APPROACH TO AN UNSOLVED PROBLEM OF NEWCASTLE DISEASE VIRUS IN POULTRY

KNOW THE VIRUS THAT'S KILLING

Dr. Prakash B. Reddy., *Ph. D*

D. G. M.-Technical

E.mail: prakash.reddy@venkys.com

NOVACON
CONference on InNOVAtion

Venworld
THE BEST IN ANIMAL HEALTHCARE

1. REASONS FOR ENDEMICITY OF CENTURY OLD NDV

2. NDV PANDEMICS AND EVOLUTION OF NDV GENOTYPES

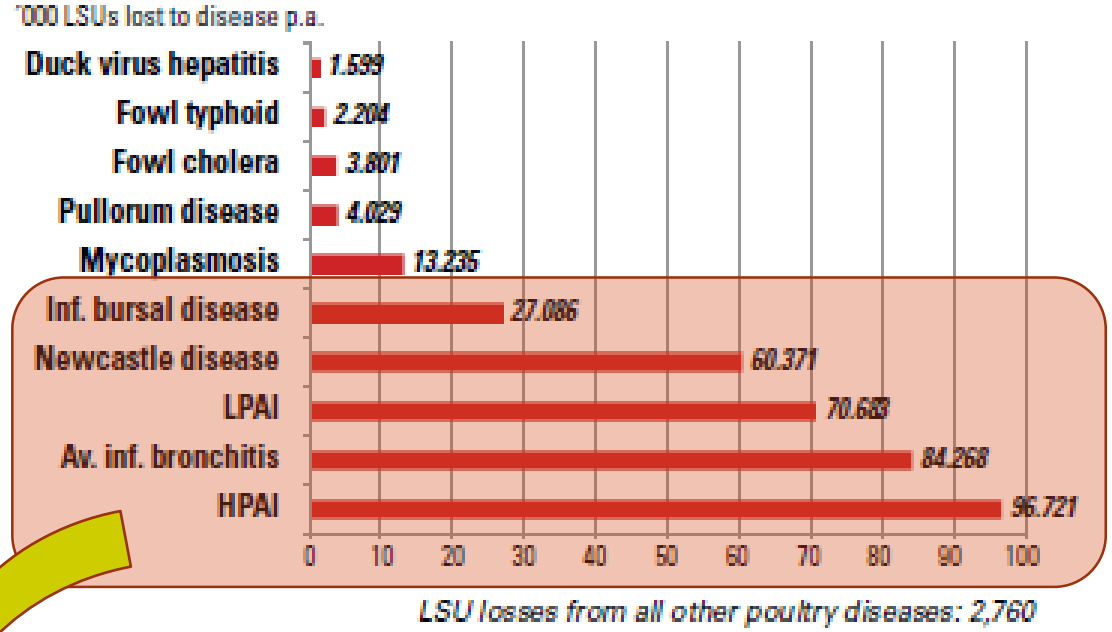
3. VACCINE DEVELOPMENT FOR THE LAST 90+ YEARS

4. GOALS OF NDV VACCINATION

5. VACCINE OR VACCINATION FAILURE?

6. HOW TO PREVENT ND OUTBREAKS?

1. REASONS FOR ENDEMICITY OF CENTURY OLD NDV AROUND THE WORLD.



Data around the world in 2014

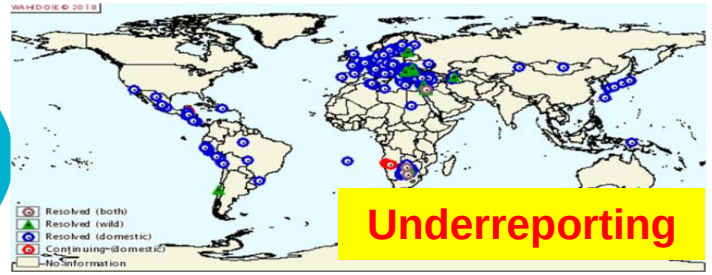
A. RNA Viruses

Virus family	**Paramyxoviridae**
Genetic material	Negative sense, Single stranded RNA, **Non-segmented**
Number of proteins	8
Virulence	Depending on the cleavage of fusion protein (F0)
Pathotypes	Lentogenic Mesogenic Velogenic
Genotypes	>20
Serotypes	Single
Live vaccine	Lentogenic and Mesogenic strains
Clinical signs and PM lesions	Details in next slides
Incubation period	1-6 days in vvND

B. Epidemiological Features In ND Endemic Countries

Vaccines and Vaccination procedures

No Stamping out policy



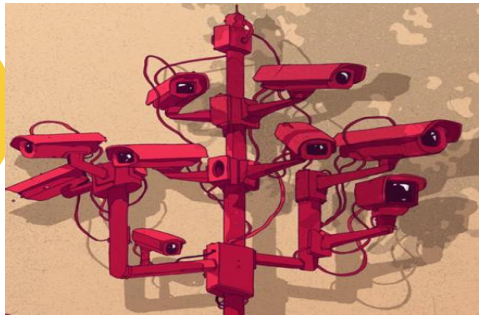
Underreporting

High density of poultry

Untreated poultry manure in agriculture

Complex biosecurity protocols

Lack of surveillance programs



C. Epidemiology of transmission

Live poultry
(Dirty pens: 6-14 days)

Slaughter waste disposal/
Dead bird disposal

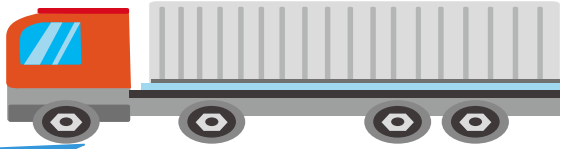
Infected Premises
Secretions and excretions

Droplet
Inhalation

Contact

?

Feeding and
drinking



Vehicle / Equipment's

Feces and Manure
RT: 94 days; >37^{0}C: 56 days

Contaminated eggs

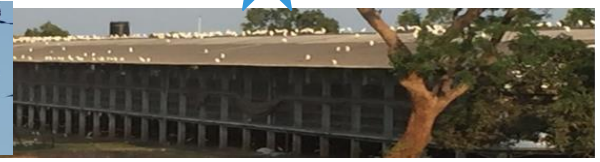
People/Vaccinator crew

Contaminated feed and water

Vector
mediated

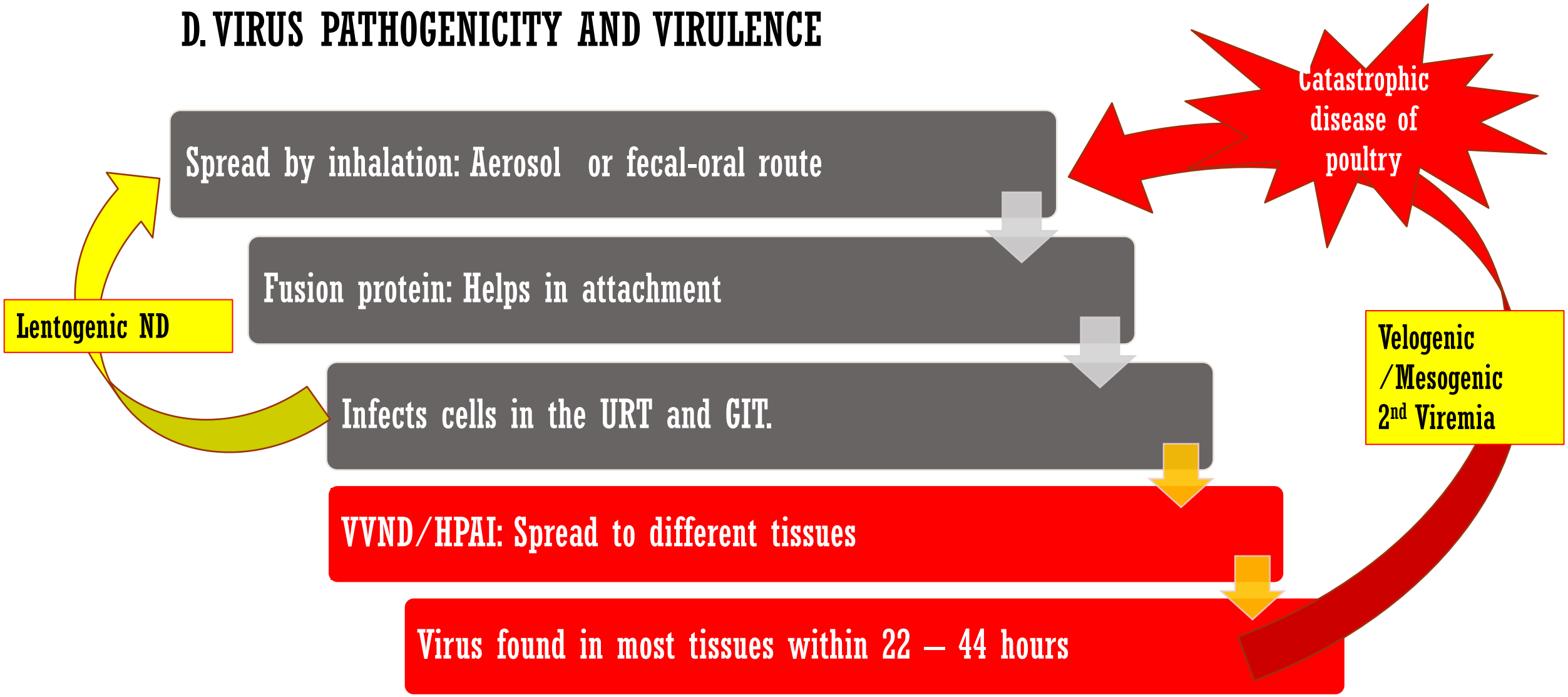
Pest / rodents / animals

Wild birds



250 spp. Of birds

D. VIRUS PATHOGENICITY AND VIRULENCE



E. CLASSIFICATION OF NDV ISOLATES BASED ON VIRULENCE

Virus Strain	IVPI (0-3)	ICPI (0-2)	MDT (24-120 hrs)	Pathogenicity Classification	Fusion protein cleavage site (amino acid position 112-117)	Virulence	Immunogenicity
V4	0	0.0	>120	Apathogenic	G R Q G R L		
PHY.LMV.42	0	0.0-0.16	>120	Apathogenic	G R Q G R L		
Ulster 2C	0	0.00	>120	Apathogenic	G R Q G R L		
VH	0	0.15	>120	Apathogenic	G R Q G R L		
Hitchner B1	0	0.2	>120	Lentogenic	G R Q G R L		
F	0	0.25	>120	Lentogenic	G R Q G R L		
VG/GA	0	0.35	120	Lentogenic	G R Q G R L		
Clone LaSota	0	0.36	106	Lentogenic	G R Q G R L		
LaSota	0	0.4	106	Lentogenic	G R Q G R L		
Mukteswar	0	1.4	44	Mesogenic	R R Q K R F		
Komarov	0	1.41	48	Mesogenic	R R Q K R F		
Roakin	0	1.45	48	Mesogenic	R R Q K R F		
Velogenic- CA 1083 (VVNDV)	2.6	1.8	48	Velogenic	R R Q K R F		
Velogen- Texas GB (VVNDV)	2.6	1.7	56	Velogenic	R R Q K R F		
Genotype VII (XIIIb)-India	2.8	1.9-2.0	<48	Velogenic	R R Q K R F		
Genotype VIIi	2.8-3.0	1.9-2.0	<48	Velogenic	R R Q K R F		

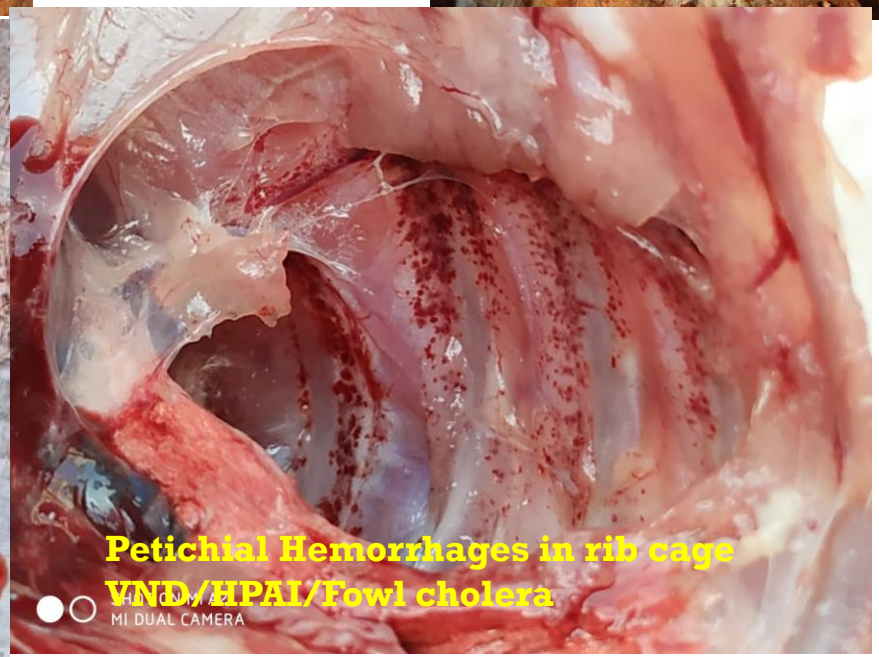
Cleavage site

F. PATHOTYPES AND TISSUE TROPISM

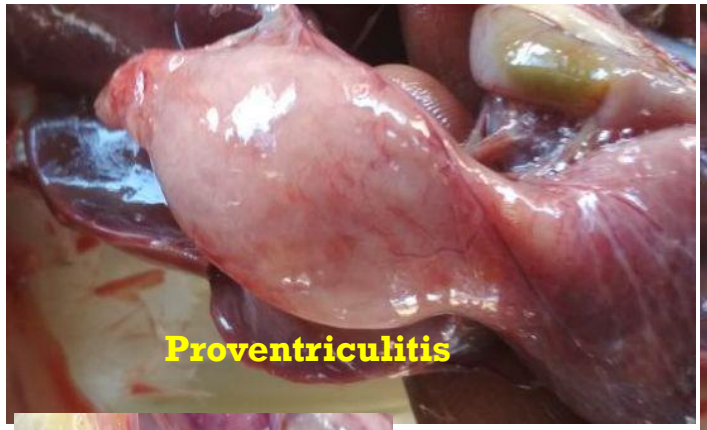
Pathotypes		Main tropism	Respiratory	Digestive	Reproductive	Nervous	Mortality
Asymptomatic		Enterotropic	-	-	-	-	-
Lentogenic		Respiratory / Enterotropic	+	-	-	-	+/-
Mesogenic		Respiratory	++	-	-	+/-	+
Velogenic	Neurotropic	Neurotropic/ Respiratory	+++	-	+++	+++	++
	Viscerotropic	Enterotropic/ Neurotropic/ Respiratory	+++	+++	+++	+++	+++

