repeat most of their work.

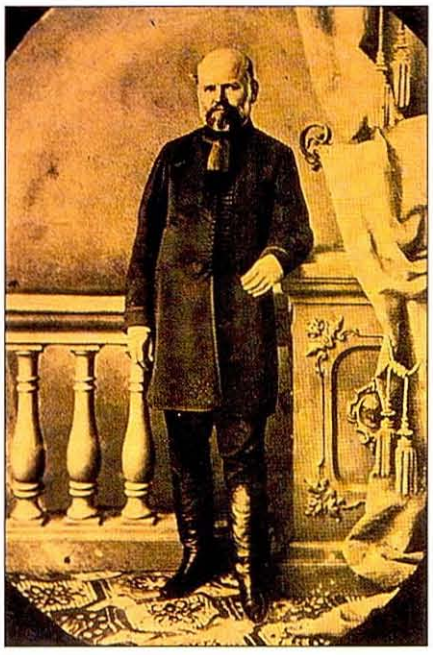
Holmes was born in Boston USA and initially entered Harvard College in 1826 to study law.[7] Four years later he turned to medicine and changed to Boston Medical College. Although the usual subjects in

Table 1: The association of epidemic puerperal fever and epidemic erysipelas.

	Year								
Epidemic	**1786**	**1787**	**1788**	**1789**	**1790**	**1791**	**1792**	**1793**	**1794**
Puerperal fever	0	0	0	0	23	28	0	0	9
Erysipelas	0	0	0	0	52	41	0	0	15

Figures taken from the Aberdeen Dispensary 1786–1794.[5]

Oliver Wendell Holmes.



Ignaz Philipp Semmelweis.

medicine were taught, there was no instruction in pathology or histology. Microscopes were not used in America at that time. Only two years into his three-year apprenticeship, Holmes went to Paris in 1833 to study in the Hôpital de la Pitié under Pierre Louis, the premier physician in France. Louis taught medicine as a science, particularly pathology. When Holmes returned to Boston in 1835 he was years ahead of his American contemporaries. Two months after his return he was granted the Harvard degree of Doctor of Medicine.

In the Spring of 1842, small 'epidemics' of puerperal fever arose in the Boston area. A doctor and two medical students developed fever and inflammation following autopsy on a case of puerperal fever. One of the medical students died. Later a doctor died following examination of a case of puerperal sepsis. Holmes was deeply concerned and thoroughly researched the literature available to him. He was appalled at the neglected evidence he uncovered from 18th century English physicians. In 1843 he published a paper 'The Contagiousness of Puerperal Fever' in the *New England Quarterly Journal of Medical Surgery*. Holmes stated that the disease was dangerously contagious and was spread by doctors, nurses and midwives who delivered babies. He prescribed the following rules:

> *No doctor preparing to deliver a child should take part in a puerperal fever autopsy. Following autopsy, the doctor should wash thoroughly, change his clothes and wait 24 hours before attending his patients. Doctors and midwives, discovering a single case of puerperal fever among their patients, should give up obstetric practice for at least a month.*

He was very much against the habit of doctors carrying organs removed at autopsy in their jacket pockets, for teaching purposes. Unfortunately, this powerful message was lost because the Journal ceased publication. Eleven years later, in 1854, Holmes produced a new comprehensive publication in which he attacked all his medical colleagues who had vilified him. A final furious outburst against Holmes was put down by the American Medical Association. They supported evidence from the work of Ignaz Semmelweis and within a year the Holmes–Semmelweis theory was generally accepted in American medical practice.

Ignaz Philipp Semmelweis, born in Buda (Hungary) was sent to Vienna to study law. He also changed to medicine and in 1844, aged 26 years, obtained a Doctorate in Medicine with diplomas in obstetrics. A reputation for Hungarian nationalism did not help him in a very hostile political climate in Vienna. His appointment as an unpaid assistant to Professor Klein (Obstetrics) in the German hospital, who was a powerful, political and autocratic figure, did not bode well for Semmelweis's future. Professor Boer, Klein's predecessor, had brought cleanliness and order from Dublin. Boer had also used models (phantoms) to teach midwifery. Klein overthrew all of this, using both live and dead patients for teaching purposes. Maternal mortality from puerperal fever began to rise and reached horrific levels. Since Klein supported the Galenic theory of epidemics, he saw no association of this with his medical practices. The leading pathologist in Vienna at that time was Karl Rokitantsky (1804–1878) who carried out more than 30,000 autopsies in his working life time. The total commitment of the medical profession to dissection and autopsy was based on the belief that diseases could be identified and classified postmortem. Medical students were encouraged to learn from the mortuary. The introduction of forceps, in the latter part of the 18th century, to shorten difficult labours was also a significant factor in these puerperal epidemics. Training doctors to use forceps required instruction in obstetrics and the creation of Lying-in hospitals as teaching centres. Thomas Lightfoot in 1850 asked why mothers entered 'these gates that led to death'.[8]

