

SARS vaccine development:
experience of vaccination against
avian infectious bronchitis coronavirus
(IBV)

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Avian Pathology, 32 (6), 2003.

IBV is the long-known coronavirus of the chicken (domestic fowl; *Gallus domesticus*)

It most obviously causes respiratory disease:
rhinitis, tracheitis, bronchitis.

Can also damage oviduct.
Some strains cause nephritis.
Recently proventriculitis observed.



IBV replicates in

Harderian gland

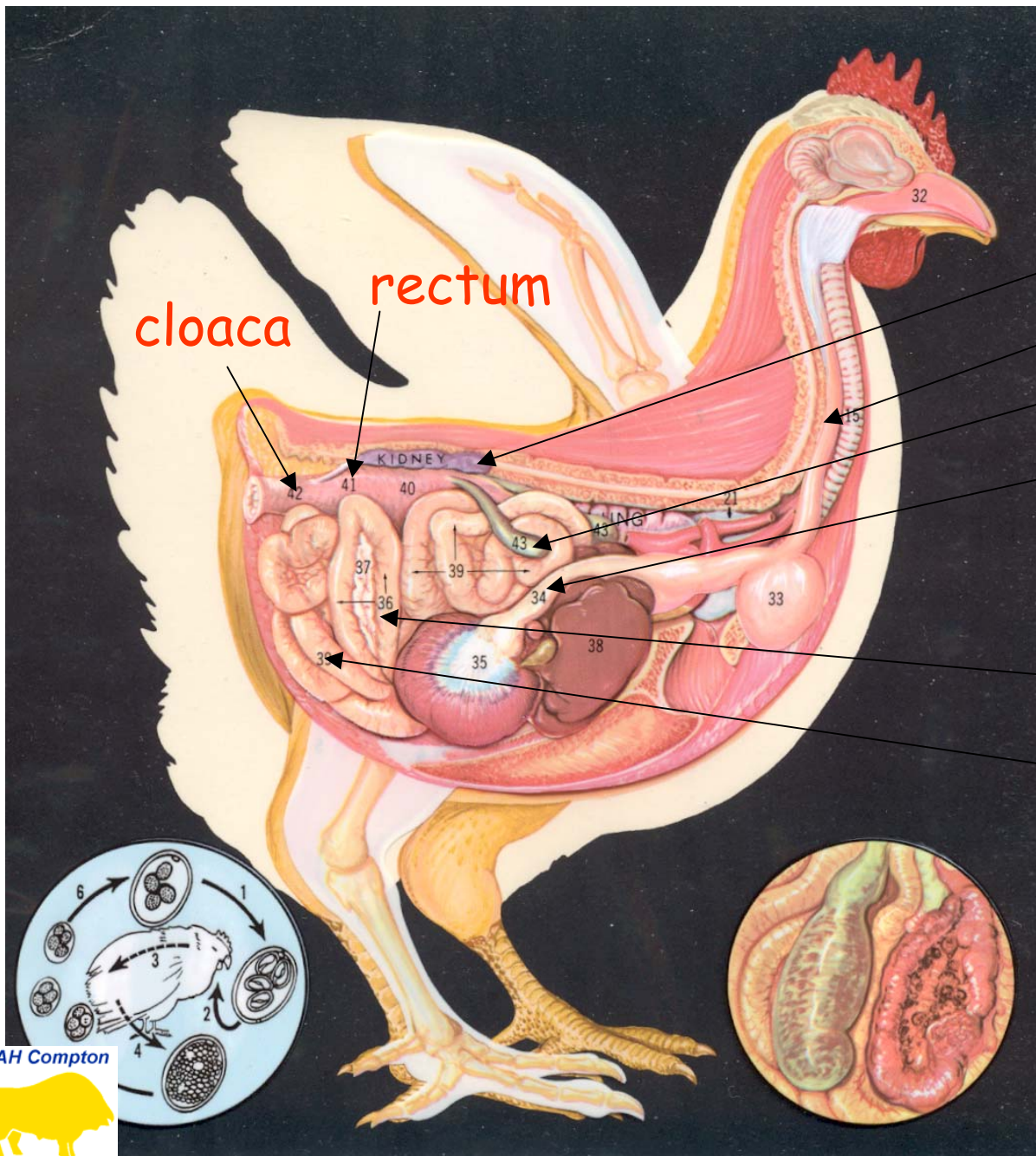
nose

trachea

lung

air sacs





IBV also replicates in kidney

oesophagus

caecum

proventriculus

duodenum

ileum

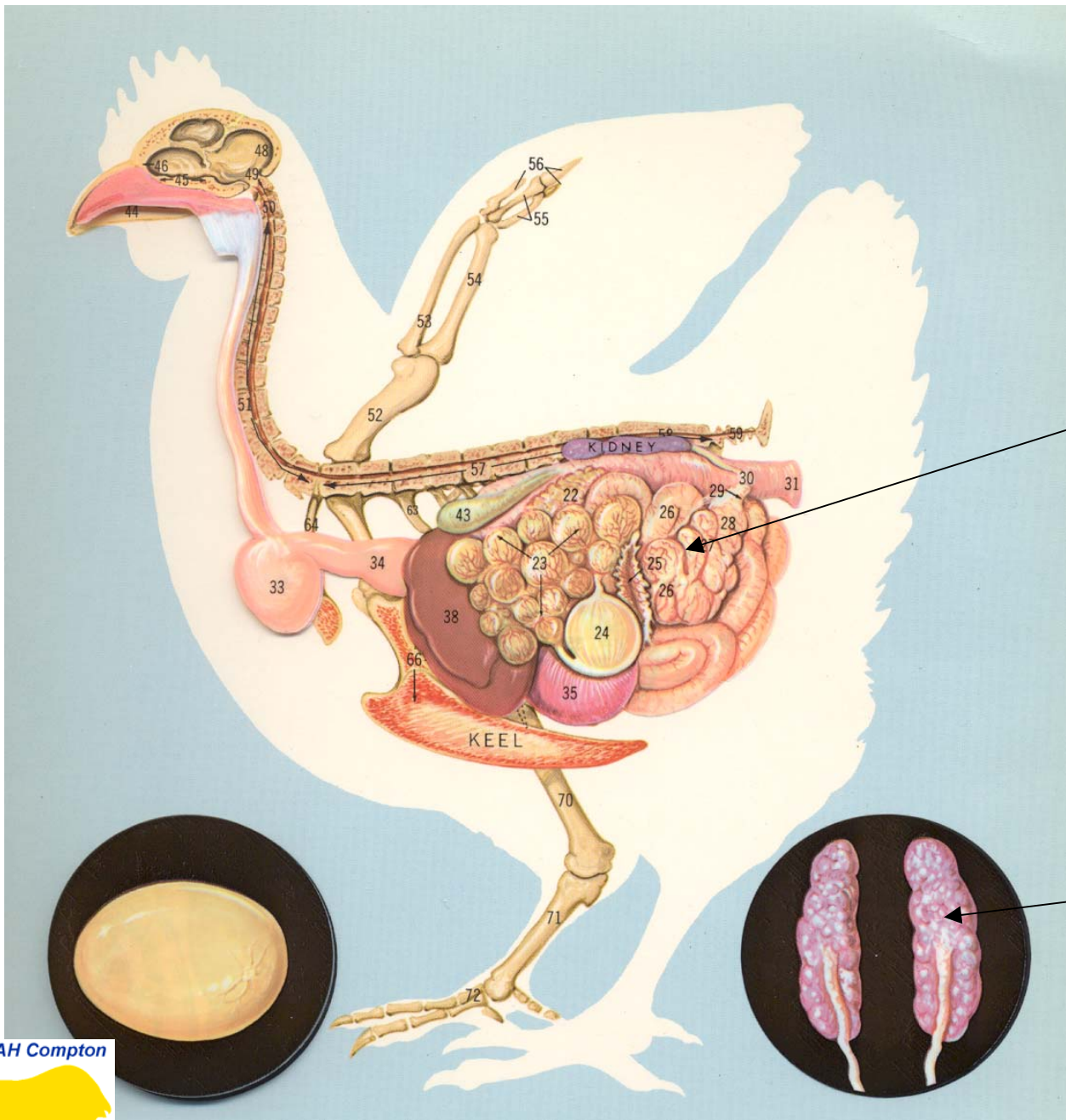
IBV can be isolated from cloaca later than from respiratory tract



... and also replicates in

oviduct

swollen kidney with urates



IBV

There are genetically very closely related CoVs in **turkeys** (*Meleagris gallopavo*; enteric disease)