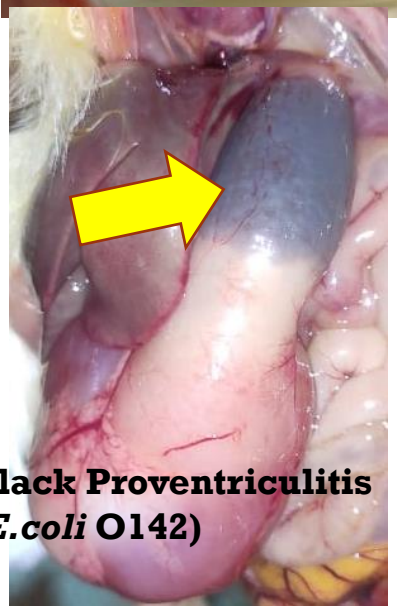
G. CLINICAL PICTURE AND DIFFERENTIAL DIAGNOSIS

Respiratory lesions

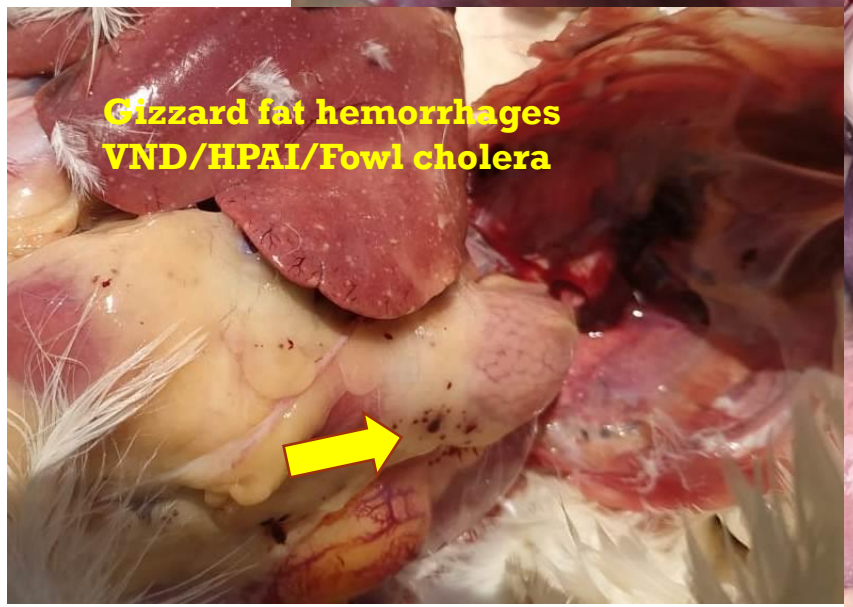


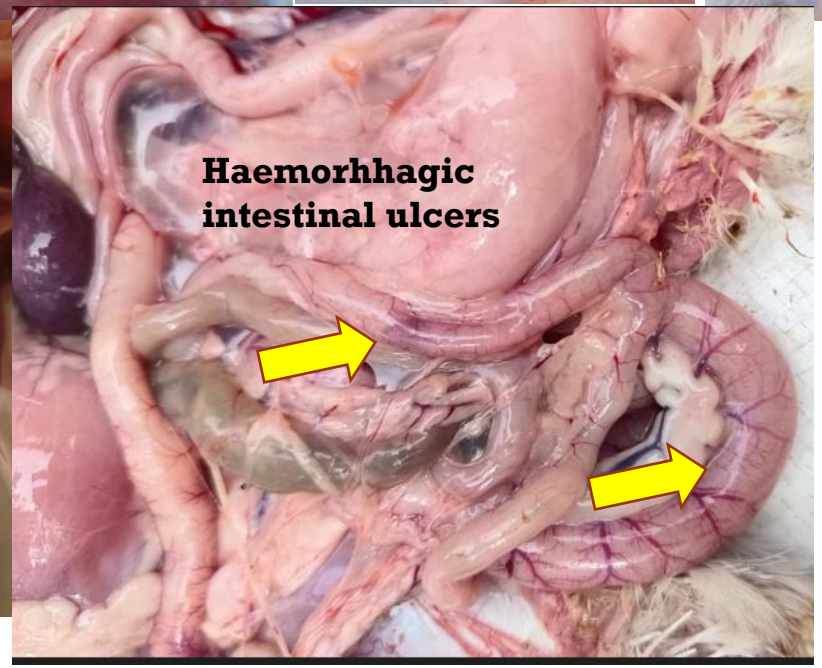
DIGESTIVE TRACT/ INTESTINAL LESIONS



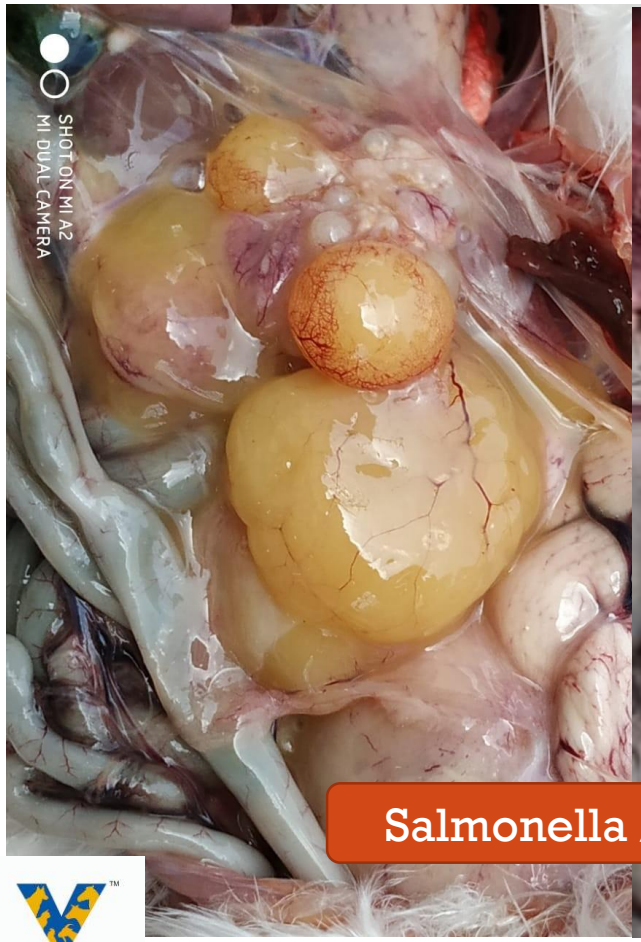


Black Proventriculitis (*E.coli* O142)





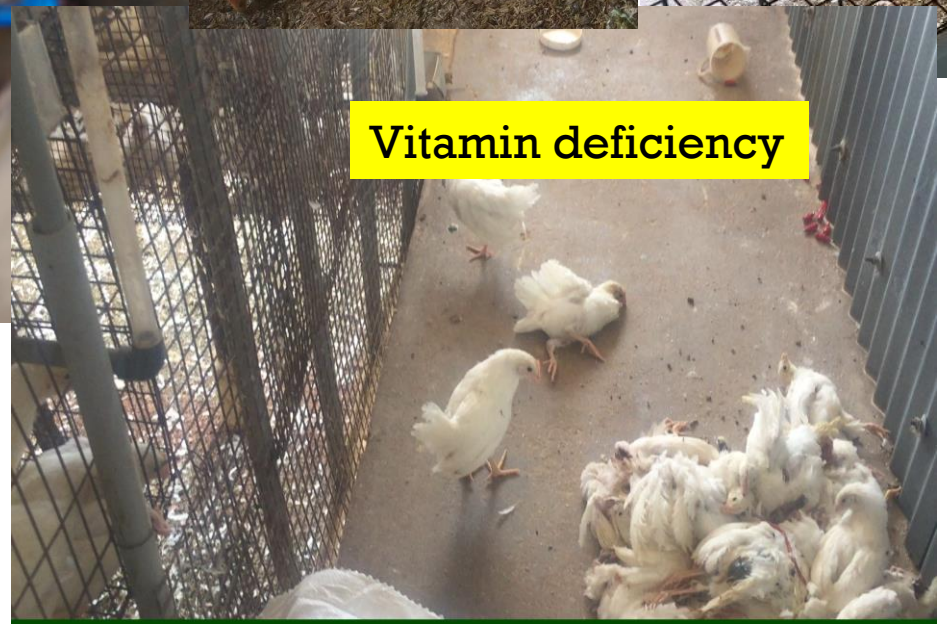
REPRODUCTIVE LESIONS: OOPHORITIS AND EGG ABNORMALITIES



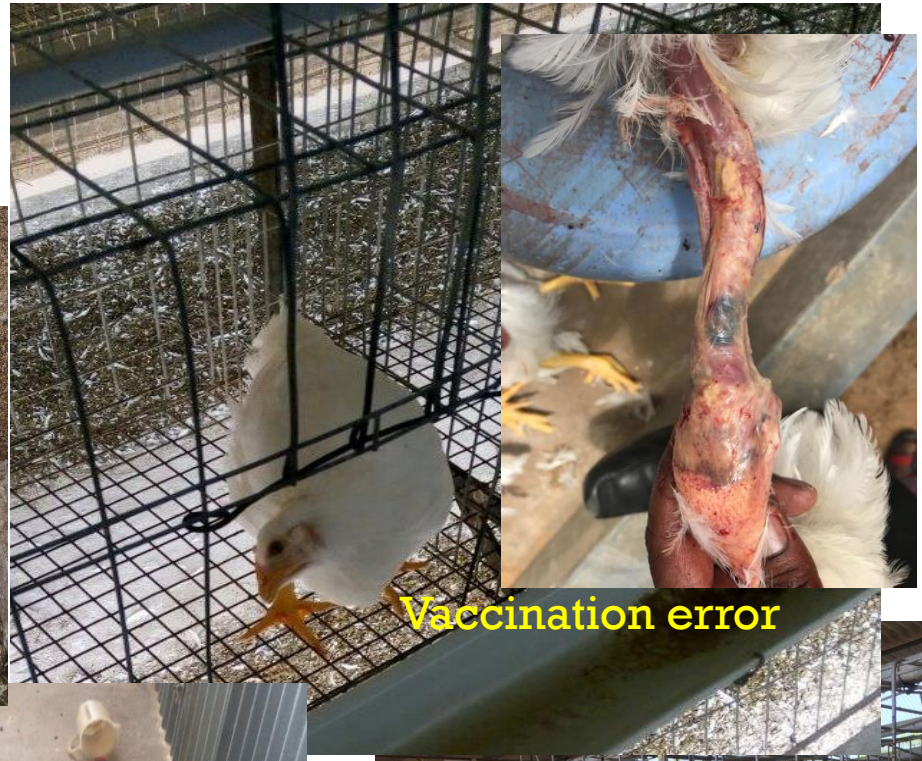
Salmonella / Fowl cholera

NEUROLOGICAL / TORTICOLLIS

AEV



Vitamin deficiency



Vaccination error

VVND/HPAI

Brief Communication

Otitis and meningoencephalitis associated with infectious coryza (*Avibacterium paragallinarum*) in commercial broiler chickens

Journal of Veterinary Diagnostic Invest
2018, Vol. 30(5) 784–788

DOI: 10.1177/1040638718792964
jvdi.sagepub.com

Pathogens can colonize the inner ear following migration from the nasal and oral cavity to the middle ear, through the Eustachian tube