In the case of the German Hospital in the garrison city of Vienna, the attraction for the numerous unmarried mothers was that treatment would be free and the child taken to the Foundling Hospital but only if the mother presented herself whilst still in labour. Giving birth in the street (Gassengeburten) which was a comparatively safe procedure, did not qualify. There were two clinics for obstetrics in the German Hospital, which formed the largest Lying-in unit in the world. After 1840, deliveries were performed by physicians and medical students in the First Clinic and by midwives in the Second Clinic. The First Clinic was the larger and had a higher mortality rate from puerperal fever than the Second Clinic. By the time Semmelweis was appointed in 1846, the cycling of doctors and students through the autopsy room and back into the Clinic, was well established. The death rates per 100 confinements in the First Clinic in this year were: July 13.10%, August 18.05%, September 14.39% and October 14.98%. Several Commissions of Enquiry investigated the possible causes of the appalling death rate but to no useful purpose. It has to be remembered that for most of the 19th century, hospitals were rarely free from septic diseases. The introduction of anaesthetics in 1840 made a bad situation worse by creating greater opportunities for infection with bolder surgical procedures. Patients, sometimes two or three to a bed, created a human 'miasma' which seemed to explain the persistence and spread of contagious diseases in hospitals, ships and prisons.[8] Semmelweis looked for answers in the autopsy room every morning, before embarking on his obstetric rounds in the Clinic.

He discarded Klein's Galenic theory because it could not explain the difference in mortality between the First and Second Clinics. Similarly, the miasmic theory did not explain why the much more overcrowded Second Clinic had much smaller death rates (**Table 2**). In contrast to Holmes, he appeared not to consult any earlier publications on the disease. However, the answer came to him in similar circumstances to Holmes. Semmelweis returned from holiday to learn that his friend Jakob Kolletschka, Professor

Table 2: Comparative % death rates for the First and Second Clinics. (Adapted from Lancaster[1].)

Year	First Clinic (Physicians)	Second Clinic (Midwives)
1841	7.7%	3.5%
1842	18.8%	7.5%
1843	8.9%	5.9%
1844	8.2%	2.3%
1845	6.8%	2.0%

of Forensic Medicine, had died following a wound received during dissection. Studying the postmortem report, Semmelweis saw that the pyaemia described was the same as the puerperal sepsis. From that moment he was convinced that Kolletschka and the puerperae had died from the same disease. He had become a convinced Liebigian, suggesting that any autopsy material could induce a pyaemic, usually fatal, disease. Thus he and all his medical associates had unwittingly carried the noxious substances from autopsy to the labour ward. Washing with soap and water could not remove the persistent odour of the autopsy room and he looked for a disinfectant to remove the 'corpse-poison'. He chose chloride of lime, partly because of its de-odourising properties. From May 1847 onwards, he made it compulsory for doctors, students and nursing staff to disinfect their hands in this solution before attending patients. Good results appeared immediately, the death rate fell to 2.38% in June, 1.20% in July and 1.89% in August. Later, small 'outbreaks' of fatalities were shown to be associated with cross-infection from other patients. Chloride of lime ablutions were then fully carried out, including bed linen, walls and floors. The iatrogenic epidemic was over.

Semmelweis considered that he stood equal with Lister and Jenner but his reward from the German Hospital was banishment and he returned to Budapest. It is clear from **Table 3** that Professor Klein could not tolerate this man near him. Unfortunately, Semmelweis was prevented from publishing his results immediately,[9] although friends carried the message across Europe.

It was 13 years later, in 1861, that his full results were published in German 'Die Aetiology, der Begriff und die Prophylaxis des Kindbettfiebers'.[1] In this paper he analysed the mortality figures in the German Hospital and showed clearly that he and his colleagues had infected the patients. For this he was bitterly attacked, even Virchow the great German pathologist, reacted indignantly to this accusation.

In a series of open letters, Semmelweis conducted a vituperative debate with his opponents. He became increasingly mentally disturbed and in July 1865 was finally admitted to a mental institution in Vienna. He died two weeks later, on the 13 August 1865. Most accounts of Semmelweis's death ascribe it to blood poisoning from a wound received in the operating theatre. As in a Greek tragedy, Semmelweis became a corpse in the very room where he dissected so many mothers. Lancaster[1] cites Nuland for the true story of his death. Semmelweis, a difficult patient, was beaten by the asylum staff and died from his injuries.

Table 3: Effect on death rates of Klein's appointment, routine autopsies and disinfection. (Adapted from Lancaster[1].)

