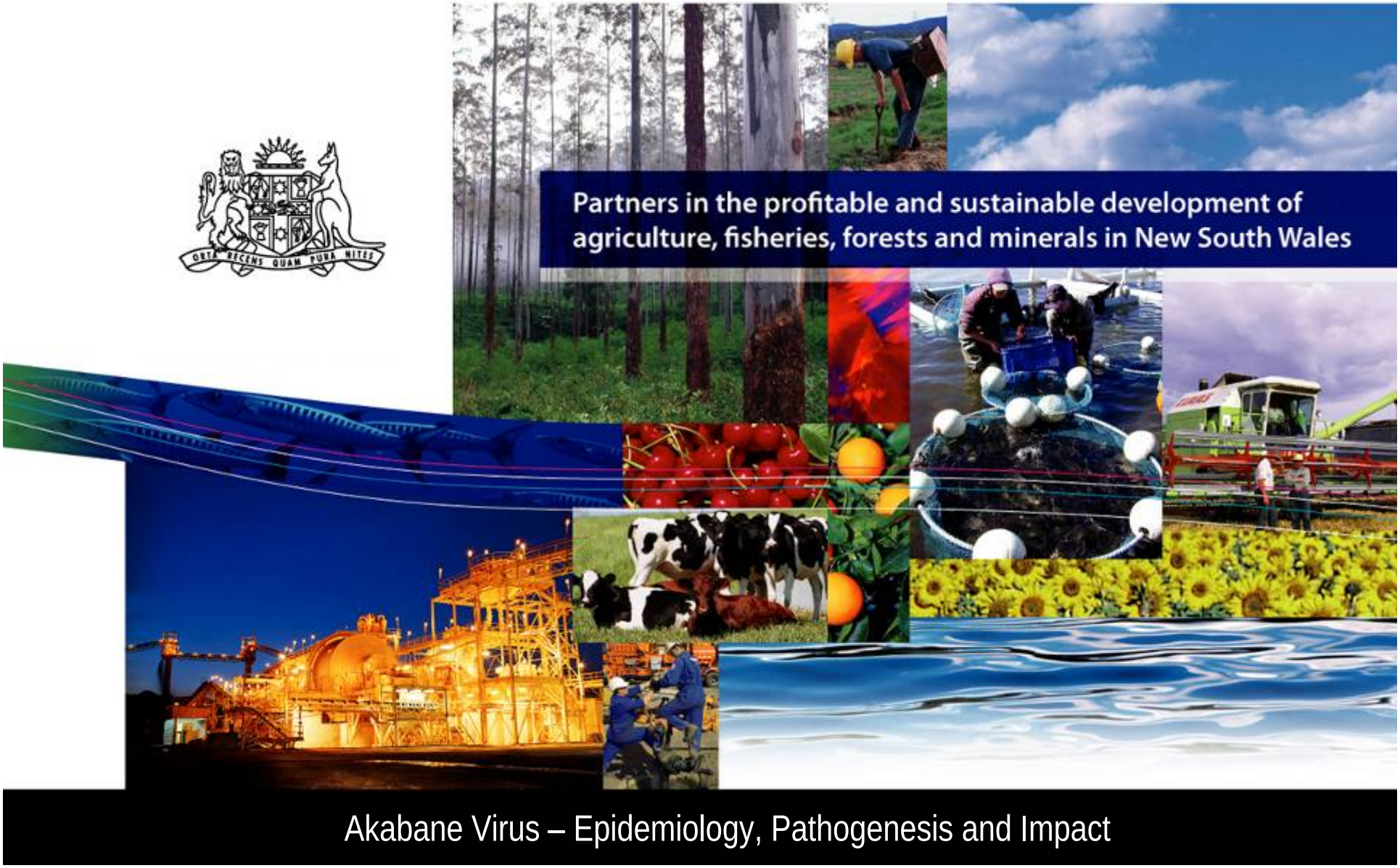


Akabane Virus – Epidemiology, Pathogenesis and Impact

P.D. Kirkland, EMAI, Camden NSW Australia.