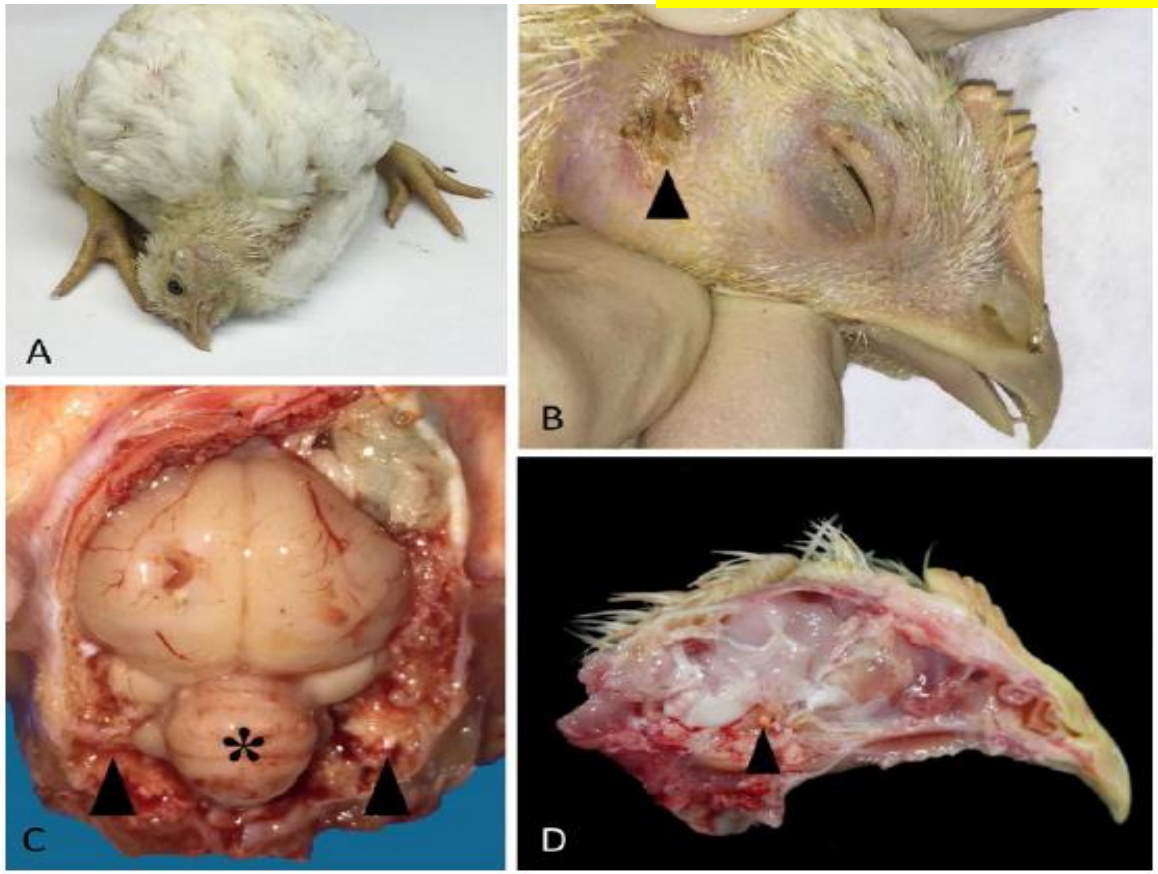


Figure 1. Clinical signs and macroscopic lesions in 29-d-old broiler chickens with otitis and meningoencephalitis associated v
Avibacterium paragallinarum infection. **A.** Severe torticollis. **B.** External ear. Accumulation of dry, yellow-brown caseous exudate on the
feathers (arrowhead). **C.** Cerebral edema and petechial hemorrhages visible on the cerebellum (asterisk), after the removal of
ria. Symmetrical discoloration of cranial bones, as a result of accumulation of necrotic exudate, is also present (arrowheads). **D.**
linal section of a head. Focal accumulation of necrotic exudate within a cranial bone (arrowhead).

Scientific References

1 Crispo, Manuela, et al.. **Otitis and meningoencephalitis associated with infectious coryza (Avibacterium paragallinarum) in commercial broiler chickens** *Journal of Veterinary Diagnostic Investigation 30.5* (2018)

2 Graham, Jennifer E., ed. **Blackwell's Five-Minute Veterinary Consult: Avian**. *John Wiley & Sons* (2016)

3 Banani, M., et al.. **Isolation of Ornithobacterium rhinotracheale from the brains of commercial broiler breeder chickens with meningitis and encephalitis** *Archives of Razi Institute* (2016)

4 Davies, Gaynor. **Common ailments of pet hens** *Veterinary Nursing Journal* (2016)

5 G Damerow **The Chicken Health Handbook**. *Storey Publishing* (2015)

6 Hauck, R., Richard P. Chin, and H. L. Shivaprasad.. **Retrospective Study on the Isolation of Ornithobacterium rhinotracheale from Chickens and Turkeys in Central California: 294 cases (2000–12)** *Avian diseases 59.1* (2015)

7 Nakamura, A. A., & Meireles, M. V. **Cryptosporidium infections in birds-a review** *Revista Brasileira de Parasitologia Veterinária* (2015)

8 Martel, An, et al. **Treatment of otitis externa associated with Corynebacterium kroppenstedtii in a peach-faced lovebird (Agapornis roseicollis) with an acetic and boric acid commercial solution** *ournal of avian medicine and surgery 23.2* (2009)

9 Moreno, B., et al.. **Nervous signs associated with otitis and cranial osteomyelitis and with Ornithobacterium rhinotracheale infection in red-legged partridges (Alectoris rufa)** *Avian pathology 38.5* (2009)

10 Shivaprasad, H. L., P. Cortes, and R. Crespo.. **Otitis interna (labyrinthitis) associated with Salmonella enterica arizonae in turkey poults** *Avian diseases 50.1* (2006)

11 Rival, F. **Auricular diseases in birds**. *8th European AAV Conference* (2005)

Venworld
THE BEST IN ANIMAL HEALTHCARE

Outbreak with NDV Genotype VIIi

National & World Ag News Headlines

Newcastle Disease Hits Pakistan Poultry Sector

USAgNet - 04/30/2012

Poultry producers in Pakistan are suffering heavy losses to Newcastle disease, with almost 45 million broilers succumbing to the virus in the past five months, according to local press reports. Cost to producers in the Punjab alone are estimated at around PKR6 billion, speakers told a meeting at the University of Veterinary & Animal Sciences in Lahore.

(Miller et al., Infec Genet Evol, 2015)

logical situation of ND. The epidemiological work described here represents recent ND outbreaks, which emerged in the northern region of Pakistan from November 2011 until March 2012, causing losses in the broiler industry worth more than USD 6 million. This ND outbreak also affected wild and exotic birds that died in public zoos and domestic poultry in backyard farms, however, no official figures on the numbers birds lost in the field have been released. The incidence of ND has continued at all levels of production facilities despite the use of full time veterinary services developed to control avian influenza in the most advanced commercial production facilities. Ironically, in 2009 in Pakistan 60% of the commercial broilers initially reported as having died from AI were later confirmed dead due to ND (Khan, 2009). The emergence of AI has facilitated increased surveillance and improved bio-security; surprisingly, the focus on AI has not been enough to prevent the

Phlebitis

tion facilities. Ironically, in 2009 in Pakistan 60% of the commercial broilers initially reported as having died from AI were later confirmed dead due to ND (Khan, 2009). The emergence of AI has facilitated increased surveillance and improved bio-security; sur-

2. NDV PANDEMICS AND EVOLUTION OF NDV GENOTYPES

First reported in 1926 in Newcastle-upon Tyne, England

1920-1960

- Genotype I, II, IV
- Lentogenic
- Mesogenic

Europe in late 1960s

- Genotype III, IV, IX and X

Middle East during 1980s

- Genotype VI

Asia, Africa, Europe and even isolated in S. America, Since 1984

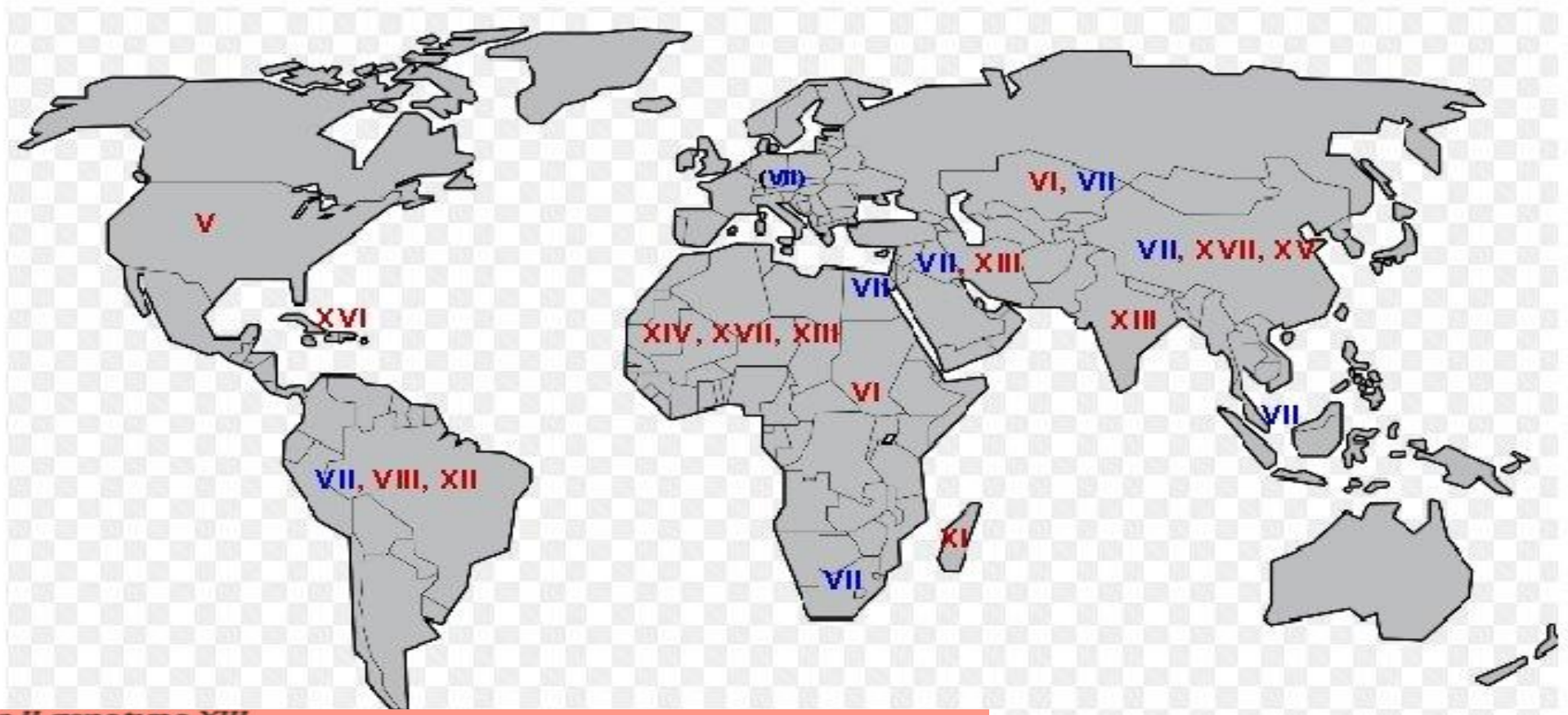
- Most variable Genotype VII,
- Sub-genotypes of VII (XIII)

Latest Indonesia Israel and Pakistan

- **VIIi (XIX)**

A. Recent distribution of Class II NDV genotypes

(Late genotypes) Since 2000



2.14. Class II genotype XIII

Full fusion gene sequences for class II genotype XIII viruses have been detected mainly in Eurasia and Africa and are currently divided into two sub-genotypes with the most ancestral strain being recovered from a cockatoo (family Cacatuidae) sampled in India in 1982 (Benson et al.,

