し、台湾での狂犬病の再流行に関する情報を収集した。具体的には、国立感染症研究所・獣医科学部の井上智博士の講演に参加することで情報収集を行った。

2)韓国における狂犬病の流行状況に関する調査

韓国の動植物検疫局の Dong Kun Yang 博士より1970～2013年における人および動物における狂犬病の発生状況に関する情報を入手した。

3)オーストラリアにおける狂犬病対策に関する調査

オーストラリア政府・各自治体によって共同運営される非営利団体「Animal Health Australia」のホームページから、同国の狂犬病対策を記載した資料「AUSVETPRAN Rabies」をダウンロードし、その内容を確認した。

(倫理面からの配慮について)

該当なし

C. 研究結果

1) 台湾における狂犬病の再流行の状況に関する調査

台湾では、1961 年以降、狂犬病の清浄地域となっていた。しかし、2013 年 7 月、前年に採取された野生のイタチアナグマの死体から狂犬病ウイルスの遺伝子が検出され、台湾における狂犬病の再流行が確認された。その後の本格的な調査の結果、2013 年 12 月の時点で、イタチアナグマ 256 頭、ジャコウネズミ 1 匹、犬 1 頭において狂犬病が確認された。ウイルス遺伝子の解析の結果、台湾では、3系統のウイルスが流行しており、その系統は地域によって異なることが明らかとなった。また、これらのウイルスは、中国における流行株と遺伝的に比較的近縁であることが判明した。

2)韓国における狂犬病の流行状況に関する調査

韓国では、1985～1992 年の清浄期間を経て、1993 年に狂犬病の再流行が確認されている(資料 1 参照)。1930～1938 年の狂犬病の流行では、犬が病原巣になっていたのに対し、1993 年以降の流行ではタヌキと犬における流行が主体となっている。これらの動物から感染したと考えられるウシの症例も数多く報告されている。また、1993～2004 年の期間において、計 8 名の人の犠牲者も確認されている。2002 年(動物の狂犬病の発生数:78 例)をピークとして、狂犬病の発生数は著しく減少している。2012 年における動物における発生は 7 例にとどまっている。

3)オーストラリアにおける狂犬病対策に関する調査

「AUSVETPLAN rabies」(資料 2 参照)の第 1 章には、狂犬病に関する様々な基本的な情報が掲載されており、狂犬病が侵入した場合にその制圧に従事する関係者が知っておくべき基本事項が整理された形で記載されている。例えば、様々な動物における狂犬病の症状の特徴、基本的な病態形成機序、診断法・診断体制の概略、ウイルスの不活化法などの情報が記されている。

第 1 章の情報によると、1867 年にタスマニア

島において狂犬病の発生と考えられる事例が報告されている。これ以外に、オーストラリアにおける狂犬病の流行は確認されていない。一方、1987 年および 1990 年では、それぞれ 1 例ずつの輸入症例(患者はいずれも子供)が報告されている。

オーストラリアでは、Nobivac Rabies (Intervet 社)が唯一の認可された動物用狂犬病ワクチンとなっている。本ワクチンは、国外に輸出する動物を予防接種する目的で使用されており、それ以外の目的では認可されていない。したがって、オーストラリアで狂犬病が発生した場合には、上記の目的以外の使用に関して認可を受ける必要がある。

第 2 章では、狂犬病が発生した場合の制圧法・撲滅法の基本原理が記載されている。特に、ワクチン接種による制圧の重要性が強調されている。野生動物に狂犬病が発生した場合に、経口生ワクチンを使用する可能性について言及しているものの、実際の使用については安全性の担保など、多くの課題がある。

第 3 章では、オーストラリアで狂犬病が発生した場合の、より具体的な対応について記載されている。作業者の安全確保に必要な基礎的情報の他、感染拡大を防ぐための制限区域(Infected premises, Restricted area, Transmission area、 Control area)の設定の意義が記載されている。また、感染源動物の特定のための基本的な考え方についても記されている。

第 4 章では、設定された制限区域における動物の移動制限および検疫について詳しく記載されている。基本的に被疑動物の移動は禁止されている。一方、それ以外の動物に関しては、条件が満たされれば、特別な許可によって、移動が認められる。

なお、オーストラリアにおける狂犬病対策をより詳細に調査する目的で、2014 年 2 月に岐阜大学・伊藤直人准教授らがビクトリア州政府の環境・一次産業部門および CISRO オーストラリア動物衛生研究所を訪問する予定となっている。日本の狂犬病対策の現状を説明した上で(資料 3 参照)、オーストラリアにおける同対策の現状について調査・討議を行う予定である。