Akabane virus – some history

- Prior to 1975, bovine ephemeral fever (a rhabdovirus infection of cattle) caused intermittent major epizootics of disease sweeping from the tropical north to the far south of Australia;
- The virus spread over several thousand kilometres in 1-2 months.
- A vector-borne aetiology was suspected;

Geography of Australia – a large continent

Akabane virus discovered

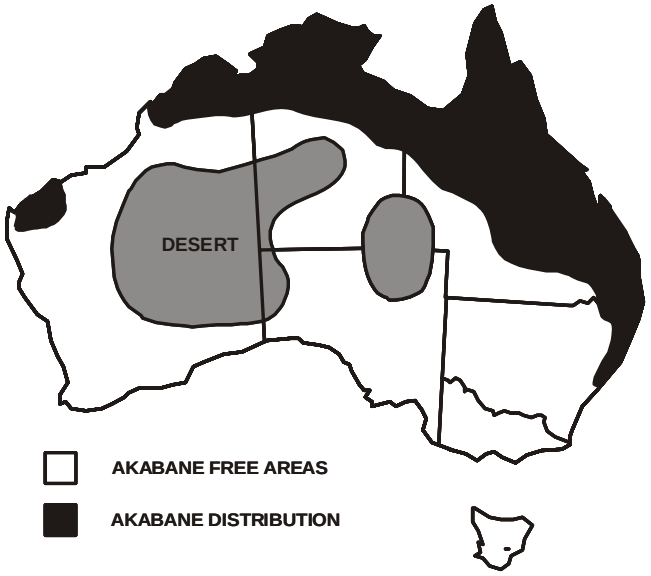
- During the search for the vector of BEF, mosquitoes and midges (Culicoides spp) were caught and virus isolation attempted;
- Many viruses isolated. In 1968, a bunyavirus from the Simbu serogroup was isolated from Culicoides brevitarsis – virus identified as B8935.
- Serological surveys using VNT show high prevalence of infection in cattle, also infection of sheep, goats and horses;
- No known association with between B8935 infection and disease in cattle;

Akabane virus epidemiology

- In 1974, Akabane virus shown to be associated with the arthrogryposis- hydranencephaly (AG/HE) of cattle in Japan. In August 1974, B8935 virus and Akabane shown to be identical and also involved in AG/HE epizootics in Australia
- Systematic studies of the epidemiology of Akabane infection of cattle commenced in 1975, using sentinel cattle;
- Sentinel cattle aged 5-7 months at recruitment (first year of exposure to virus);

Akabane virus epidemiology

- Geographical distribution of Akabane virus in Australia shown to match the distribution of Culicoides brevitarsis;



Akabane virus epidemiology

- High prevalence of Akabane virus infection in sentinel cattle – ie most young cattle (<15 mths) seroconvert in endemic area;
- Seroprevalence often lower in sheep; goats similar to cattle;
- Infection rates may be higher in intact males than females or castrated males;

Akabane virus epidemiology

- Monitoring of sentinel cattle demonstrates regular annual transmission of Akabane virus within range of C. brevitarsis

SIMBU ELISA													
LISMORE	2001												
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN
1	1				-		+	+	+	+	+	+	+
2	2				-		-	+	+	+	+	+	+
3	3				-		-	+	+	+	+	+	+
4	4				-		+	+	+	+	+	+	+
5	5				-		+	+	+	+	+	+	+
6	6				-		-	+	+	+	+	+	+
7	7				-		+	+	+	+	+	+	+
8	8				-		+	+	+	+	+	+	+
9	9				-		+	+	+	+	+	+	+
10	10				-		+	+	+	+	+	+	+
At Risk (A)					?		10	3	0	0	0	0	0
No S/C (S)					0		7	3	0	0	0	0	0
TOTAL (T)					10		10	10	10	10	10	10	10