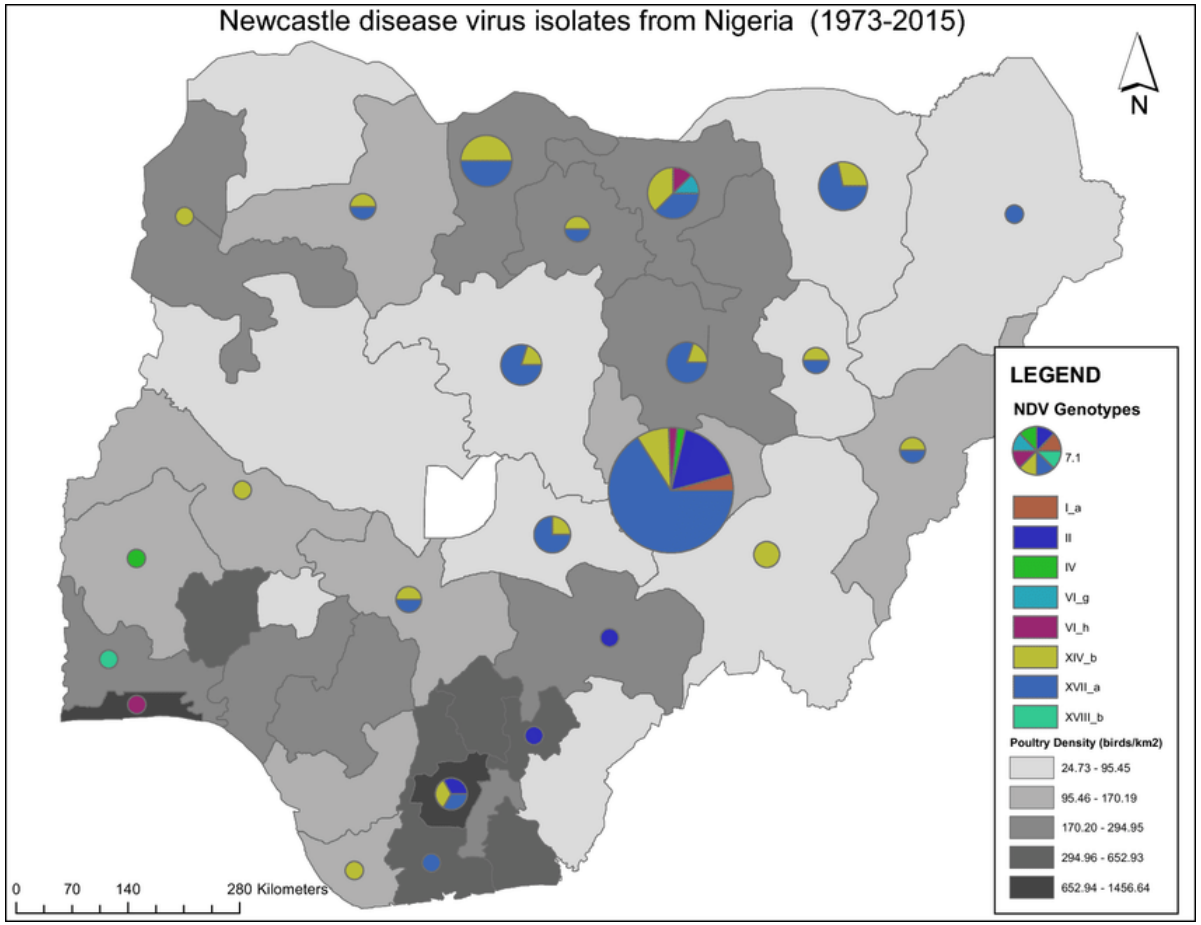
OIE REFERENCE LABORATORY FOR NEWCASTLE DISEASE

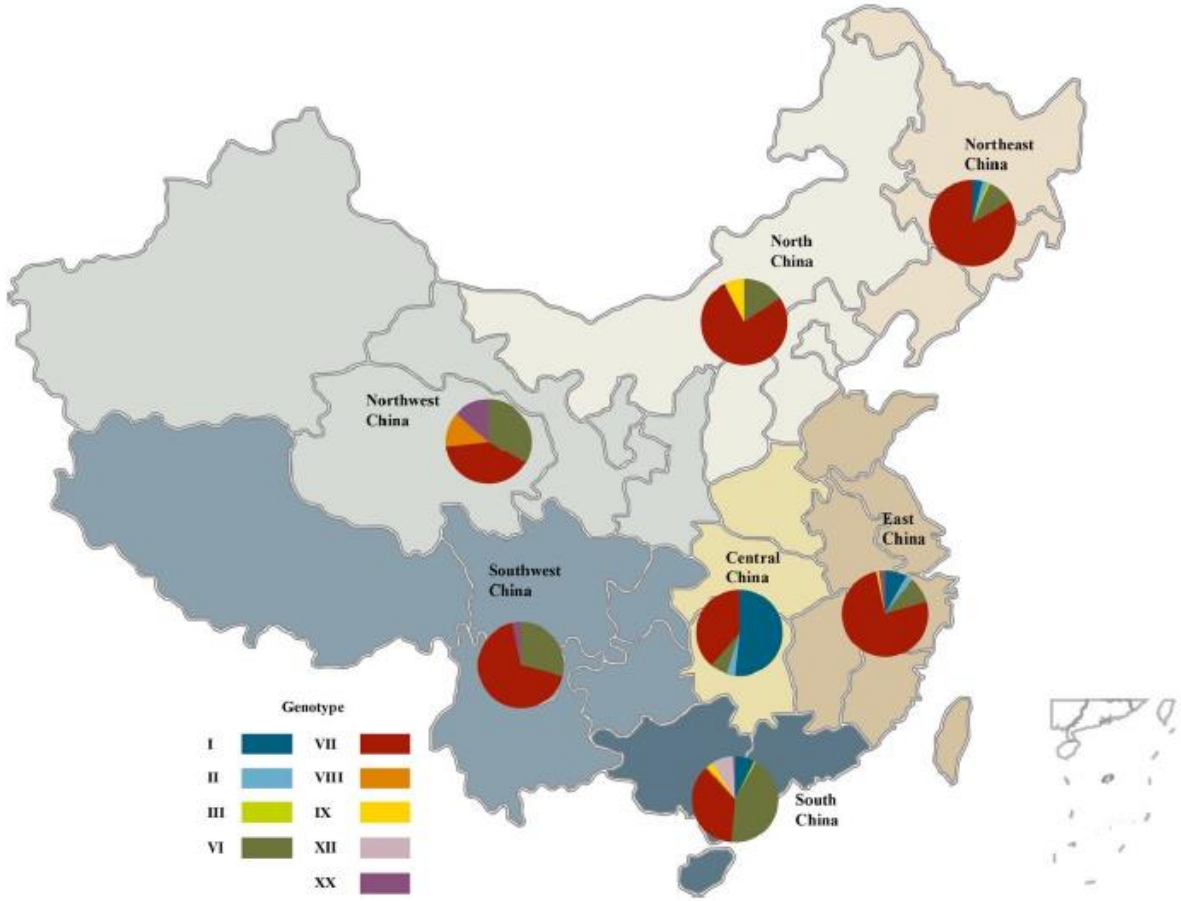
B. WHAT IS THE CHANGE IN NDV GENOTYPES AFTER 2013?

(DIEL *ET AL.*, 2013)

Former classification		Latest	Main geographic distribution
Lineage	Genotype	Genotype	
1	I	I	Worldwide
2	II	II	Worldwide
3	III	III	Far East 1960
3	IV	IV	Europe before 1970s
3	V	V	North America
4	VI	VI	Worldwide
5	**VII**	VII	Worldwide
3	VIII	VIII	S. Africa, SEA
3	IX	IX	SEA
2	II	X	N. America
3	-	XI	Africa, Madagascar

Former classification		Latest	Main geographic distribution
Lineage	Genotype	Genotype	
-	-	XII	China, S. America
5	**VII b**	XIII	ME, Asia (India)
7	**VII ?**	XIV	Africa
5	**VII d**	XV	Asia and ME
-	-	XVI	Central America
7	**VII ?**	XVII	Africa
7	-	XVIII	Africa
7	**VII i**	**XIX**	**Pakistan, Indonesia, Israel, ME, Asia**
7	**VIIj**	?	China, Ukraine, Iran
7	**VIIk**	?	Indonesia, China


Newcastle disease virus isolates from Nigeria (1973-2015)
N
LEGEND
NDV Genotypes
7.1
I_a
II
IV
VI_g
VI_h
XIV_b
XVII_a
XVIII_b
Poultry Density (birds/km2)
24.73 - 95.45
95.46 - 170.19
170.20 - 294.95
294.96 - 652.93
652.94 - 1456.64
0
70
140
280 Kilometers


Northeast China
North China
Northwest China
East China
Central China
Southwest China
South China
Genotype
I
II
III
VI
VII
VIII
IX
XII
XX

Global spread of newly emerging NDVs

VIIh, VIIi, XIIIb: Pandemic potential?

EVPA Conference 2017

Newcastle disease; an old disease with new features

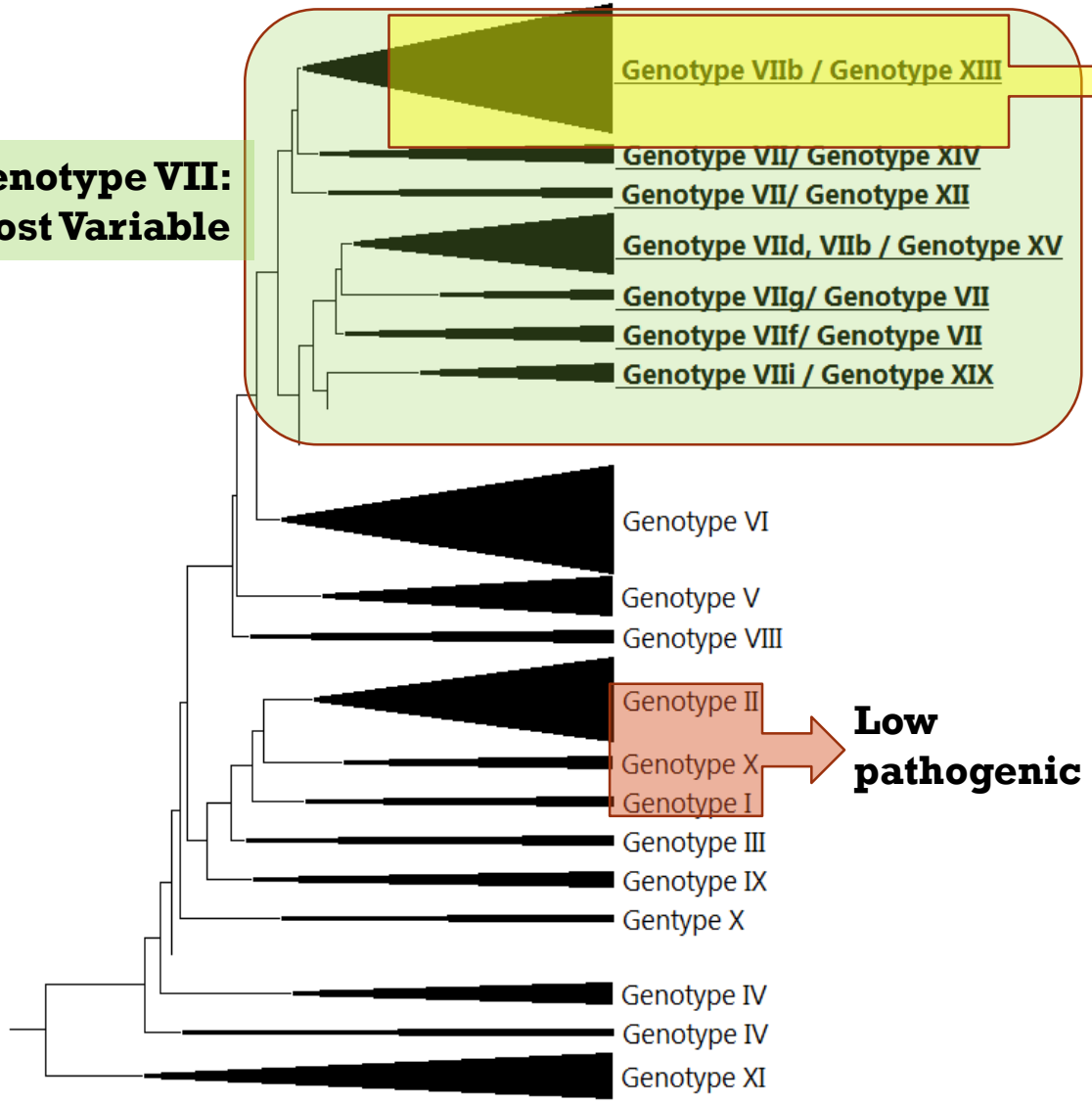
Kang-Seuk Choi /OIE expert

OIE Reference laboratory for Newcastle Disease
Animal and Plant Quarantine Agency, Korea