D. 考察

最近、台湾のイタチアナグマで流行している狂犬病ウイルスは、その遺伝子解析の結果より、他の国から新たに侵入したというよりも、以前から台湾で流行していた可能性が高いと考えられる。このことは、日本の野生動物に狂犬病の発生がないことを確認する必要性を強調するものである。また、日常的に野生動物における人獣共通病原体の発生・流行状況を監視するシステムの構築が望まれる。

韓国では、狂犬病の流行が収束傾向にあり、もう少しで本病を撲滅できるという段階にきている。同国ではタヌキにおけるウイルス感染環を遮断する目的で経口生ワクチンを使用している。同国の狂犬病対策を詳細に調査すれば、日本の野生動物に狂犬病が発生した場合に必要な対応を考える上で重要な情報が得られると考えられる。

「AUSVETPLAN rabies」には、オーストラリアで狂犬病が発生した場合の具体的な対策が記載されていた。その骨格は、我国の狂犬病対応

ガイドラインと基本的に同じと考えてよい。一方、現在の輸入動物検疫システムについての記載はほとんどないことから、現地での訪問調査によってその詳細を明らかにしていきたい。

該当なし

3．その他

該当なし

E. 結論

台湾および韓国における狂犬病の流行状況、ならびにオーストラリアにおける狂犬病対策についての情報を入手した。これらの情報は、将来の日本の狂犬病対策を考える上で重要な基礎情報となることが期待できる。

F. 健康危険情報

該当なし

G. 研究発表

1.論文発表

Yamaoka S, Ito N, Ohka S, Kaneda S, Nakamura H, Agari T, Masatani T, Nakagawa K, Okada K, Okadera K, Mitake H, Fujii T, Sugiyama M. Involvement of the rabies virus phosphoprotein gene in neuroinvasiveness. J. Virol. 2013. 87:12327-12338.