SIMBU ELISA													
LISMORE	2002												
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN
1	101						-	-	+	+	+	+	
2	102						-	-	+	+	+	+	
3	103						-	-	+	+	+	+	
4	104						-	-	+	+	+	+	
5	105						-	-	+	+	+	+	
6	106						-	-	+	+	+	+	
7	107						-	-	+	+	+	+	
8	108						-	-	+	+	+	+	
9	109						-	-	-	+	+	+	
10	110						-	-	+	+	+	+	
At Risk (A)							?	10	10	1	0	0	
No S/C (S)							0	0	9	1	0	0	
TOTAL (T)							10	10	10	10	10	10	

SIMBU ELISA												
LISMORE	2003											
ANIMAL	EARTAG	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN
1	201				-	+	+	+	+	+	+	
2	202				-	+	+	+	+	+	+	
3	203				-	+	+	+	+	+	+	
4	204				-	+	+	+	+	+	+	
5	205				-	+	+	+	+	+	+	
6	206				-	+	+	+	+	+	+	
7	207				-	-	+	+	+	+	+	
8	208				-	-	-	+	+	+	+	
9	210				-	-	?	+	+	+	+	
10	211				-	+	+	+	+	+	+	
At Risk (A)					?	10	3	0	0	0	0	
No S/C (S)					0	7	3	0	0	0	0	
TOTAL (T)					10	10	10	10	10	10	10	

SIMBU ELISA													
LISMORE	2004												
ANIMAL	EARTAG	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	
1	301			-		-	-	+	+	+	+	+	
2	302			-		-	-	+	+	+	+	+	
3	303			-		-	-	+	+	+	+	+	
4	304					-	-	+	+	+	+	+	
5	305			-		-	-	+	+	+	+	+	
6	306			-		-	-	+	+	+	+	+	
7	307			-		-	-	+	+	+	+	+	
8	308			-		-	-	+	+	+	+	+	
9	309			-		-	-	+	+	+	+	+	
10	310			?		-	-	+	+	+	+	+	
At Risk (A)				?		8	12	12	1	0	0	0	
No S/C (S)				0		0	0	12	1	0	0	0	
TOTAL (T)				11		12	12	12	13	13	12	12	

Akabane virus epidemiology

- Consistent north-south transmission pattern - North Coast NSW

SIMBU ELISA														
LISMORE	2001													
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	1				-		+	+	+	+	+	+	+	
2	2				-		-	+	+	+	+	+	+	
3	3				-		-	+	+	+	+	+	+	
4	4				-		+	+	+	+	+	+	+	
5	5				-		+	+	+	+	+	+	+	
6	6				-		-	+	+	+	+	+	+	
7	7				-		+	+	+	+	+	+	+	
8	8				-		+	+	+	+	+	+	+	
9	9				-		+	+	+	+	+	+	+	
10	10				-		+	+	+	+	+	+	+	
At Risk (A)					?		10	3	0	0	0	0	0	
No S/C (S)					0		7	3	0	0	0	0	0	
TOTAL (T)					10		10	10	10	10	10	10	10	

SIMBU ELISA														
CASINO														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	27				-		-	+	+	+	+	+	+	
2	28				-		+	+	+	+	+	+	+	
3	29				-		-	-	+	+	+	+	+	
4	30				-		+	+	+	+	+	+	+	
5	31				-		-	-	+	+	-	-	+	
6	32				-		-	-	+	+	+	+	+	
7	33				-		-	-	+	+	+	+	+	
8	34				-		-	-	+	+	+	+	+	
9	35				-		-	-	-	+	+	+	+	
10	36				-		-	-	-	+	+	+	+	
At Risk (A)					?		10	8	7	2	0	0	0	
No S/C (S)					0		2	1	5	2	0	0	0	
TOTAL (T)					10		10	10	10	10	10	10	10	