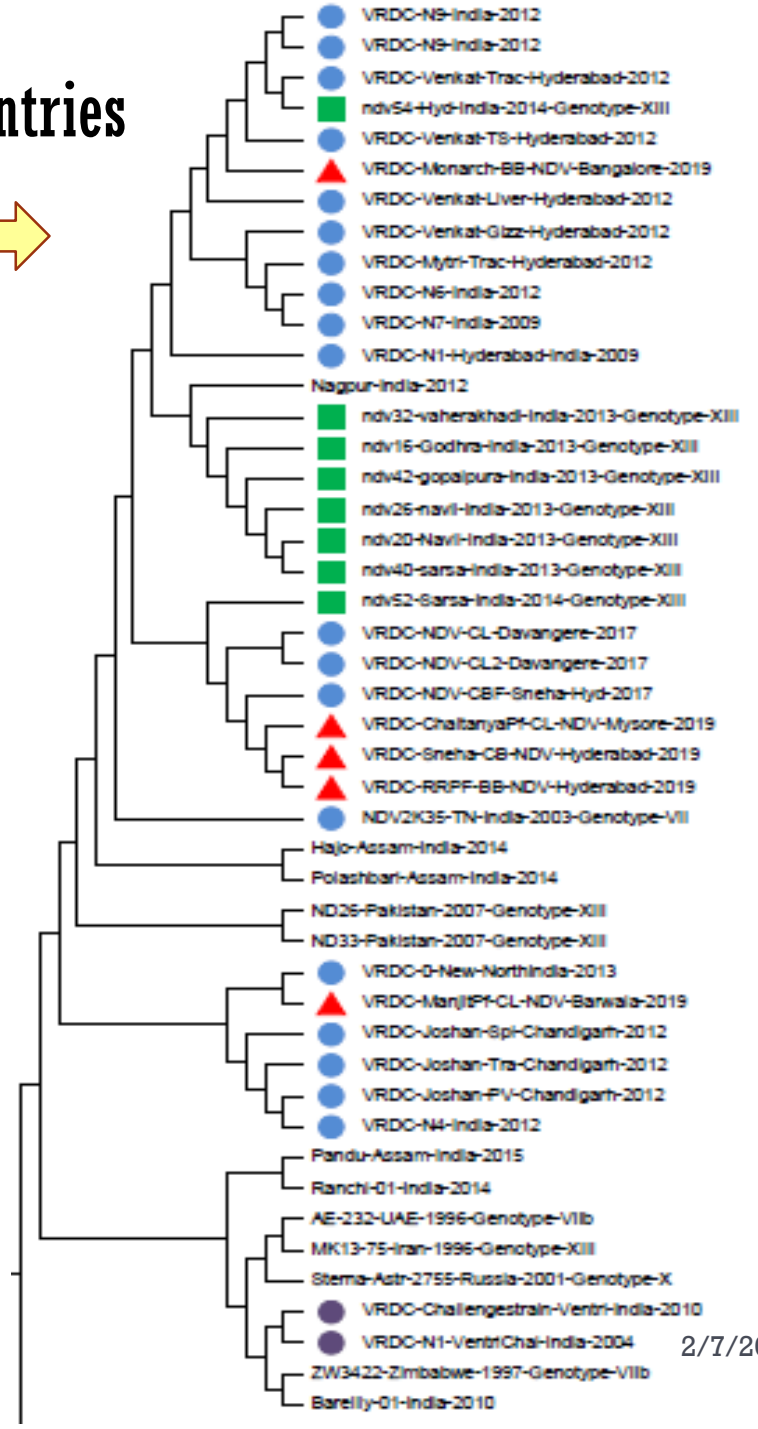
OIE
REFERENCE LABORATORY FOR NEWCASTLE DISEASE

C. Phylogeny of NDV isolates in India and Neighboring Countries

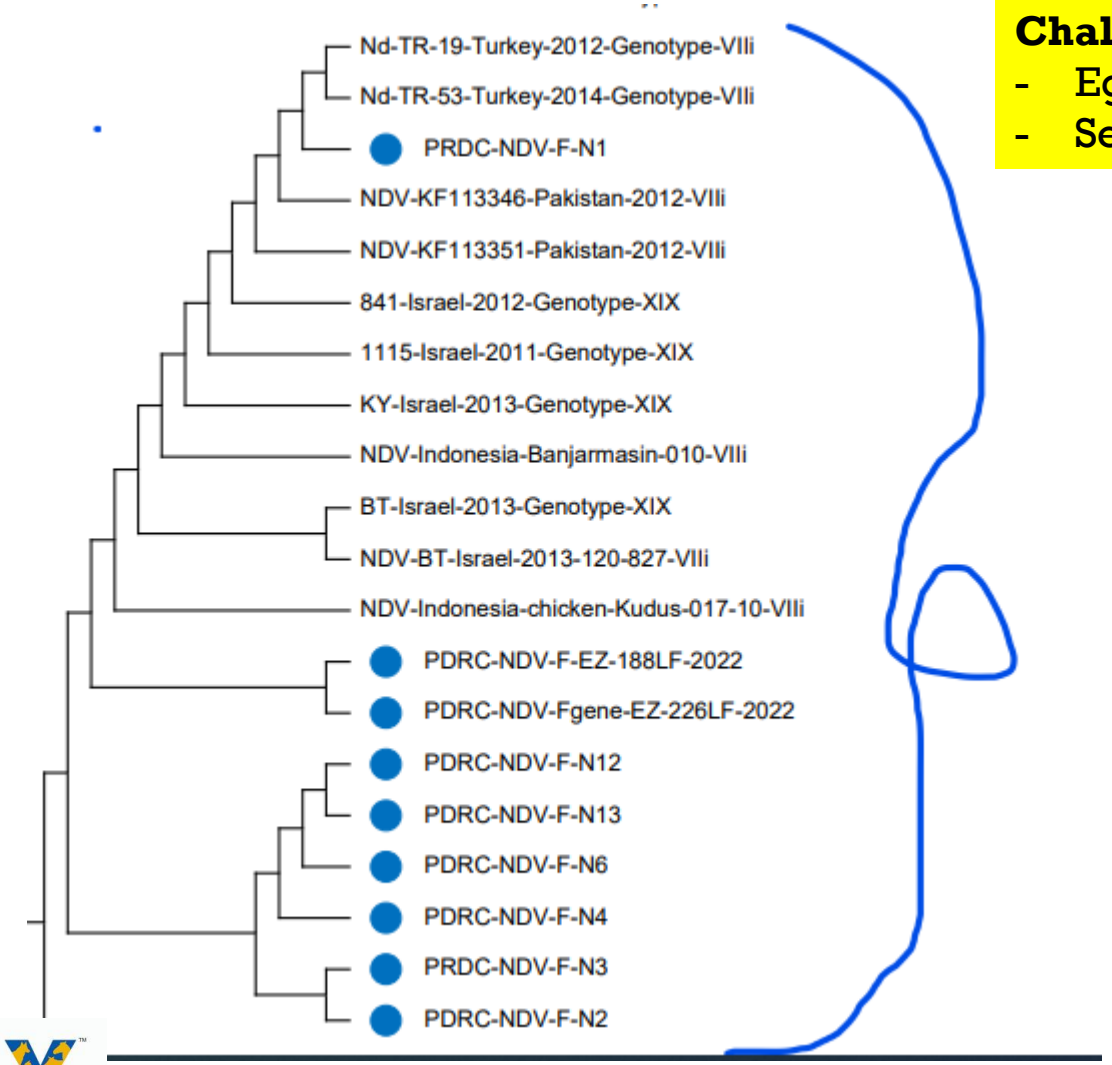
Genotype VII: Most Variable



Low pathogenic



D. CURRENT CHALLENGES WITH NDV GENOTYPE VIIi IN INDIA



Challenges in vaccinated flocks

- Egg production drop in long lived birds
- Severe mortality and clinical signs in young chicks < 6wks of age

Table 1
Epidemiological and genetic description of vNDV isolates from Pakistan, Indonesia and Israel.

GenBank accession #	Virus designation	Month	Farm type/location	Breed	Latitude	Longitude	Flock size	Age (days)	Mortality %	Cleavage site
KF113338	Chicken/Pak/University Diagnostic Lab./12/2010	Nov.	UDL, UVAS, Lahore, Punjab	Broiler	NA	NA	28000	32	60	RRQKRF
KF113339	Chicken/Pak/Lahore/30/2011	Nov.	Mashallah P/F Raiwind, Lahore, Punjab	Broiler	31.235531	74.2171	30000	30	>80	RRQKRF
KF113340	Chicken/Pak/Lahore/32/2011	Nov.	Mashallah P/F Raiwind, Lahore,Punjab	Broiler	31.235531	74.2171	30000	30	>80	RRQKRF
KF113353	Chicken/Pak/University Diagnostic Lab./33/2011	Dec.	UDL,UVAS, Lahore, Punjab	Broiler	NA	NA	NA	NA	100	RRQKRF
KF113341	Chicken/Pak/Lahore /43/2011	Dec.	S/S P/F, Barki road, Lahore, Punjab	Broiler	31.495	74.487	27000	33	>80	RRQKRF
KF113342	Chicken/Pak/Lahore/50/2011	Dec.	AM P/F, Raiwind, Lahore, Punjab	Broiler	31.235531	74.2171	20400	41	<60	RRQKRF
KF113343	Chicken/Pak/Gujranwala/56/2011	Dec.	Usman Gorya P/F Gujranwala, Punjab	Broiler	31.418	73.07757	55000	40	60	RRQKRF
KF113344	Chicken/Pak/Okara/103/2011	Dec.	Rajput P/F, Okara, Punjab	Broiler	30.8013	73.4483	26000	28	100	RRQKRF
KF113345	Chicken/Pak/KPK/117/2011	Dec.	Asad khan P/F, Nowshera, KPK	Broiler	34.006	71.9998	1500	20	10	RRQKRF
KF113346	Chicken/Pak/Khyber Pukhtun Khawa/118/2011	Dec.	Kabir P/F, Kohat road Kohat, KPK	Broiler	33.5199	71.5963	2500	20	>80	RRQKRF
KF113347	Chicken/Pak/Khyber Pukhtun Khawa /119/2012	Jan.	Haleem P/F, Warsak road, Peshawar KPK	Broiler	34.0264	71.5348	5000	26	90	RRQKRF
KF113348	Chicken/Pak/Khyber Pukhtun Khawa /162/2012	Jan.	K&N's Lab Mansehra, KPK	Broiler	34.3333	73.2	0	21	>60	RRQKRF
KF113349	Chicken/Pak/Kasure/191/2012	Jan.	Suye-Hasil, Kasur, Punjab	Broiler	31.1176	74.4499	28000	25	80	RRQKRF
KF113350	Chicken/Pak/Lahore/200/2012	Jan.	Ahad P/F, Baidian road Lahore Punjab	Broiler	31.4629	74.4356	30000	22	100	RRQKRF
KF113351	Chicken/Pak/University Vet. Animal Sci./211/2012	Jan.	QOL,UVAS, Lahore, Punjab	Layer	31.54505	74.340683	50	350	100	RRQKRF
KF113352	Chicken/Pak/University Vet. Animal Sci./212/2012	Feb.	QOL, UVAS, Lahore, Punjab	Layer	31.54505	74.340683	50	84	100	RRQKRF

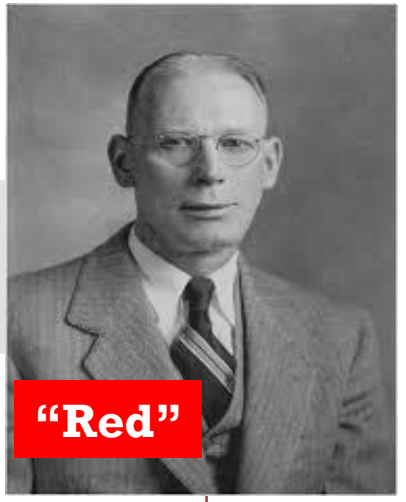
3. VACCINE DEVELOPMENT FOR THE LAST 90+ YEARS

Vaccines as Treatment?????

If a **Lie** is told loud and long enough people will begin to believe it.

-A.H

A. MESOGENIC STRAINS



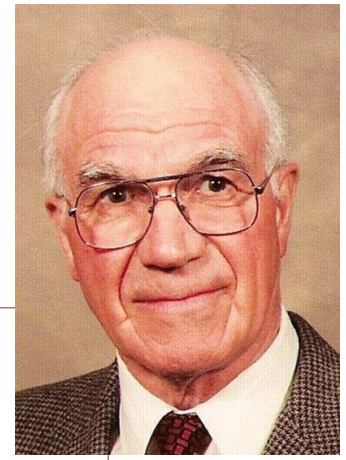
ATTENUATION OF VIRULENT STRAINS

- 1930's Iyer and Dobson (England) Passaged Hert's 33 isolate in embryonated eggs- **H- strain**
- **Beaudette (USA) screened 105 isolates: Roakin strain**
- Iyer (India)- Mukteshwar isolate passaged in embryonated eggs –**R2B strain**.
- Komarov (Palestine) Intracerebral passage in ducklings- **Komarov strain**

Though the vaccines induced very good protection

- **Capable of causing disease and high mortality in fully susceptible birds**

B. DEMAND FOR SAFER VACCINES: LENTOGENIC STRAINS



Hitchner (1947) at Virginia polytechnic institute

- Beaudette provided 8 strains of ND and one control of IBV.
- **B1 strain for day old chicks,** licensed in 1950.

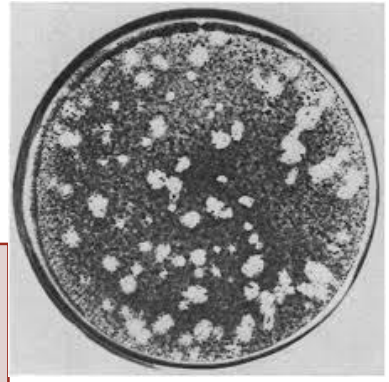
Beaudette , Poultry pathologist at New Jersey

- Revised his records on 105 strains to identify any candidate with low virulence and got 3 strains.
- The mildest strain was the isolate from **Adam LaSota's farm.**

Asplin, England (1952)

- Isolated NDV from mild respiratory disease in young chicks similar to B1 strain in virulence and immunogenicity: **F strain**.

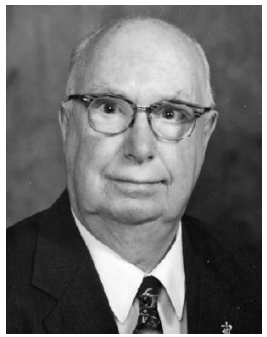
C. Cloned Vaccines– Reduce vaccinal reactions?