2.学会発表

該当なし

H. 知的財産権の出願・登録状況

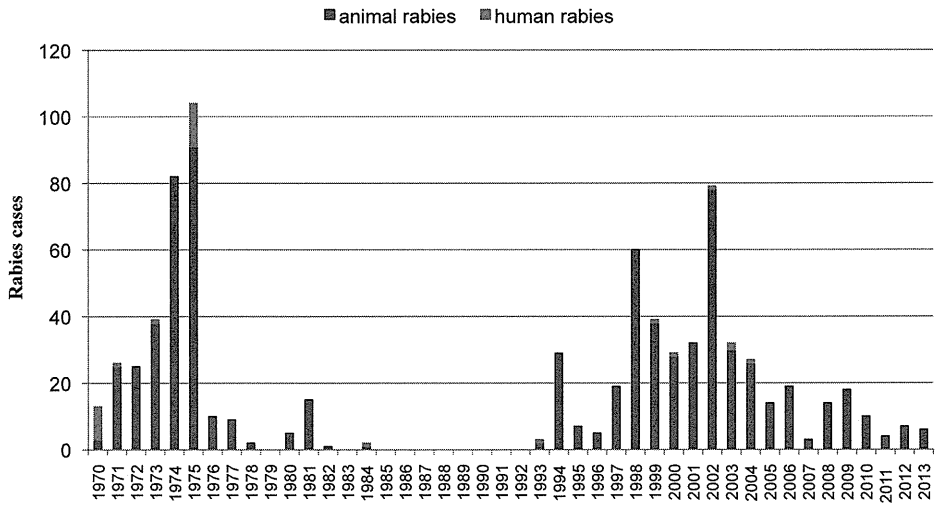
1. 特許取得

該当なし

2. 実用新案登録

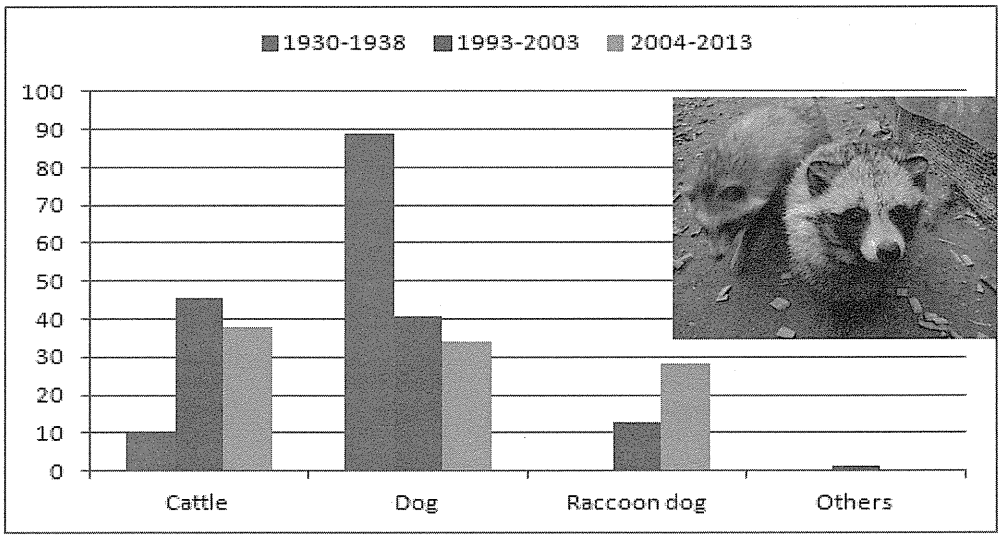
資料1

Number of reported human and animal rabies cases in Korea between 1970 and 2013



No rabies cases have been reported in human since 2004.

Incidence rate of rabies according to animal species



Rabies cases have been diminished in dog.
But, since rabies was first confirmed in a Korean raccoon dog in 1994, the cases have been increase.

AUSTRALIAN VETERINARY EMERGENCY PLAN

AUSVETPLAN

Disease Strategy

Rabies

Version 3.0, 2011

AUSVETPLAN is a series of technical response plans that describe the proposed Australian approach to an emergency animal disease incident. The documents provide guidance based on sound analysis, linking policy, strategies, implementation, coordination and emergency-management plans.

Primary Industries Ministerial Council

This disease strategy forms part of:

AUSVETPLAN Edition 3

This strategy will be reviewed regularly. Suggestions and recommendations for amendments should be forwarded to:

AUSVETPLAN — Animal Health Australia
Manager, Veterinary Services
Suite 15, 26–28 Napier Close
Deakin ACT 2600
Tel: 02 6232 5522; Fax: 02 6232 5511
email: admin@animalhealthaustralia.com.au

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Version 2.0, 1996 (major update)
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AUSVETPLAN is available on the internet at:
www.animalhealthaustralia.com.au

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DISEASE WATCH HOTLINE

1800 675 888

The Disease Watch Hotline is a toll-free telephone number that connects callers to the relevant state or territory officer to report concerns about any potential emergency disease situation. Anyone suspecting an emergency disease outbreak should use this number to get immediate advice and assistance.

Preface

This disease strategy for the management of a rabies outbreak in Australia is an integral part of the **Australian Veterinary Emergency Plan**, or **AUSVETPLAN (Edition 3)**. AUSVETPLAN structures and functions are described in the AUSVETPLAN **Summary Document**. This rabies strategy provides information about the disease (Section 1), the relevant risk factors and their treatment, and the options for the management of a disease outbreak depending on the circumstances (Section 2), and the policy that will be adopted in the case of an outbreak (Sections 3 and 4). The key features of rabies are described in Appendix 1.

This manual has been produced in accordance with the procedures described in the AUSVETPLAN **Summary Document** and in consultation with Australian national, state and territory governments and industry.

Rabies is included on the World Organisation for Animal Health (OIE) list of notifiable diseases as a multiple species disease. This obliges OIE member countries that had been free from the disease to notify the OIE within 24 hours of confirming the presence of rabies. OIE-listed diseases are diseases with the potential for international spread, significant mortality or morbidity within the susceptible species, and/or potential for zoonotic spread to humans.[1]

The strategies in this document for the diagnosis and management of an outbreak of rabies are based on the recommendations in the OIE *Terrestrial Animal Health Code* [2] and the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*.[3]

In Australia, rabies is included as a Category 1 emergency animal disease in the *Government and Livestock Industry Cost Sharing Deed In Respect of Emergency Animal Disease Responses* (EAD Response Agreement).[4]

In this manual, text placed in square brackets [xxx] indicates that that aspect of the manual remains contentious or is under development; such text is not part of the official manual. The issues will be worked on by experts and relevant text included at a future date.

Detailed instructions for the field implementation of AUSVETPLAN are contained in the disease strategies, operational procedures manuals, management manuals and wild animal manual. Industry-specific information is given in the relevant enterprise manuals. The full list of AUSVETPLAN manuals that may need to be accessed in an emergency is shown below.