SIMBU ELISA														
COFFS HARBOUR														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	385						-	+	+	+	+	+	+	
2	399				-		-	-	-	+	+	+	+	
3	381				-		+	-	-	+	+	+	+	
4	378				-		-	-	-	-	+	+	+	
5	380				-		-	-	-	+	+	+	+	
6	400				-		-	+	+	+	+	+	+	
7	401				-		-	+	+	+	+	+	+	
8	384				-		+	+	+	+	+	+	+	
9	B8				+		-	+	-	+	+	+	+	
10	387						+	+	+	+	+	+	+	
At Risk (A)					?		6	7	4	4	1	0	0	
No S/C (S)					0		1	4	0	3	1	0	0	
TOTAL (T)					7		10	10	10	10	10	10	10	

SIMBU ELISA														
KEMPSEY														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	53				-		-	-	-	-	-	+	+	
2	54				-		-	+	+	+	+	+	+	
3	55				-		-	-	-	-	?	+	+	
4	56				-		-	+	+	+	+	+	+	
5	57				-		-	+	+	+	+	+	+	
6	58				+		-	+	+	+	+	+	+	
7	59				+		-	+	+	+	-	+	+	
8	60				+		-	-	-	-	-	+	+	
9	61				+		-	+	+	+	+	+	+	
10	62				+		-	-	-	-	-	+	+	
At Risk (A)					?		5	10	4	4	4	3	0	
No S/C (S)					0		0	6	0	0	1	3	0	
TOTAL (T)					10		10	10	10	10	10	10	10	

Akabane virus epidemiology

- Consistent north-south transmission pattern - Central Coast NSW

SIMBU ELISA														
TAREE	2001													
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	B384				-		-	+	+	+	+	-	+	+
2	Y647				-		-	-	+	+	+	+	+	+
3	Y636				-		-	-	+	+	+	+	+	+
4	B381				-		-	-	-	+	+	+	+	+
5	Y612				-		-	+	+	+	+	+	+	+
6	Y646				-		+	+	+	+	+	+	+	+
7	Y614				+		-	-	+	+	-	+	+	+
8	Y615				-		-	-	+	+	+	+	+	+
9	Y613				-		-	-	+	+	+	+	+	+
10	NT (133899)				+		+	+	+	+	+	+	+	+
At Risk (A)					?		8	8	6	0	0	0	0	0
No S/C (S)					0		1	2	6	0	0	0	0	0
TOTAL (T)					10		10	10	10	10	10	10	10	10

SIMBU ELISA														
PATERSON														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	3493						-	-	+	+	+	+	+	+
2	3497						-	-	+	-	-	+	+	+
3	3498						-	-	+	+	+	+	+	+
4	3518						-	-	+	+	+	+	+	+
5	3520						-	-	+	+	+	+	+	+
6	3522						-	-	+	+	+	+	+	+
7	7054						-	-	+	+	+	+	+	+
8	7055						-	-	+	+	+	+	+	+
9	7059						-	-	+	+	+	+	+	+
10	9177						-	-	-	+	+	+	+	+
At Risk (A)							?	10	10	1	0	0	0	0
No S/C (S)							0	0	9	1	0	0	0	0
TOTAL (T)							10	10	10	10	10	10	10	10

SIMBU ELISA														
SINGLETON														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	1					-	-	-	-	+	ns	+	+	
2	2					-	-	-	-	+	+	+	+	
3	3					-	-	-	-	+	+	+	+	
4	4					-	-	-	-	+	+	+	+	
5	5					-	-	-	-	+	+	+	+	
6	6					-	-	-	-	-	+	+	+	
7	7					-	-	-	-	+	+	-	-	
8	8					-	-	-	-	+	+	+	+	
9	9					-	-	-	-	+	+	+	+	
10	10					-	-	-	-	+	+	+	+	
At Risk (A)						?	10	10	10	10	1	0	0	
No S/C (S)						0	0	0	0	9	1	0	0	
TOTAL (T)						10	10	10	10	10	10	10	10	