Vial of virus is a heterogeneous population

- Milder or stronger viruses
- Less post vaccination reaction and better immunogenicity .
- Heat resistant strains

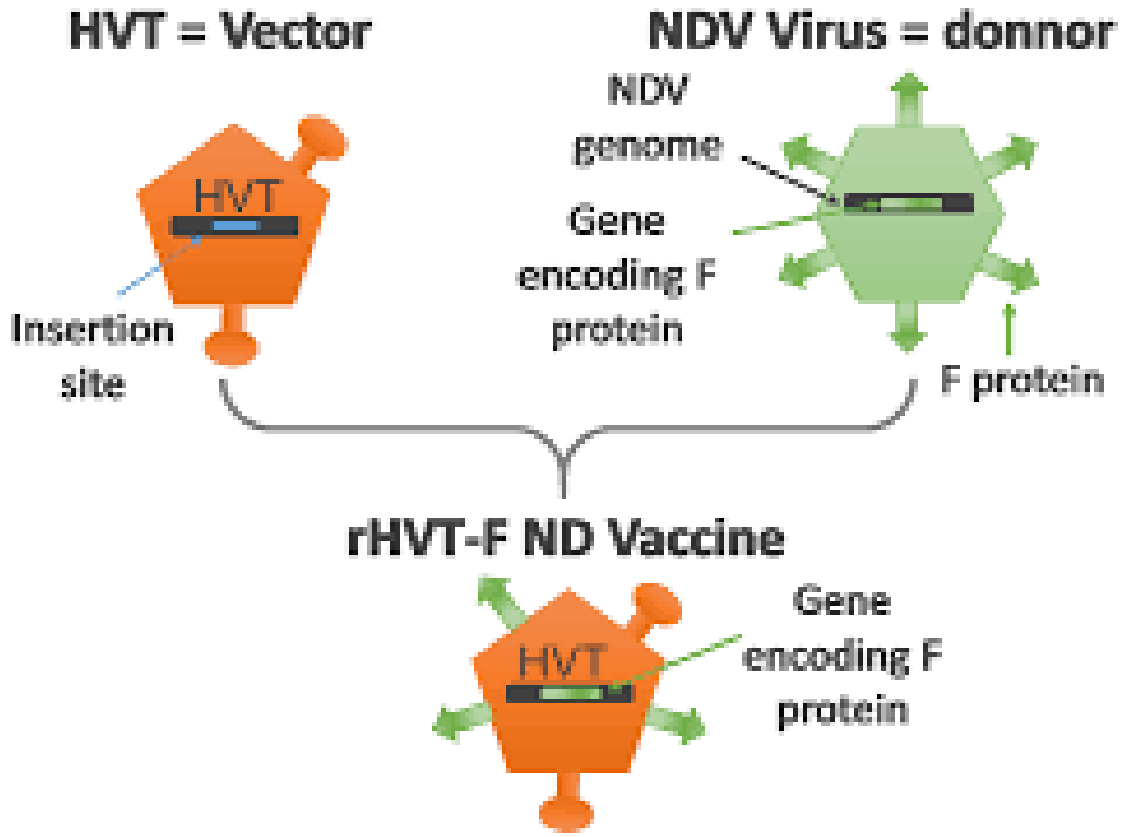
LaSota	: Clone 30, CL/79, Master Clone
B1	: C2
Local lentogenic	: VH strain
Heat resistant strains	: V4-HR, I2



In January 1982, Hiram made seven specific predictions on the future of the vaccine industry. Hiram rarely hesitated to speak his mind and did so with the confidence that reflected his 30 years of experience in poultry vaccines. This list serves to document issues that Hiram thought to be important at that point in time. Armed with 20-20 hindsight, it is interesting to reflect on these predictions 25 years later.

- *Cloned vaccines will be more popular.* This did not happen.
- *Inactivated vaccines in stable water-in-oil emulsions will be more popular.* This has happened.
- *Inactivated vaccines with several antigens will be used at point-of-lay.* This has happened.

D. RECOMBINANT VACCINES



Immunogenic protein with Antigenic Variation
- F protein
- HN protein ?

Latency with Marek's virus as vector?

Local Mucosal immunity in the early stage?

Long lasting immunity high protective titers to counter Velogenic ND challenges

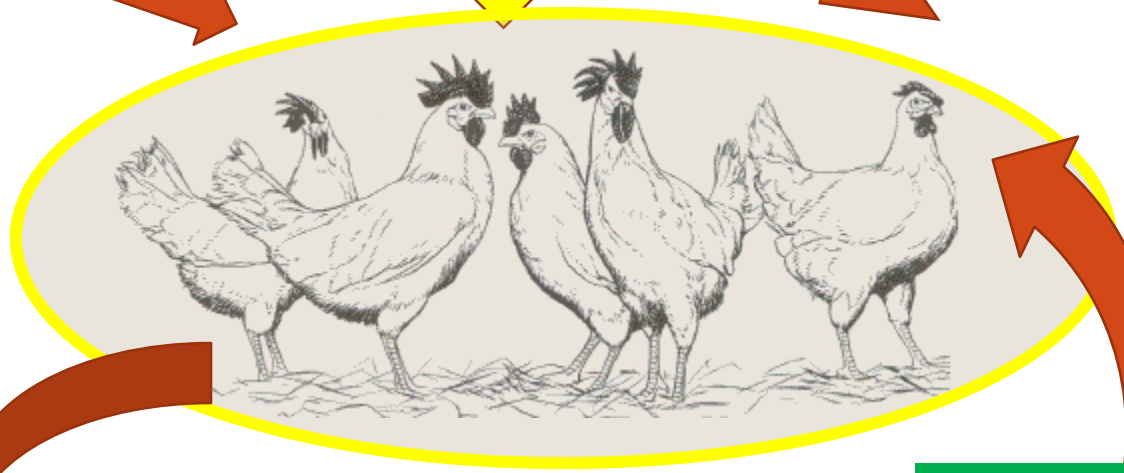
Useful For Endemic Countries with very virulent NDV ?

4. GOALS OF NDV VACCINATION

Genotype XIII/ VIIi

Resistant to infection

Clinical protection
-Mortality
-Egg production drop
-Growth retardation



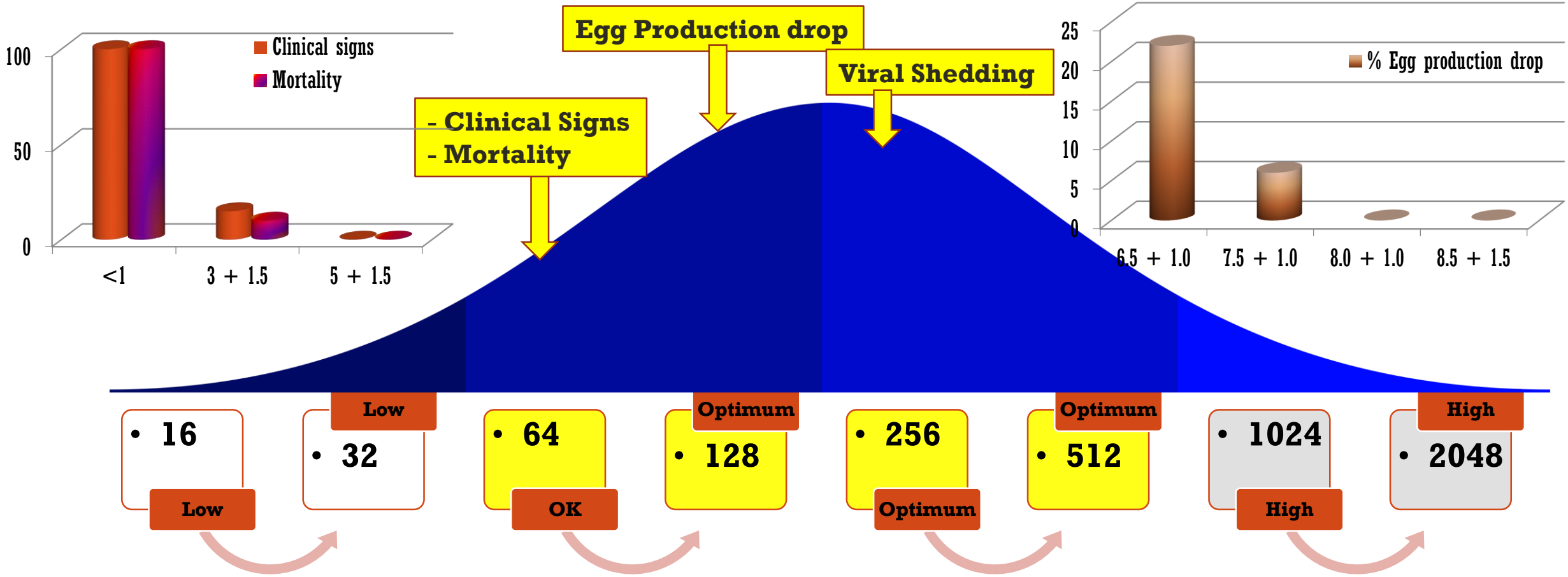
Sterile Immunity?

Homologous vaccine : Reduce the amount of Virus Shedding

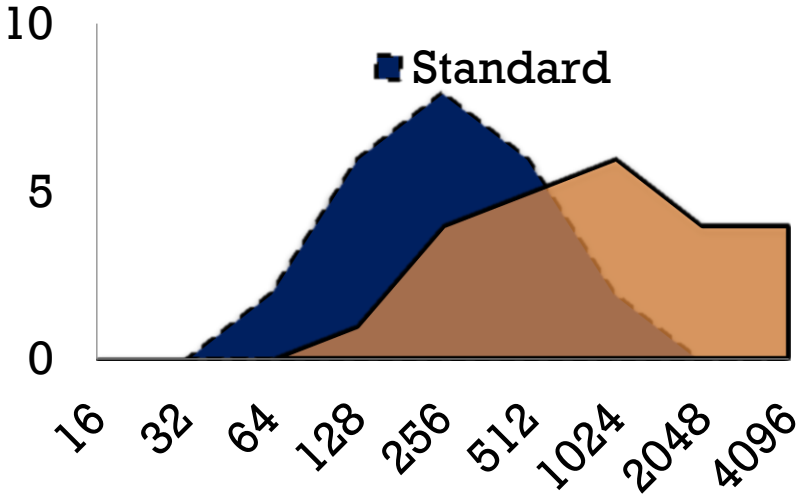
Increase the dose of Challenge virus

A. NDV TITERS AND IMMUNE RESPONSE

Herd Immunity?