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[1] These criteria are described in more detail in Chapter 1.2 of the *OIE Terrestrial Animal Health Code* (www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.1.2.htm)

[2] www.oie.int/index.php?id=169&L=0&htmfile=chapitre_1.8.10.htm

[3] www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.13_RABIES.pdf

[4] Information about the EAD Response Agreement can be found at www.animalhealthaustralia.com.au/programs/eadp/eadra.cfm

In addition, *Exotic Diseases of Animals: A Field Guide for Australian Veterinarians* by WA Geering, AJ Forman and MJ Nunn, Australian Government Publishing Service, Canberra, 1995 (to be updated) is a source for some of the information about the aetiology, diagnosis and epidemiology of the disease.

AUSVETPLAN manuals[5]

Disease strategies

- Individual strategies for each of 35 diseases
- Bee diseases and pests
- Response policy briefs (for diseases not covered by individual manuals)

Operational procedures manuals

- Decontamination
- Destruction of animals
- Disposal
- Livestock welfare and management
- Public relations
- Valuation and compensation

Enterprise manuals

- Artificial breeding centres
- Feedlots
- Meat processing
- Saleyards and transport
- Poultry industry
- Zoos

Management manuals

- Control centres management (Parts 1 and 2)
- Laboratory preparedness

Wild animal response strategy

Summary document

[5] The complete series of AUSVETPLAN documents is available on the internet at: www.animalhealthaustralia.com.au/programs/eadp/ausvetplan/ausvetplan_home.cfm

Contents

Figures

1 Nature of the disease

This AUSVETPLAN manual considers only rabies caused by lyssaviruses that are maintained and transmitted in warm-blooded terrestrial animals and bats. Infection with Australian bat lyssavirus is covered in a specific AUSVETPLAN disease strategy manual.

Rabies is a viral encephalitis of mammals that is almost invariably fatal. It is usually transmitted by bites and has a variable incubation period of days to years. Globally, the disease is of both public health and animal health significance.

Although an endemic lyssavirus is present in bats in Australia and can cause a fatal encephalitis – which is indistinguishable from rabies in humans – Australia is free from the rabies virus. Rabies is a disease that is present in most of the world, and is maintained in various hosts such as dogs and other carnivores, and bats.

1.1 Aetiology

Rabies is caused by infection with viruses of the genus *Lyssavirus,* family *Rhabdoviridae.* Lyssaviruses are genetically and serologically related, and all cause similar diseases in mammals. The genus is classified phylogenetically into seven genotypes, with four proposed new genotypes each from central Asian microchiropterid bat (Table 1.1). Lyssavirus genotypes can be further classified into variants or biotypes, defined by their maintenance-host species. A virus biotype is adapted to a single maintenance-host species, where infection and transmission by members of this species are highly efficient. Other species may also be infected by the virus biotype, but these hosts may be too inefficient as vectors or may not be numerous enough to maintain a cycle.

Example of classification:
Family: *Rhabdoviridae*
Genus: *Lyssavirus*
Genotype: for example, classical rabies = genotype 1

Rabies infection in people causes a fatal encephalitic disease. It is a significant public health issue in those areas of the world where it is present. It is virtually always fatal in humans once symptoms appear, and medical advice should be immediately sought if there is a risk of infection.

Table 1.1 Lyssavirus genotypes: common name, numerical genotype classification, geographic location, maintenance hosts and known spillover hosts

Name	Genotype designation	Locality	Maintenance hosts	Spillover hosts reported
Rabies virus	1	Worldwide (with exceptions) Bat biotypes are confined to the American continents — insectivorous bats mainly in North America, haematophagous bats in South and Central America, and the Caribbean.	Multiple American insectivorous bats: highest frequency in *Eptesicus fuscus*, *Lasionycteris noctivagens*, *Lasiuris* spp., *Myotis* spp., *Pipistrellus* spp., *Tadarida brasiliensis* Haematophagous (vampire) bats: *Desmodus* spp. Carnivores	Insectivorous bat strains: humans, foxes, skunks Vampire bat rabies: mainly cattle, horses, humans Carnivore rabies: several spillover hosts reported, including cats, dogs, humans, cattle, horses and wildlife
Lagos bat virus	2	Sub-Saharan Africa One case from France in a fruit bat imported from West Africa (1999)	Fruit bats: *Eidolon helvum*, *Micropterus pusillus*, *Epomophorus wahlbergi* Single isolate from insectivorous bat: *Nycteris gambiensis*	Cats, dogs, *Atilax paludinosus* (water mongoose)
Mokola virus	3	Sub-Saharan Africa	Not known. Has been isolated from shrews (*Crocidura* spp.)	Cats, dogs, humans, shrews
Duvenhage virus	4	Southern and eastern Africa	Insectivorous bats: *Nycteris thebaica*, possibly *Miniopterus schreibersi*	Humans
European bat lyssavirus 1	5	Europe (continental)	Insectivorous bats, particularly *Eptesicus serotinus*	Sheep, stone martens (*Martes foina*), cats, humans
European bat lyssavirus 2	6	Europe (continental, United Kingdom)	Insectivorous bats, particularly *Myotis daubentonii*, *Myotis dasycneme*	Humans
Australian bat lyssavirus	7	Australia	Flying foxes (*Pteropus* spp.) Insectivorous bat: *Saccolaimus flaviventris*	Humans
Aravan, Khujand, Irkut, West Caucasian bat virus (WCBV)	Undesignated Proposed new genotypes	Central Asia	Single isolates from insectivorous bats: *Myotis blythi* (Aravan virus), *Myotis mystacinus* (Khujand virus), *Murina leucogaster* (Irkut virus), *Miniopterus schreibersi* (WCBV)	None recorded