SIMBU ELISA														
SCONE														
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	8					-	-	-	-	+	-	+	+	
2	138					-	-	-	-	+	-	+	+	
3	161					-	-	-	-	+	+	+	+	
4	183					-	-	-	-	+	-	-	+	
5	202					-	-	-	-	-	+	-	+	
6	231					-	-	-	-	+	+	+	+	
7	237					-	-	-	-	+	+	+	+	
8	371					-	-	-	-	-	+	+	+	
9	425					-	-	-	-	+	+	+	+	
10	463					-	-	-	-	+	+	+	+	
At Risk (A)						?	10	10	10	10	2	0	0	
No S/C (S)						0	0	0	0	8	2	0	0	
TOTAL (T)						10	10	10	10	10	10	10	10	

Akabane virus epidemiology

- Consistent north-south transmission pattern - South Coast NSW

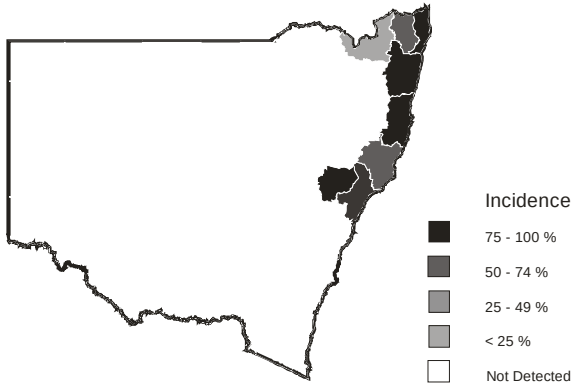
  & southern limit of spread

SIMBU ELISA																SIMBU ELISA													
CAMDEN	2001															NOWRA													
ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL		ANIMAL	EARTAG	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL
1	1568					-	-	-	-	+	+	+	+			1	410						-	-	-	-	-	-		
2	1570					-	-	-	-	-	ns	+	ns			2	412						-	-	-	-	-	-		
3	1571					-	-	-	-	+	+	+	-			3	413						-	-	-	-	-	-		
4	1572					-	-	-	-	-	+	+	ns			4	414						-	-	-	-	-	-		
5	1574					-	-	-	-	+	ns	+	+			5	415						-	-	-	-	-	-		
6	1575					-	-	-	-	-	+	+	-			6	416						-	-	-	-	-	-		
7	1577					-	-	-	-	-	+	+	+			7	417						-	-	-	-	-	-		
8	1578					-	-	-	-	-	+	+	+			8	418						-	-	-	-	-	-		
9	1579					-	-	-	-	-	+	+	+			9	419						-	-	-	-	-	-		
10	1580					-	-	-	-	+	+	+	-			10	421						-	-	-	-	-	-		
At Risk (A)						?	10	10	10	10	5	1	0			**At Risk (A)**							?	12	10	10	10	10		
No S/C (S)						0	0	0	0	4	5	1	0			**No S/C (S)**							0	0	0	0	0	0		
TOTAL (T)						10	10	10	10	10	8	10	10			**TOTAL (T)**							12	12	10	10	10	10		