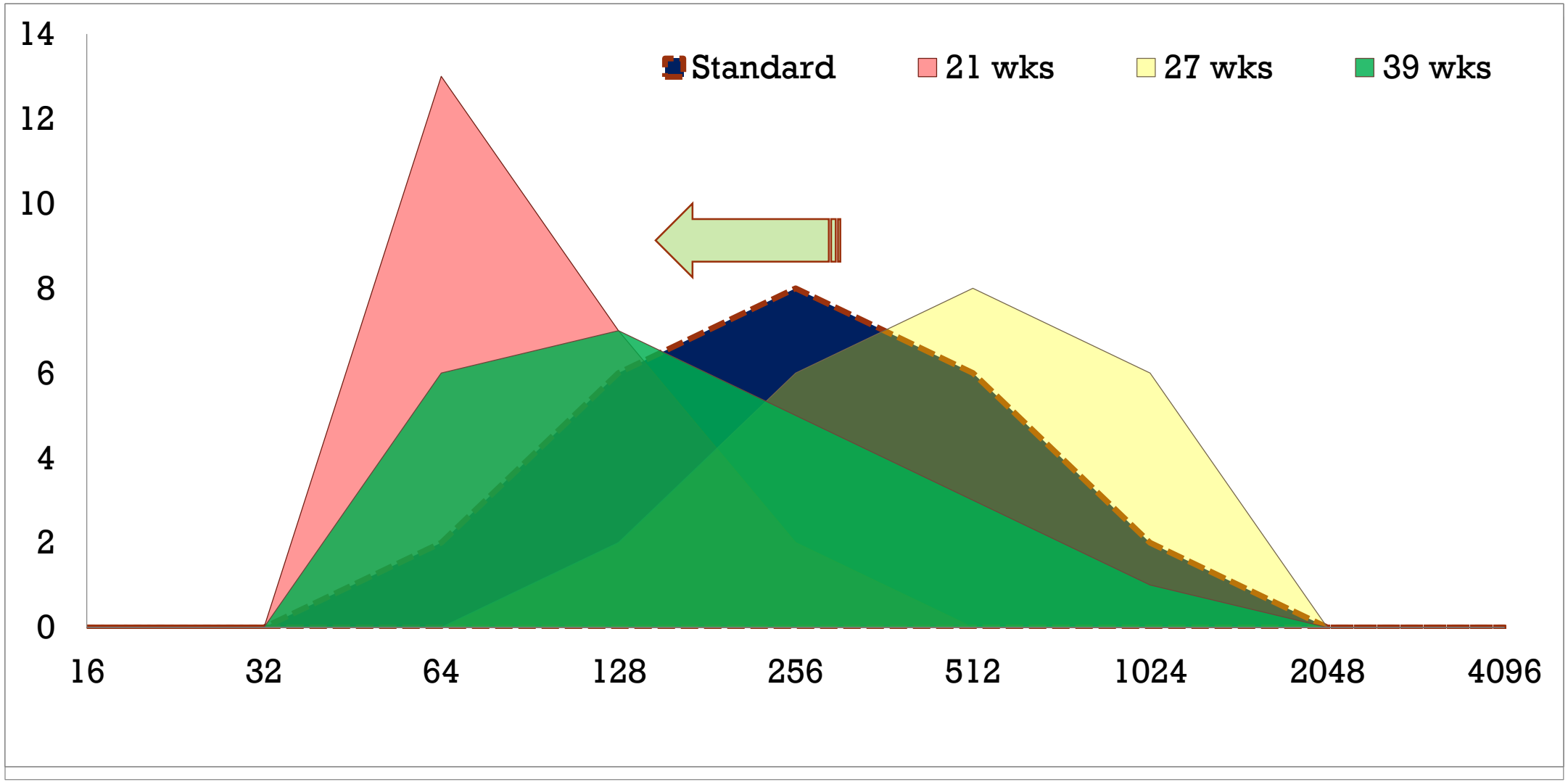


B. IMMUNE RESPONSE TO CHALLENGE

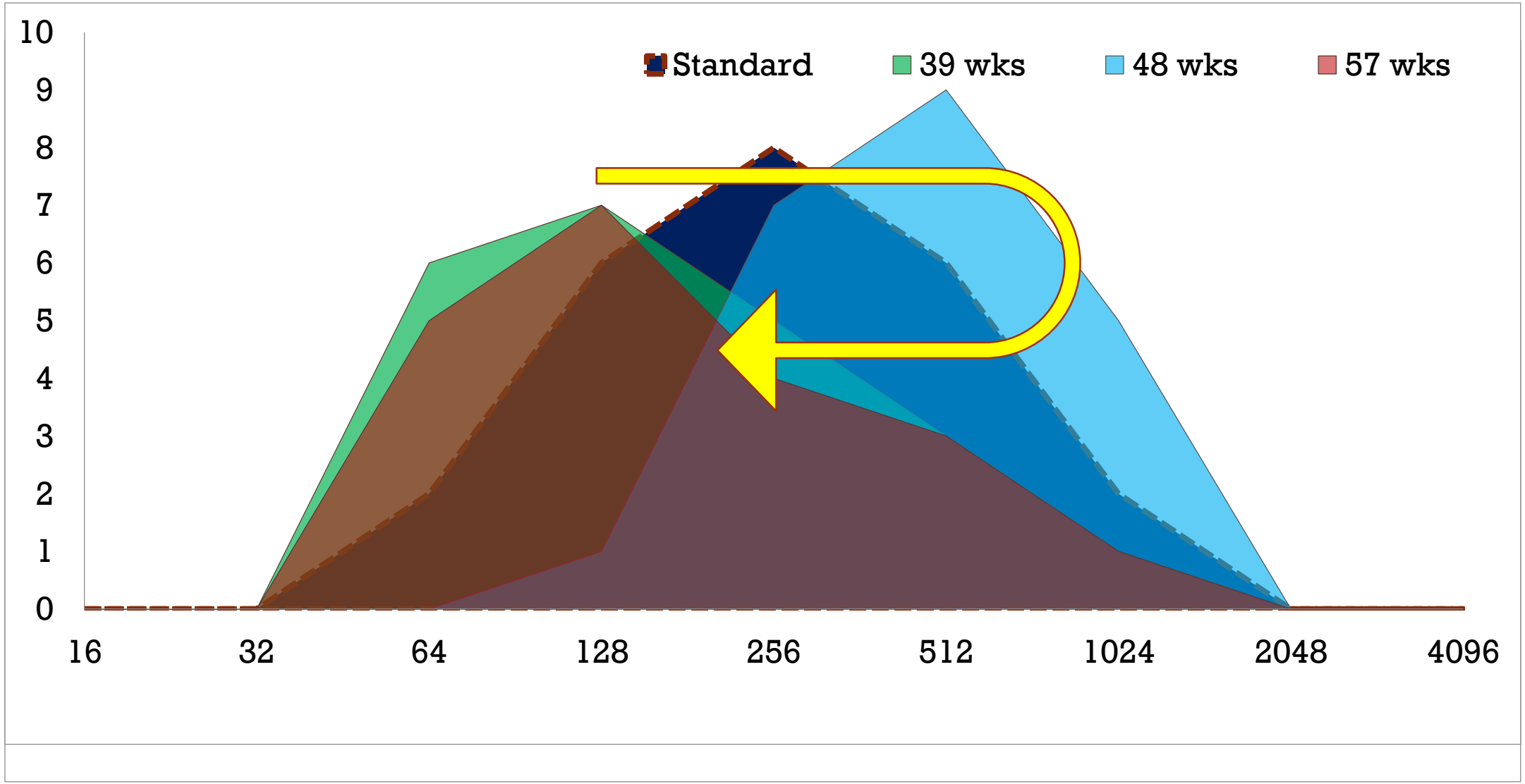


Challenge : VVND (Velogenic)
ICPI: 1.9-2.0

C. SERO-MONITORING OF NDV TITERS IN BREEDERS



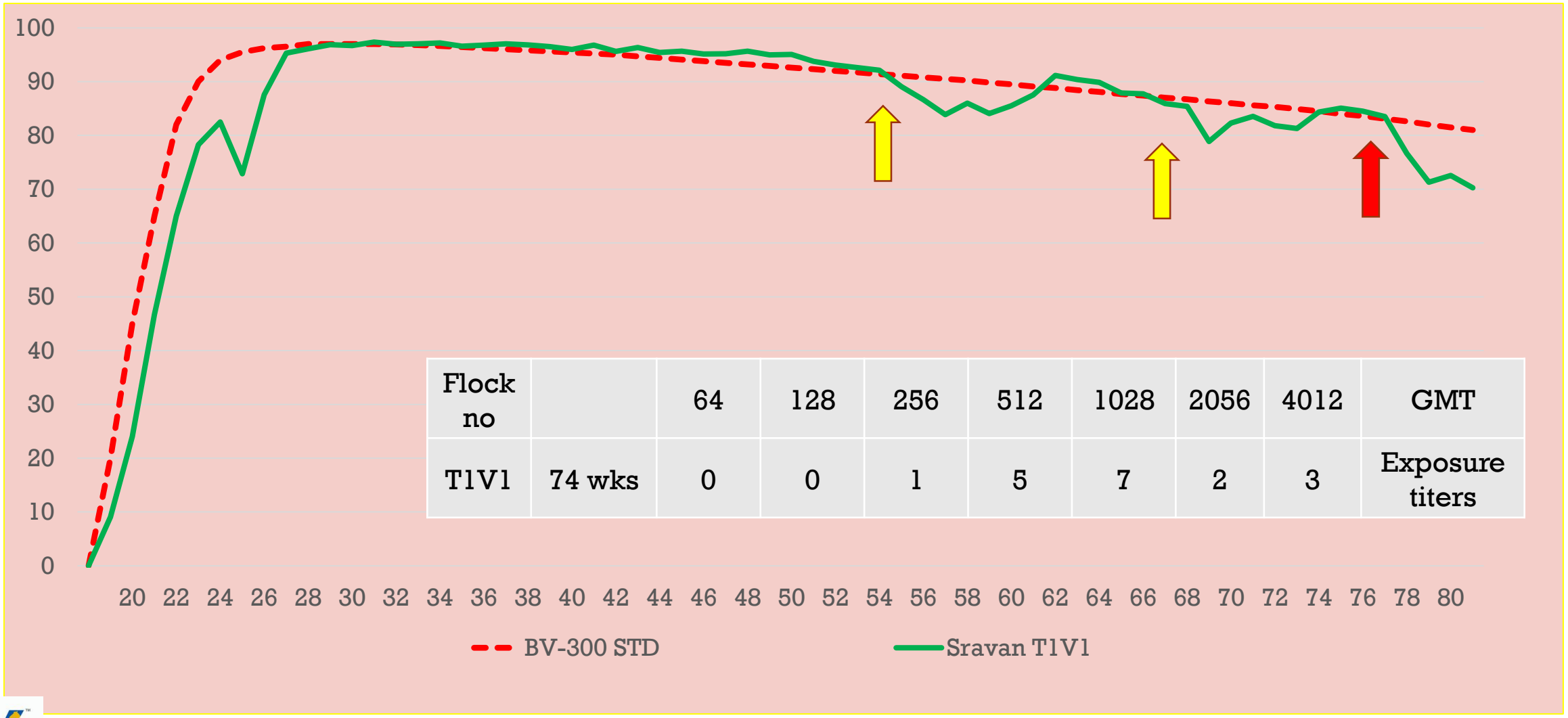
SEROLOGY OF POST MID-LAY VACCINATION



ND TITER MONITORING IN COMMERCIAL LAYER FLOCK

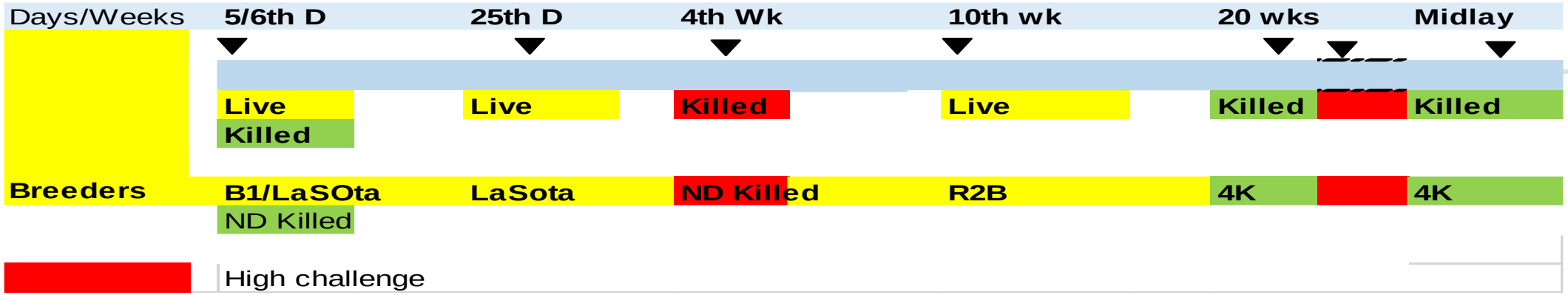
Flock Age	HI titers							
	64	128	256	512	1028	2056	4012	GMT
12 wks	2	8	7	2	1	0	0	7.6 (128-256)
18th week	1	5	6	7	1	0	0	8.1 (256)
37th week	0	2	6	4	1	0	0	8.3 (256-512)
51st week	0	3	2	2	3	0	0	8.5 256-512)
60th week	7	1	2			0	0	6.6 (64-128)

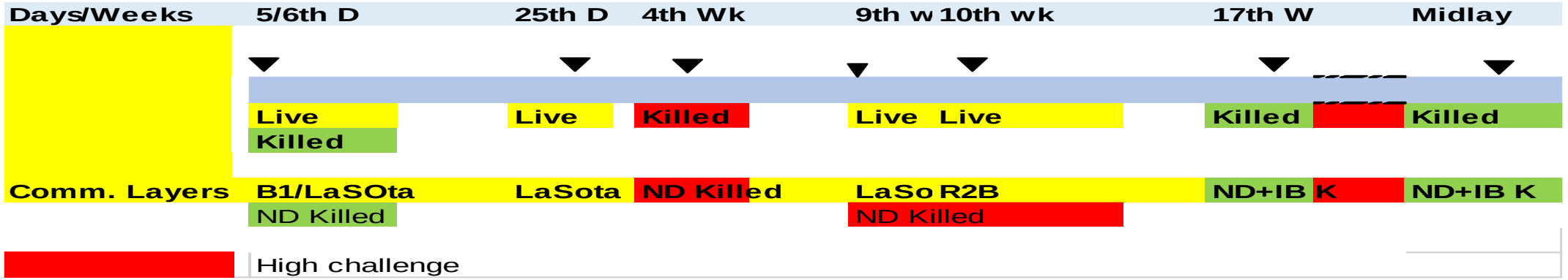
MID-LAY LIVE VACCINE



Flock no		64	128	256	512	1028	2056	4012	GMT
T1V1	74 wks	0	0	1	5	7	2	3	Exposure titers