1.2 Susceptible host species

Lyssaviruses infect warm-blooded animals. However, rabies virus (genotype 1) can be further classified into variants or biotypes that have adapted to a specific host species and are referred to as the host biotype. The term biotype, defined by its maintenance-host species, will be used throughout this document for purposes of control and management.

The rabies virus life cycle involves maintenance-host species and spillover-host species:

- *Maintenance host.* The species that principally sustains the virus life cycle is highly susceptible to its biotype, but less susceptible to other biotypes. Successful control of rabies in the maintenance host will lead to eradication of the virus cycle in the ecological community.
- *Spillover host.* Infected hosts that belong to species that do not normally maintain the virus biotype in question. These hosts are not maintenance hosts and have no epidemiological significance in sustaining rabies epidemics. Spillover hosts are often, but not always, dead-end hosts. They may transmit infection to other hosts, although such events are relatively uncommon. Spillover hosts include humans and other primates, horses, cattle, sheep, pigs and some wild species.

The virus dose required to cause infection is higher for nonmaintenance species than for the maintenance host. The probability of establishing infection is also lower, the clinical and pathological course of the disease is less consistent, and virus shedding, and therefore transmission, is less effective.

The maintenance hosts of rabies virus are usually members of the orders Carnivora and Chiroptera. Domestic dogs are a major maintenance host in much of the world, as they were in Europe and North America before the early decades of the 20th century. Dogs still cause the majority of human rabies in the world today. In some areas of the world where dog rabies has been controlled, wildlife species have become more important for maintenance of the disease. This includes the red fox and raccoon dog in Europe; striped skunks, raccoons, red and grey foxes, and coyotes in North America; side-striped and black-backed jackals, various mongoose species (particularly the yellow mongooses) and bat-eared foxes in southern Africa; and the Arctic fox in the northern polar areas. Table 1.2 gives examples of terrestrial maintenance-host species and their localities.

Other hosts include many species of American bats. The disease appeared in the Americas during the 20th century following ecological changes that allowed major increases in bat density.

Although most, if not all, warm-blooded animals are susceptible to infection with rabies virus, rabies is not regarded as a disease of avian species. In most cases where the infection has been observed in birds, it was experimentally induced (Gough and Jorgenson 1976; Scott 1993). Birds therefore do not play a significant part in the maintenance or spread of rabies virus. The susceptibility of Australian native animals is unknown.

Table 1. 2 Examples of maintenance-host species for rabies virus (genotype 1) biotypes

Maintenance host	Locality
Family Canidae	
Domestic dog (*Canis lupus*)	Africa, Asia, and Central and South America
Arctic fox (*Alopes lagopus*)	Arctic regions
Raccoon dog (*Nyctereutes procyonoides*)	Eastern Baltic states
Red fox (*Vulpes vulpes*)	Europe,[a] Canada (Ontario), USA (northeast)
Bat-eared fox (*Otocyon megalotis*)	South Africa (Cape)
Black-backed jackal (*Canis mesomelas*)	Southern Africa
Side-striped jackal (*Canis adustus*)	Zimbabwe
Other Carnivora	
Striped skunk (*Mephitis mephitis*)	USA, Canada
Raccoon (*Procyon lotor*)	USA, Canada
Indian mongoose (*Herpestes auropunctatus*)	Caribbean
Yellow mongoose (*Cynictis penicillata*)	South Africa

USA = United States of America
a Rabies has been eradicated in western Europe.