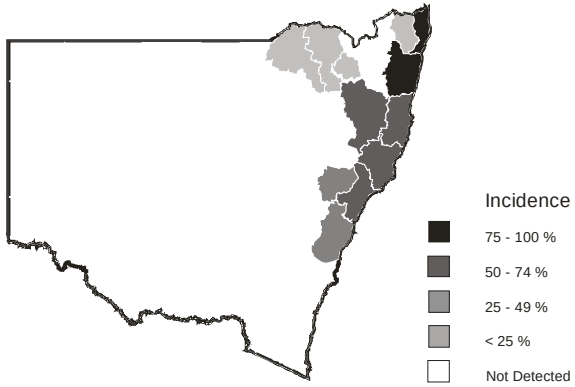
Akabane virus epidemiology

- Annual transmission patterns regular and ‘predictable

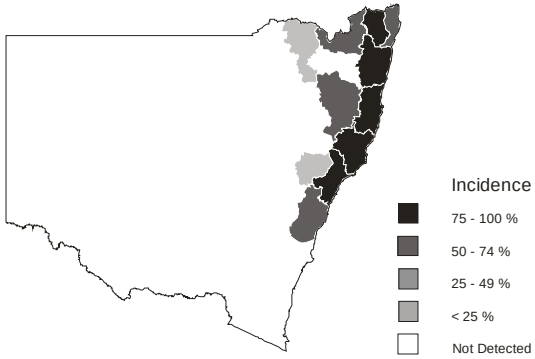
Distribution of Akabane Virus: 2004-2005.



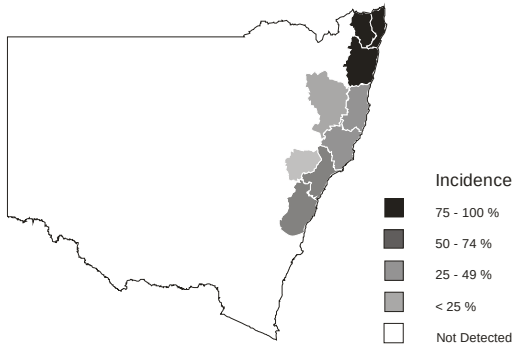
Distribution of Akabane Virus: 2005-2006.



Distribution of Akabane Virus: 2006-2007.



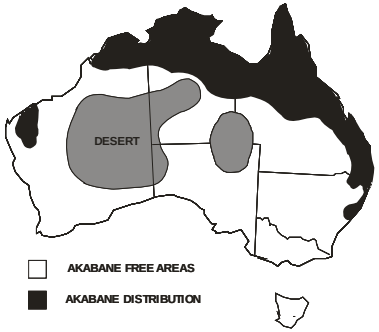
Distribution of Akabane Virus: 2007-2008.