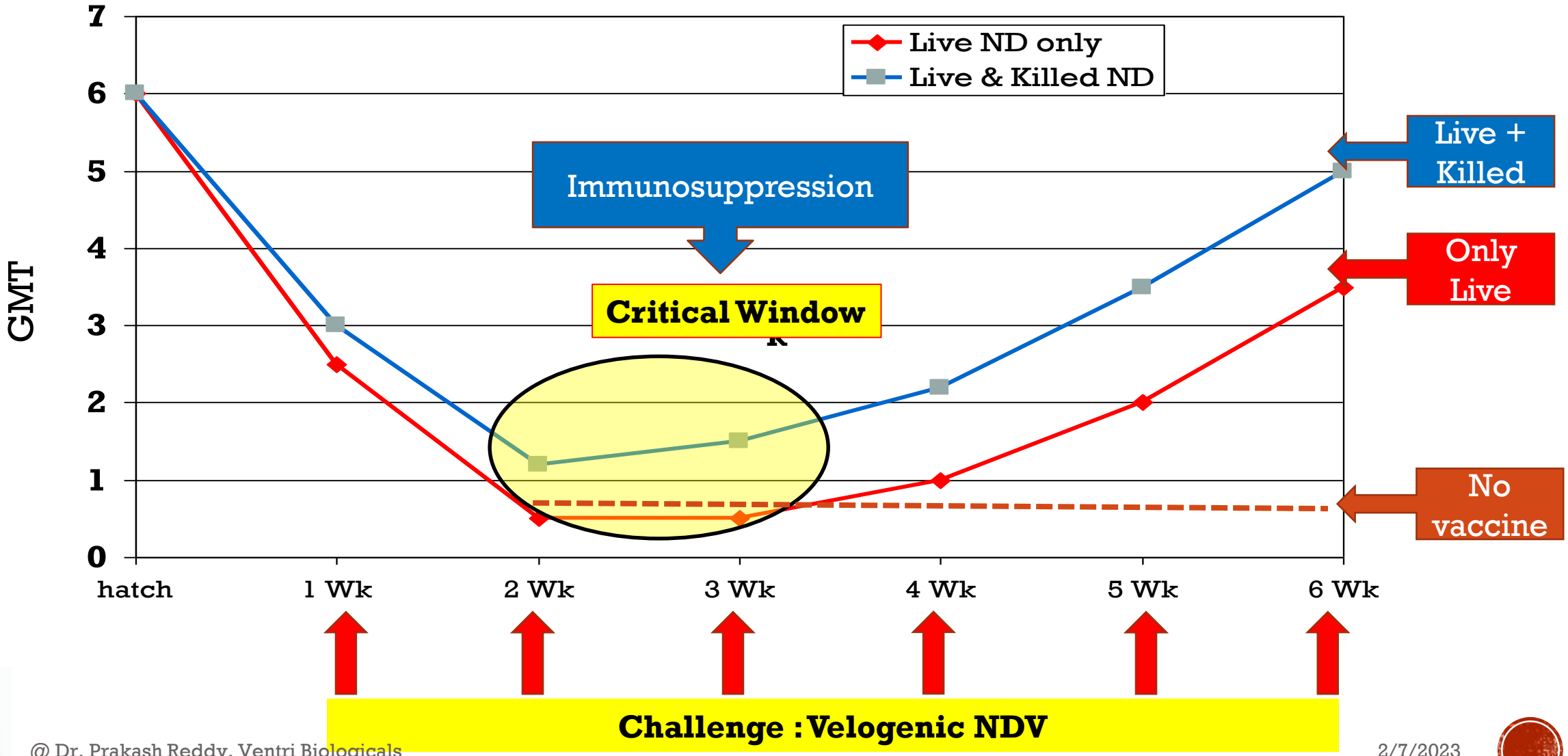
E. VACCINATION PROGRAM IN LONG LIVED BIRDS





Stop Repeating Live vaccines during lay?

D. CONCEPT OF EARLY PROTECTION (<6 WKS OF AGE)



HATCHERY VACCINATION

ND KILLED + IMMUNE COMPLEX IBD

F. VACCINAL REACTION

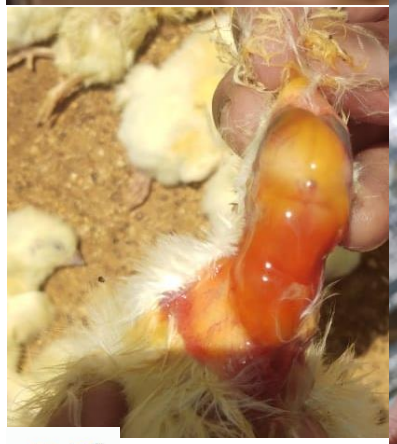
?

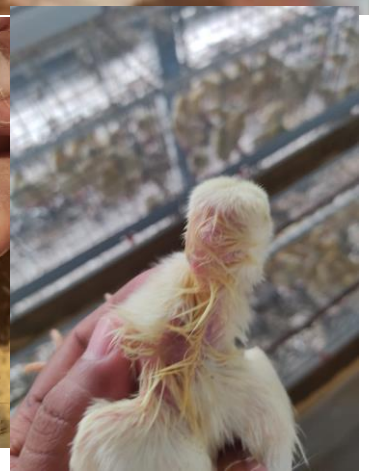
Lentogenic strains	Factors influencing vaccinal reactions
• Mild respiratory disease • Airsacculitis • Egg production drops • Eggshell changes • Wider range of signs	MG/MS positive flocks
	Immunosuppressed /Compromised respiratory system
	Strong lentogenic viruses as primer
	Poor vaccination techniques
	Spray vaccination
	Large amount of NH3 or dust

5. VACCINE OR VACCINATION FAILURE?

A. VACCINATION ERRORS: EYE DROP

VACCINATION ERRORS: SUBCUTANEOUS/ INTRA-MUSCULAR





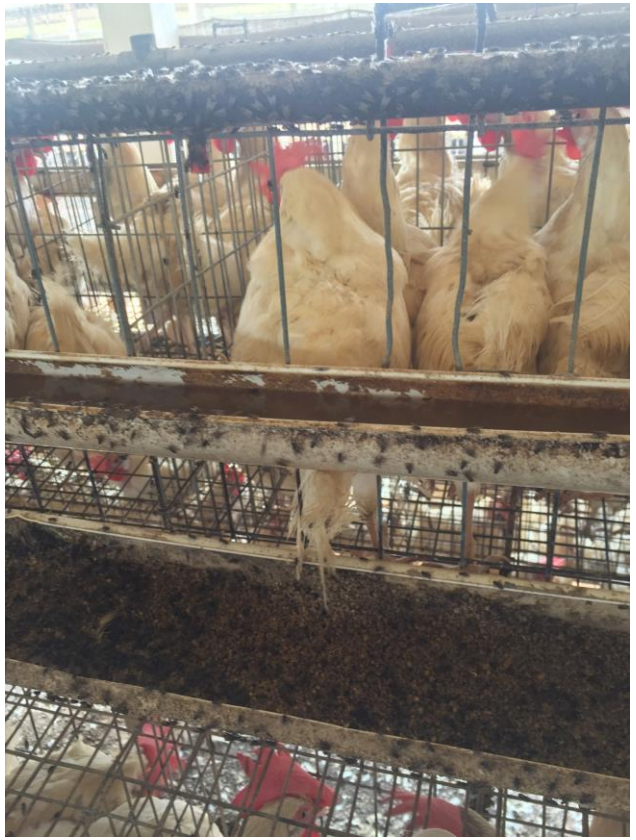
B. NUTRITION AND MANAGEMENT

5th Day	IB +Lasota Drops
17th Week	ND+IB killed-0.5ml /bird -s
19th Week	ND Killed -s/c-0.5ml
24th Week	IB+Lasota D/w-2.0Dose

F.NO : 6
AGE: 28Wks
TYPE : C/L

Body weight 1-1.1 kg

Titre	Number	Titre	Number
2	0	2	0
4	0	4	0
8	0	8	0
16	0	16	0
32	8	32	5
64	10	64	12
128	3	128	5
256	1	256	0
512	0	512	0
1024	0	1024	0
2048	0	2048	0
4096	0	4096	0

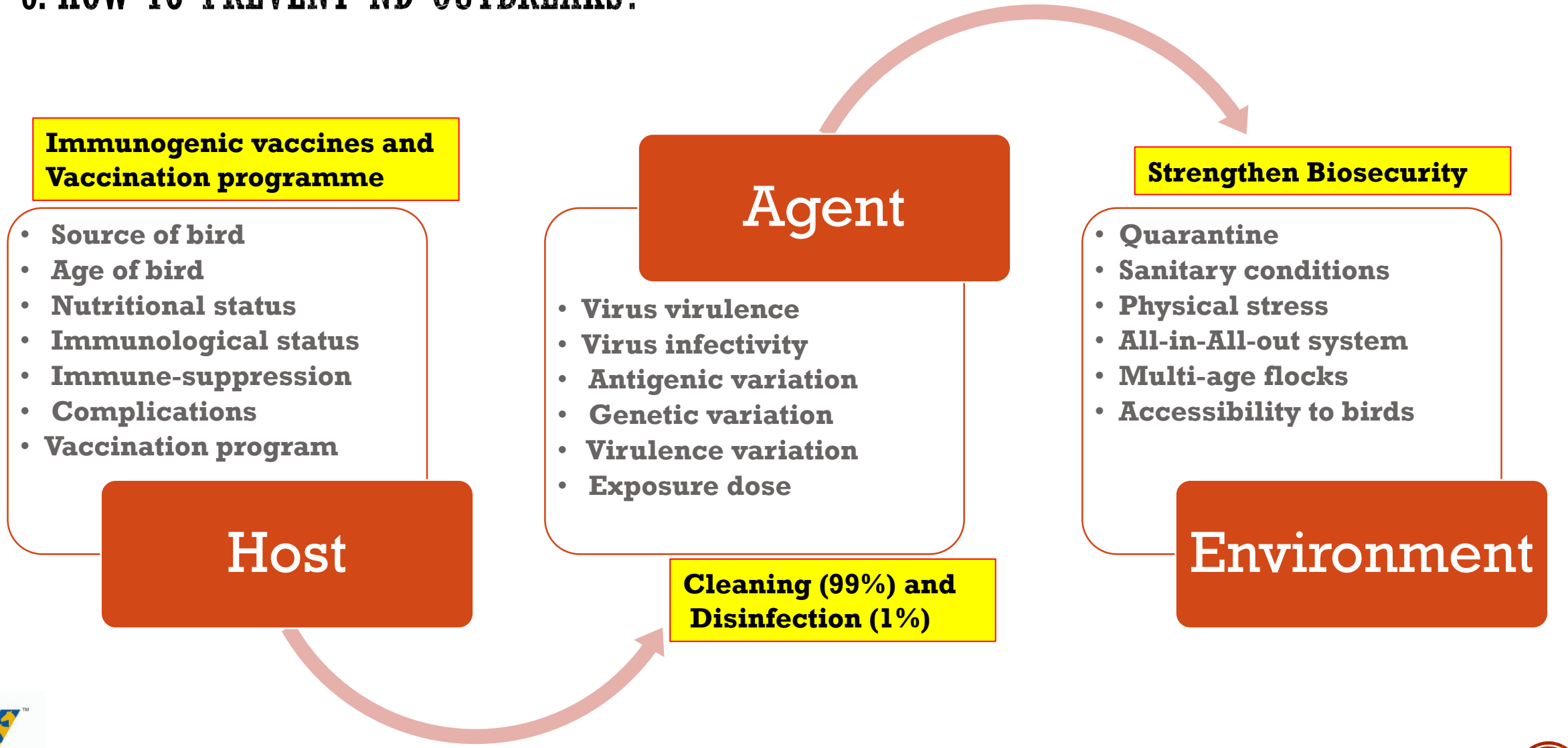


Egg production:

- Didn't reach peak

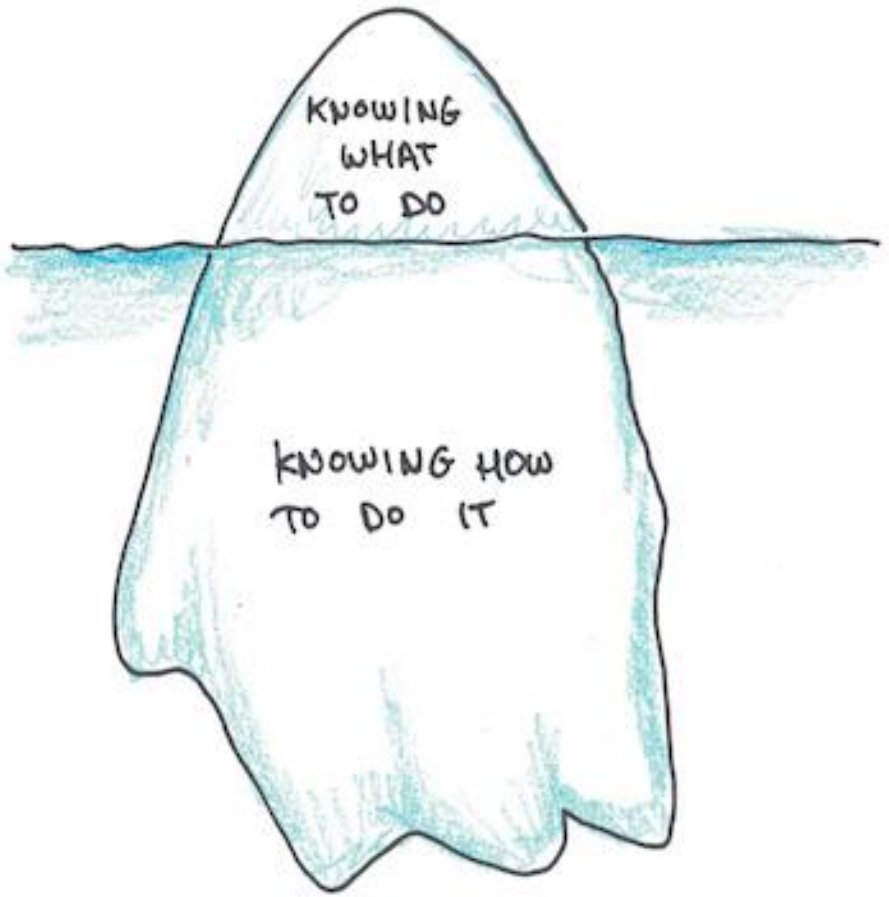
- Egg production drop of ~30% less than STD

6. HOW TO PREVENT ND OUTBREAKS?



DISEASES DON'T HAVE TO MAKE HEADLINES.

WE CAN STOP THEM BEFORE THEY SPREAD WIDELY.



THANKS