1.3 World distribution and occurrence in Australia

Rabies virus occurs throughout most of the world except in Australia, New Zealand, Papua New Guinea, Japan, Great Britain and Ireland, and many small island nations. In some areas of the world (eg parts of western Europe), effective management of rabies in animals has reduced the frequency of occurrence of rabies in humans, and led to its eradication. However, the number and size of rabies-free countries, territories or areas is small compared with those of rabies-affected areas. Recently, there has been an outbreak of rabies in Indonesian islands such as Bali and Flores; previously, these islands had been considered rabies free.

Human rabies is found wherever animal rabies is found. Globally, human deaths from rabies are estimated to be between 55 000 and 100 000 per year. About 95% of these deaths occur in Asia and Africa. World Health Organization (WHO) data on human and animal rabies are available from the WHO website.[6] The most up-to-date information on the global rabies situation is given in the World Animal Health Information Database (WAHID) Interface.[7]

In Australia, there was one probable occurrence of transmission of rabies. This occurred in Tasmania in 1867 and involved several dogs, a pig and a child bitten by one of the dogs. In two more recent cases (1987 and 1990), individual children who contracted the infection in endemic countries developed the clinical disease in Australia after a protracted incubation.

[6] http://apps.who.int/globalatlas/default.asp
[7] www.oie.int/wahid-prod/public.php?page=disease_outbreak_map

1.4 Diagnostic criteria

1.4.1 Clinical signs

Animals

It is important to recognise the variability of the clinical syndrome. The clinical signs of rabies can, in many instances, be subtle and even unremarkable.

Clinical signs of the disease are attributable to the neurological effects of the infection. Clinical signs may change as the disease progresses and may be intermittent, alternating between different states during the course of the disease. They fall into six main categories:

- *Excitation.* This includes unprovoked aggression, overreaction to external or perceived stimuli, aimless wandering, restlessness, self-inflicted trauma (eg scratching, biting).
- *Paralysis.* This can affect any of the motor systems, causing ataxia; knuckling of distal limbs; paresis; the inability to swallow, close the jaws and lips, or retract the tongue; and facial asymmetry, including drooping ears and eyelids.
- *Loss of normal social and behavioural responses.* Wild animals will often lose their natural fear of humans. These animals may wander into urban areas and into buildings, and can be attacked and killed by dogs. Frequently, this happens at unusual times; for example, nocturnal animals may appear during the day. In companion animals, owners may report a 'personality change'.
- *Unusual vocalisation.* Many rabid animals will vocalise relentlessly. In dogs, the tone is altered, due to muscular incoordination of the larynx, causing a characteristic low-pitched, hoarse howling.
- *Pica.* Rabid animals, particularly carnivores, will chew, and often swallow, anything in their environment, including soil, plant material and bedding.
- *Coma.* This is seen in the terminal stage of the disease.

A rabid animal's signs can often rapidly change; for example, a dog may change, without provocation, from resting quietly to running frenziedly. Cats may attack suddenly and without warning. In addition to the above, animals may suffer from signs secondary to the direct neurological changes, including dehydration, red eyes, salivation, poor condition, unkempt pelage and signs of trauma. However, cases have been reported where death has occurred with few, if any, premonitory signs.

In much of the traditional literature, the clinical signs of rabies are classified into furious and dumb syndromes. While this may have been a useful classification, particularly for dog rabies, the clinician must take care not to let this bias prevent them from noticing other manifestations of the disease.

Dogs

There is a prodromal stage, which lasts 2–3 days, but is often missed by the dog's owner. During this stage, there is a sudden change in temperament. Dogs that are normally friendly towards people may suddenly become snappy and uncertain, and shy dogs may become affectionate. There may be a rise in temperature, dilation of the pupils and hyperaesthesia at the wound site.

A rabid dog will typically become unusually restless, seldom lying or sitting in one place for more than a short time. If confined, it will move around ceaselessly. At certain periods, the dog may seem possessed of abnormal strength and insensitivity to pain. Bars of cages, furniture and other objects are frequently attacked to the point where the animal's teeth are reduced to stumps and the mouth lacerated. If the dog is not under restraint, this excitable energy is manifested by furious, aimless running (sometimes for long distances), and by snapping at animate or inanimate objects in its path. Alternatively, the dog may remain quiet and lethargic; it may hide behind cover and bite only when provoked.