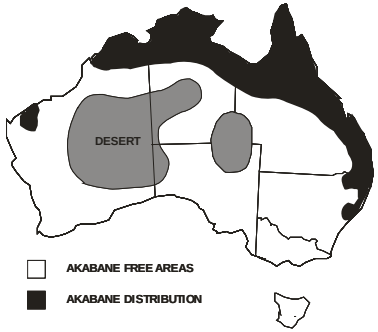
Akabane virus epidemiology

- Annual transmission patterns regular and ‘predictable

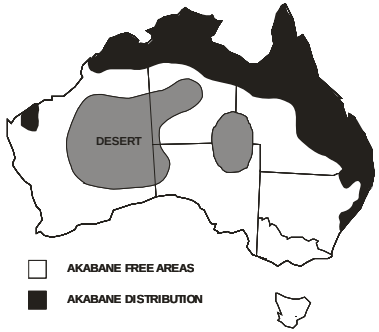
LIMITS OF AKABANE VIRUS 2005/2006



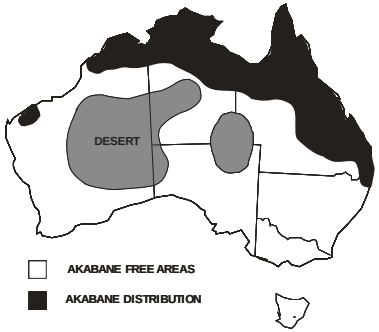
LIMITS OF AKABANE VIRUS 2006/2007



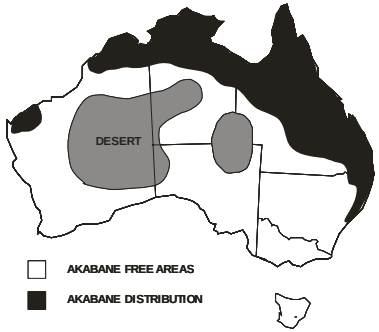
LIMITS OF AKABANE VIRUS 2007/2008



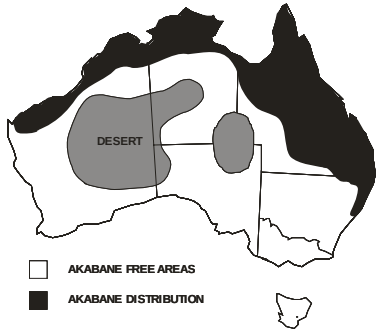
LIMITS OF AKABANE VIRUS 2008/2009



LIMITS OF AKABANE VIRUS 2009/2010



LIMITS OF AKABANE VIRUS 2010/2011



Akabane virus epidemiology

- Akabane and related viruses transmitted with high efficiency – especially compared to bluetongue viruses;
- Transmission occurs even with small vector populations;
- Distribution of Akabane and other Simbu viruses a reliable indicator of ‘effective’ vector populations.

Akabane disease

- Akabane virus is predominantly a foetal pathogen;
- Australian strains of Akabane virus have not been associated with disease following postnatal infection;
- Some strains of Akabane virus in Japan have caused disease in both neonates and older cattle.

Akabane disease occurrence

- Disease is ONLY observed with a disruption or alteration to the endemic cycle (females become immune prior to breeding age);
- Disease can occur as a result of:

  - a reduction in the size of the ‘normal’ endemic zone (eg following adverse climatic conditions - drought) due to reduced vector activity;

  - an expansion of the distribution of vectors (following favourable climatic conditions).

  - the introduction of susceptible animals into the endemic zone

Akabane disease - cattle

- Clinical outcome depends on stage of pregnancy at which a susceptible female is infected.
- Due to the longer gestation period, disease in cattle is observed over a longer time span although infection may be restricted to a few weeks;
- Disease in cattle occurs following infection from about 70 days of gestation through to term;
- Highest incidence of defects follow infection at 3-4 mths of gestation

Akabane disease – sheep and goats

- Disease less likely to occur in small ruminants due to shorter gestation period;
- Different clinical presentations seen in cattle tend to merge in sheep and goats;
- Affected progeny may have wide range of defects;
- Highest incidence of defects follow infection at 28-60 days of gestation
- Can be absence of disease in sheep and goats in areas where cattle affected – only as a result of later seasonal breeding

Akabane disease incidence

- Severity of disease can be strain related;
- Experimentally, some strains cause defects in 80% of lambs, others 15%;
- In the field, in cattle, disease has been observed in 50% of progeny of infected cows
- Some strains of virus cause a higher incidence of abortions

Akabane disease pathogenesis in cattle

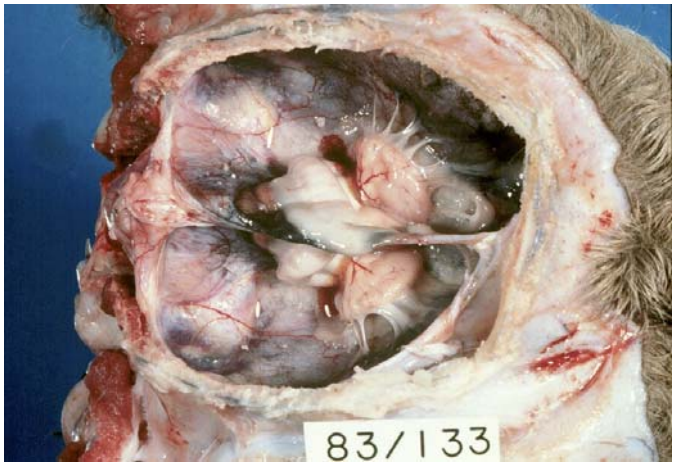
- Clinical outcome depends on stage of pregnancy at which a susceptible cow is infected.
- Sequential appearance of different clinical presentations in year round calving herds;
- Seasonally (especially autumn) calving herds may not see a problem;
- Spring calving herds have greatest losses (many cows in early pregnancy during virus transmission period)
- Losses reduced in year round calving herds