Years	Death per 100 confinements
1780–1789	0.86
1790–1799	1.11
1800–1809	0.92
1810–1819	1.9
1820–1822	1.7
Professor Klein appointed 1823	
1823–1829	5.1
1830–1833	4.7
Routine autopsies started 1833	
1834–1839	6.6
Separation of First and Second Clinics 1840	
1840–1846	7.2
Jan–May 1847	12.24
Semmelweis disinfection process started May 1847	
June-Dec 1847	2.98
1848	1.28

Conclusions

The science of pathology began in the 18/19th centuries, with the increasing practise of autopsy to discover the cause of death and the anatomical effects of disease. Thousands of parturient women paid a terrible price for this iatrogenic infection. The lesson preached in the 1770s, for more hygiene and less dissection was largely ignored until the 1850s. Although the epidemics were over, not all the lessons were learnt because up to the early 1930s, puerperal fever continued to be a major cause of maternal death.[10] Then, for unexplained reasons, the virulence of *Streptococcus pyogenes* began to decline.

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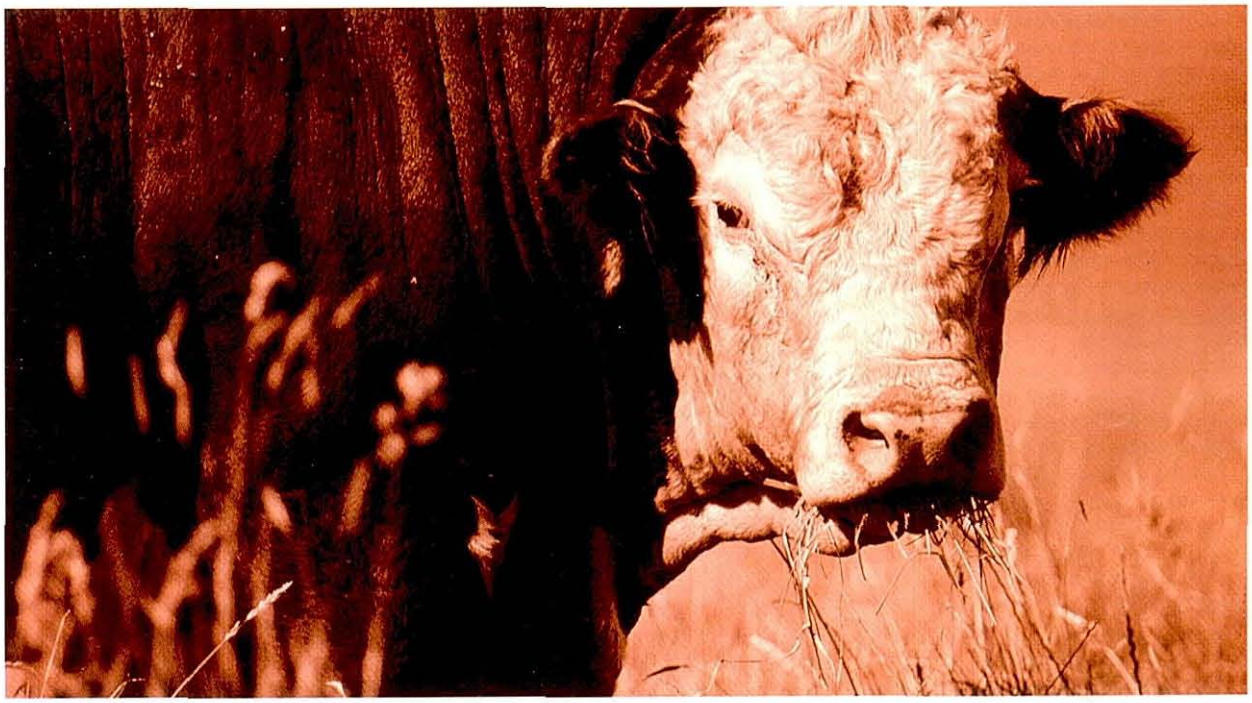

Be aware.

Verotoxin-producing *E. coli* contamination is often associated with cattle. Transmission to humans can be through food, water or person-to-person, and contact with cattle manure has been implicated. Symptoms can be severe, and sometimes fatal.

So don't be fooled. It's dangerous to make assumptions about Verotoxin production just by testing for the presence of suspect *E. coli* organisms.

The Oxoid VTEC-RPLA test removes all doubt by detecting, not the organisms, but the toxins themselves.

It reacts clearly to the presence of specific vero-cytotoxins (VT1 and VT2) in cultured samples by reverse passive latex agglutination.

Extensive evaluation has shown the sensitivity of the Oxoid VTEC-RPLA test to be 1-2ng/ml. And it can be used with isolates cultured from both food and faecal specimens.

Which is just as well. Because, when you're testing for possible VTEC contamination, toxin detection is your most effective solution.

OXOID
TOXIN DETECTION
KITS

UNIPATH ISO 9002 REGISTERED FIRM

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