In many cases of rabies, the animal's pupils are dilated, there is loss of the corneal reflex, and there is sometimes a squint. The animal assumes a watchful, puzzled or apprehensive look, and may snap at imaginary objects. There is a change in phonation, often with a characteristic low-pitched, hoarse howling. Their appetite for usual foods decreases, and animals start to eat stones, sticks, earth and other objects. There may be muscle tremors and paralysis of the hindquarters, the jaw ('dropped jaw') and the tongue, which hangs flaccidly from the mouth. There may be drooling from the mouth. Often, the rabid dog is unable to eat or to lap water, although it may repeatedly try to do so. In contrast to human rabies, hydrophobia is a rare sign in dogs and other animals. Within 1–4 days of the onset of symptoms, there is rapidly progressing ataxia. Death supervenes within a few days, usually from paralysis of respiratory muscles.

Cats

The clinical signs in cats are generally similar to those in dogs, but unprovoked aggression is a more common presenting sign. Rabid cats often retreat into hiding, from where they spring to attack humans or other animals ferociously when approached. Their pupils are dilated. They may mew continuously and the vocalisation becomes hoarse. As the disease progresses into the paralytic phase, the animal shows marked incoordination, followed by posterior paralysis. The muscles of the head become paralysed, and the animal soon lapses into a coma and dies.

Horses

Clinical signs of rabies in horses are highly variable and can be easily confused with other diseases affecting the nervous system, such as cervical vertebral malformation or other viral encephalitides.

Periods of marked excitation and aggressiveness alternate with periods of relative calm. In periods of excitation, affected animals become restless, stare, paw, move their ears, draw their upper lips back and forth continually, and salivate excessively. There may be intense sexual excitement. Animals frequently grind their teeth, whinny as if in great pain, and show signs of acute colic, which may present as oesophageal obstruction. They may lash out with great fury at any perceived threat or restraint (donkeys will often attack and bite other animals and people). They often bite or rub at the site of exposure, causing self-mutilation. As

paralysis develops, they fall repeatedly, finally remaining down with their legs thrashing. In some cases, the excitatory phase is absent and there is dysphagia, aimless wandering or staggering, and a rapidly developing paralysis. Equine rabies progresses rapidly, with most affected animals becoming depressed, recumbent and comatose before dying within 5 days of the onset of clinical signs.

Cattle

In cattle, there is initial depression and cessation of milk production. Paralysis of throat muscles with grinding of teeth and excess salivation is common, and may lead to a false diagnosis of oesophageal obstruction. Cattle may bellow frequently in a low-pitched voice. There is increased sexual excitement. Some animals develop one or more furious stages, and may attack other animals or objects; they charge and butt, but seldom bite. Other animals show little excitement.

As paralysis develops, cattle knuckle over at the fetlocks, stumble and fall frequently. Finally, they are unable to rise, lapse into a coma and die.

Sheep

In sheep, a period of excitement occurs, during which affected sheep move restlessly, salivate and grind their teeth. They also show twitching of the lips and oscillation of the tongue, pulling of wool and aggressive butting of other sheep or objects. Rams exhibit sexual excitement. Sheep may either be silent or emit frequent hoarse bleats. The excitation stage is followed by depression, increasing weakness, paralysis and recumbency. Sheep generally die within 72 hours of the onset of clinical signs.

Pigs

Affected pigs tend to stand trembling in a darkened corner, but may dash out and bite if provoked. They may rub or gnaw at the bite site. There is abnormal deep grunting. Depraved appetite is common. There may be alternating periods of intense activity and recumbency. Sows may kill their offspring. There is increasing dullness, incoordination and paralysis.

Foxes

In foxes, the normal fear of people and other animals is lost. The normal social etiquette between foxes, particularly with regard to territoriality, is not observed by the rabid fox, leading to conflict. Anorexia, agitation and a characteristic abnormal cry occur. A rabid fox may charge at and bite passing people, animals and even vehicles. As the disease progresses, the fox becomes more confused and uncoordinated. With the onset of paralysis, it falls and may be unable to rise. It may attempt to drag itself before finally lapsing into a coma and dying.

Other wildlife species

In other wildlife species, the clinical signs are variable. The most important common feature is loss of normal shyness and fear of people and other animals. This makes such animals particularly dangerous to children, who wrongly interpret this behaviour as indicating friendliness.

Humans

The clinical manifestations of rabies in humans are well described (Heymann 2008), and the disease is almost invariably fatal.

1.4.2 Pathology

Gross lesions

Usually, no remarkable gross pathological signs are evident; when present, they are secondary to the neurological effects. Carcasses are often dehydrated and in poor physical condition, and may have physical signs of recent trauma; for example, broken teeth. In carnivores, signs of pica, such as soil and plant material in the mouth and stomach, may be present.