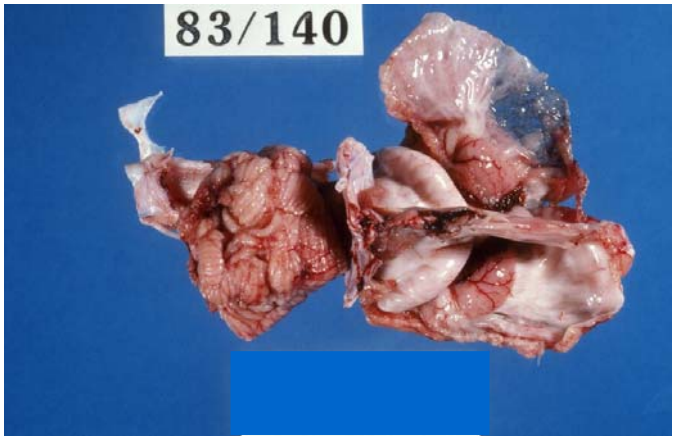
Akabane disease pathogenesis in cattle

- Infection in very late pregnancy or sometimes newborn – non-suppurative encephalitis – clinically a flaccid paralysis
- Infection 5-6 months – arthrogryposis (AG) – initially 1 or 2 joints; later cases (earlier infection) involve multiple joints and all limbs;
- Lesions primarily a neurogenic muscular atrophy;
- Degeneration/necrosis of ventral horn motor neurones of spinal cord

Akabane pathogenesis

- Infection 3-4 months – hydranencephaly (HE)– some overlap with AG – small cystic lesions initially; early infection – severe HE;
- More likely to be abortions after early infection;
- Sheep and goats – have both AG & HE together





Akabane pathology

- In cattle, at term, lesions confined almost exclusively to the CNS (brain and/or spinal cord);
- Lesions of AG predominantly a neurogenic muscular atrophy;
- Degeneration/necrosis of ventral horn motor neurones of spinal cord;
- Occasionally a residual myositis;
- Hydranencephaly a result of virus induced degeneration of developing CNS;
- In sheep and goats, impaired development of other organs eg pulmonary & thymic hypoplasia

Akabane diagnosis

- Virus can be isolated from aborted bovine foetuses or calves with late-term infections;
- Residual RNA detected by PCR over a longer period;
- Most calves that are delivered at term have no infectious virus present;
- In colostrum deprived calves, elevated IgG levels (a screening tool);
- Specific antibody can be demonstrated (VN/ELISA) in most animals with elevated IgG

Akabane – semen & embryos

- Period of viraemia very short;
- No evidence of persistent infections;
- Conflicting results from limited studies of the semen of bulls;
- Virus has been detected in semen following inoculation of sheep but it little is known about the quality of the semen and presence of blood;
- Akabane virus has not been detected in limited studies of bovine embryos

Other Simbu viruses

- Four other viruses that infect livestock – Aino, Douglas, Peaton and Tinaroo viruses;
- All spread by same vector as Akabane;
- Epidemiology and geographical limits the same;
- Usually one Simbu virus dominates transmission although a second can sometimes be spread later in season;

Other Simbu viruses

- Dual infections can occur in one animal in the same season but infection with more than 2 viruses uncommon
- Some viruses appear to give cross protection/partial immunity against Akabane infection under field conditions;
- Aino associated with disease outbreak 35 years ago, but despite transmission in apparently susceptible populations, disease outbreaks has never been observed;
- No known disease due to infections with other Simbu viruses.