



Avian Influenza: A New Emerging Infectious Disease

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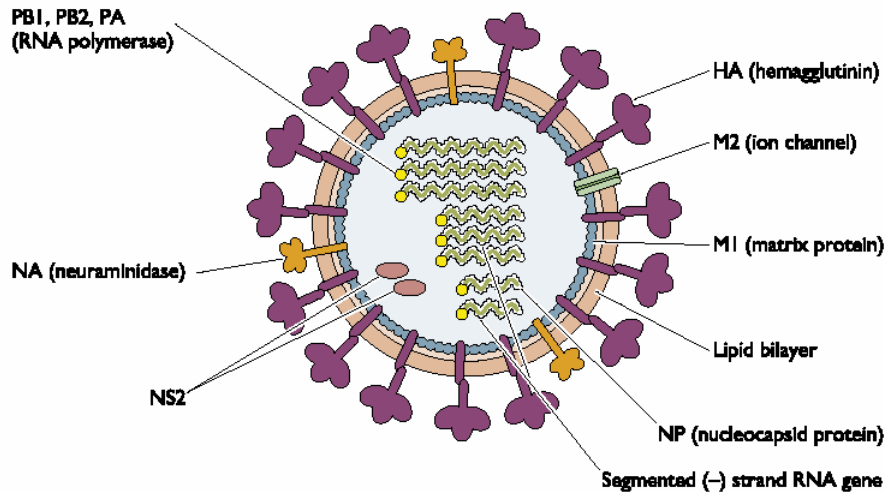
Aspects to be covered:

- **The viruses**
- **The disease**
- **The emergence of H5N1**
- **Laboratory Diagnosis**
- **Real Time PCR**
- **R&D responses to the Asian epidemic**
 - **Vaccine evaluation**
 - **Point of sampling diagnostics evaluation**



Avian Influenza

The Virus(es)



Type

- Type A, B or C based on matrix (MA) and non-structural (NS) proteins

Subtype

- H1 - H16 based on HA protein
- N1 - N9 based on NA protein

Molecular pathotype

- HPAI or LPAI strains
- Molecular pathotype based on HA cleavage region of H5 or H7 strains

Molecular Basis of Pathogenicity: Proteolytic Activation of H

Inactive Precursor H_0 (76 kD)

Activated H_1 (47 kD)

H_2 (29 kD)

A/Chicken/Vietnam/8/2004 (H5N1) HPAI

CCT	CAA	AGA	GAG	AGA	AGA	AGA	AAA	AAG	AGA	GGA	TTA	TTT
Pro	Gln	Arg	Glu	Arg	Arg	Arg	Lys	Lys	Arg*	Gly	Leu	Phe
P	Q	R	E	<u>R</u>	<u>R</u>	<u>R</u>	<u>K</u>	<u>K</u>	R	*G	L	F

A/Tern/Australia/75 (H5N3) LP AI

CCC	CAA	AGG	GAG	ACA	---	---	---	---	AGA	GGT	CTA	TTT
Pro	Gln	Arg	Glu	Thr	---	---	---	---	Arg*	Gly	Leu	Phe
P	Q	R	E	T	-	-	-	-	R	*G	L	F

Isolate	Cleavage sequence
Non-pathogenic H5 subtypes	
A/chicken/Mexico/31381/94	P Q R E - - - - T R ↓ G
A/chicken/Pennsylvania/1/83 (CHO+)	P Q K K - - - - K R ↓ G
A/duck/Singapore/645/97	P Q R E - - - - T R ↓ G
Pathogenic H5 subtypes	
A/chicken/Pueblo/94	P Q R K R K - - T R ↓ G
A/chicken/Queretaro/20/95	P Q R K R K R K T R ↓ G
A/chicken/Pennsylvania/1370/83 (CHO-)	P Q K K - - - - K R ↓ G
A/chicken/Hong Kong/990/97	P Q R E R R R K K R ↓ G
A/Hong Kong/156/97- (human)	P Q R E T R R K K R ↓ G
A/Hong Kong/486/97- (human)	P Q R E R R R K K R ↓ G
Non-pathogenic H7 subtypes	
A/tern/Potsdam/79	P E I P K - - - - G R ↓ G
A/duck/Victoria/76	P E I P K - - - - K R ↓ G
Pathogenic H7 subtypes	
A/chicken/Leipzig/79	P E I P K K K - - G R ↓ G
A/goose/Leipzig/137/79	P E I P K R K - - G R ↓ G
A/goose/Leipzig/187/79	P E I P K K K K - G R ↓ G
A/goose/Leipzig/192/79	P E I P K K K K K G R ↓ G
A/chicken/Victoria/76	P E I P K K K E - K R ↓ G

- Glycosylation of sites adjacent to the cleavage site can affect HA activation
- Loss of glycosylation presumably allows easier access of proteases and increased spread



High Pathogenicity Avian Influenza (HPAI) in Australia

Previous outbreaks of high-pathogenicity avian influenza (HPAI) in Australia all caused by viruses of H7 subtype

- **1997 NSW H7N4**
- **1994 Qld H7N3**
- **1992 Vic H7N3**
- **1985 Vic H7N7**
- **1976 Vic H7N7**

No cases of HP H5 in Australia



Avian Influenza

The Disease



Clinical Signs

- **Very high mortality rate (almost 100%)**
- **Wattle and comb : swollen and cyanotic**
- **Sero-mucous nasal discharges and hypersalivation**
- **Feet - petechiae**
- **Diarrhoea**
- **Depression**
- **Softened egg shells**



Depression & Diarrhoea



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sudden high mortality



Swollen head and nasal discharges



2004 1 16





Subcutaneous petechiae and swollen feet



Subcutaneous petechiae feet





4 MAR 2004