Microscopic lesions (histopathology)

Microscopically, the most significant lesions are in the central nervous system, and cranial and spinal ganglia. There is usually perivascular cuffing, focal and diffuse gliosis, neuronal degeneration, and intracytoplasmic inclusion bodies (or Negri bodies) in the neurones. Negri bodies vary in size with the host – they are large in dogs and cattle. Negri bodies are found most commonly in the neurones of the hippocampus or in the Purkinje cells of the cerebellum in cattle. They are found less frequently in the glial cells, in ganglion cells of the salivary glands and adrenal medulla, and in the retina.

Pathogenesis

Rabies virus is transmitted through saliva by the bite of a rabid animal. After the inoculation of virus into a wound, virus replicates in local tissues. Within hours to days after a bite, there is invasion of peripheral nerve endings, followed by centripetal movement of virions along axons to the central nervous system (CNS). Once the CNS is invaded by virus, clinical signs become apparent and the disease course is irreversible. CNS infection patterns and therefore clinical signs vary, but often include behavioural changes that lead to biting other animals. From the CNS, virus invades peripheral nerves, leading to virus infection of many peripheral tissues, including salivary glands. Virus infection of salivary acinar cells leads to shedding of large numbers of virions into saliva. Shedding is coincident with the behavioural changes that lead to biting of other animals.

No signs – clinical, pathological or immunological – are apparent before CNS invasion, a period referred to as the incubation period. The disease, once it appears, is acute and progressive, leading almost invariably to death of the host if the animal is not destroyed beforehand. The overwhelming neural infection is unusual in that it is slow to provoke an inflammatory response. Once the inflammatory response appears, it contributes to irreversible neurological damage. This pattern of viral invasion followed by inflammatory response causes the typical progression of excitatory to paralytic disease.

A significant proportion of bites by rabid animals do not result in transmission and development of disease. This is usually due to a low dose of virus in the bite inoculum, which does not lead to detectable seroconversion. Alternatively, infection may be initiated at the site of inoculation, but is cleared before establishment in the CNS. This is known as 'abortive infection' and does not result in clinical signs of disease, but may result in seroconversion.

Although there are some reports of dogs surviving rabies or developing chronic infection in western Africa, Ethiopia and India (Veeraraghavan et al 1971, Fekadu

1972, Aghomo et al 1989, Fekadu 1991), these findings have not be reproduced in recent years. It is generally accepted that there is no carrier or latent state for rabies.

1.4.3 Laboratory tests

Rabies may be suspected in animals that display neurological signs, including behavioural changes and paralysis, followed by death within 10 days. The diagnosis must be confirmed by laboratory tests. A positive result in any species must be notified immediately to the chief veterinary officer (CVO) of the state or territory concerned, who will immediately notify their public health department equivalent.

Specimens should initially be sent to the state or territory veterinary laboratory (or other appropriate laboratory), from where they may be forwarded to the CSIRO Australian Animal Health Laboratory (CSIRO-AAHL) for testing or confirmation of positive or suspicious test results.

Specific laboratory diagnostic tests are necessary to confirm rabies infection as neither clinical signs, nor gross or histological pathology are pathognomonic. The tests currently available for rabies diagnosis are discussed in the section 'Laboratory diagnosis', below.

Further information on testing is available on the website of the Australian Government Department of Health and Ageing (www.health.gov.au).

Specimens required

Because rabies is almost invariably fatal without vaccination, operators should take adequate precautions to prevent accidental exposure or self-inoculation when collecting specimens. If a potential exposure to rabies occurs, first-aid procedures should be undertaken immediately. Medical advice should always be sought without delay, irrespective of vaccination status, as postexposure prophylaxis may be needed. Please also refer to Section 3.2 for more information on occupational health and safety aspects.

Before shipping specimens, submitters should contact the receiving laboratory to discuss arrangements for sampling, transport and sample reception.

For all species, whole animals, severed heads or unpreserved brains should be chilled and forwarded on ice to the testing laboratory. The brain is the most important specimen for laboratory confirmation of rabies. Distribution of virus in the brain is usually diffuse, but may be localised in some cases. Of the structures of the brain, the brain stem is the most consistently reliable area for detection of infectious virus or viral antigen. Other regions of the brain, including the hippocampus, are negative in up to 5% of rabid animals. For this reason, it is important to take a composite brain sample to include several different parts of the brain in the diagnostic test. If the brain is not present, other suitable tissues include spinal cord, the trigeminal ganglion, peripheral nerves (taken from points close to the CNS) and salivary glands.

Unless the operator is vaccinated and experienced, the head or brain should not be removed before submission because of the risk of self-inoculation.