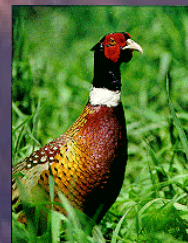


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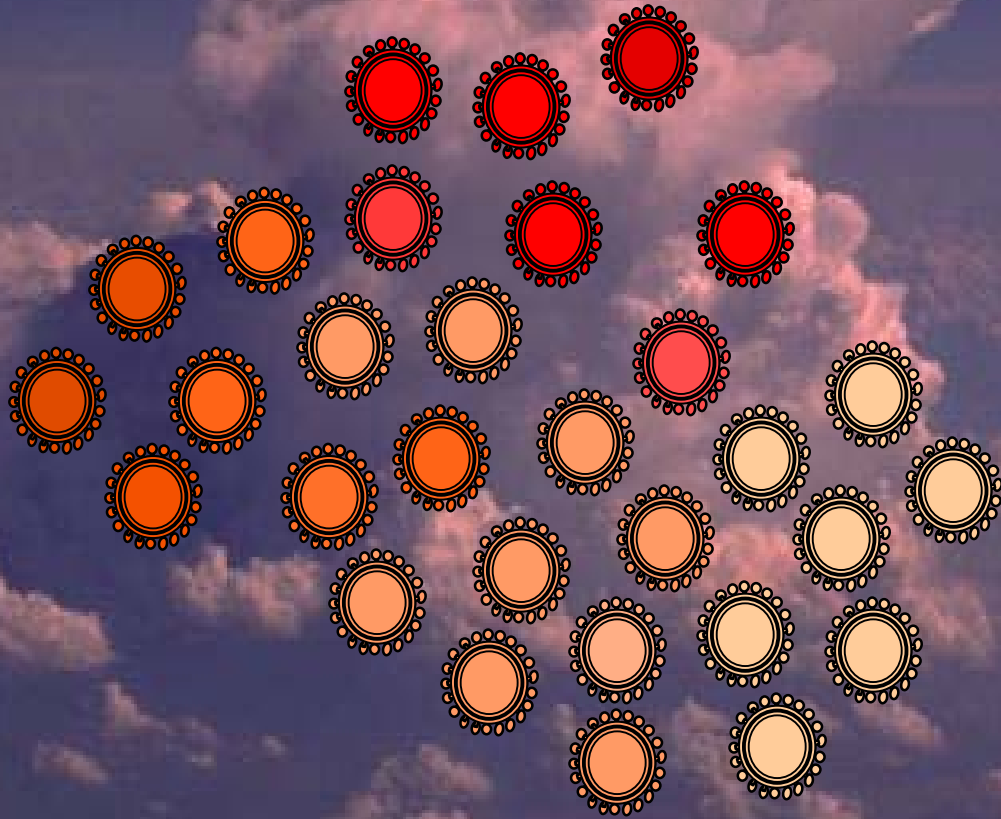
pheasants (*Phasianus colchicus*; respiratory & kidney disease).



~90% amino acid identity.



SARS CoV-like viruses?



Host genetic variation

Some strains of IBV kill young chicks.

Lines of birds differed with respect to mortality, e.g. ranging from 0% to 83%.

Initial replication of IBV was similar, but elimination of virus was slower in the more susceptible line.



Purpose of vaccination against IB

- to avoid economic loss

Meat-type chickens live only 6 weeks.

Received live vaccine at ONE day of age

Maybe re-vaccinated at 2 to 3 weeks of age.



Purpose of vaccination against IB

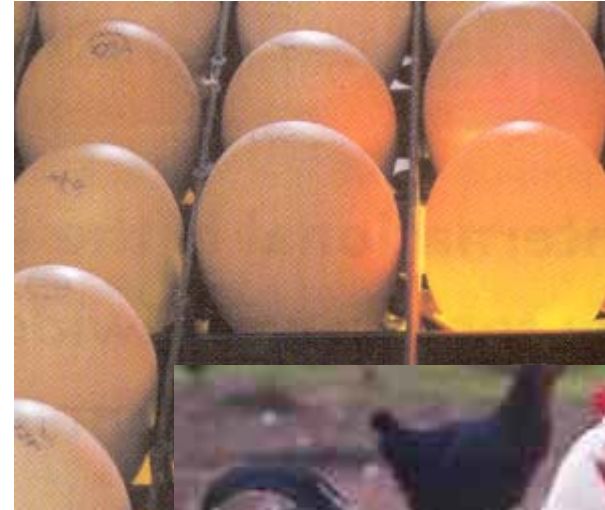
- to avoid economic loss

Egg-layers live 1 to 2 years.
Vaccinated more than once
with live vaccine during
first few weeks of age.

AND

with inactivated vaccine
at 16 weeks of age, start of
egg production period,

- to avoid drops in egg production and quality



Introduction of IB vaccines

Live attenuated 1950s

Immunity short-lived

- decrease observed after 9 weeks.
OK for meat-type birds
but not for egg-layers.

Therefore >1 live vaccine given to
young egg-layers, followed by
inactivated vaccine.

- to protect against loss of egg production.



Live attenuated IB vaccines

A single live vaccination can give sterile immunity
(against homologous challenge)
for ~ 9 weeks

Note

Approx. 10% of chickens may respond poorly
i.e. do not develop protective immunity,
even in experimental conditions.



Inactivated IB vaccines

Several investigations.

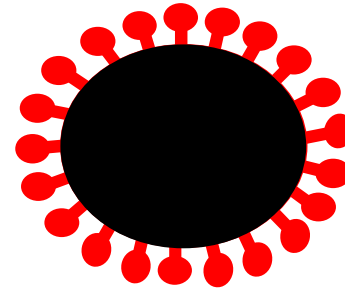
One i.m. application resulted in
<50% of chickens protected.

In some investigations
two i.m. applications resulted in
>50% protection (up to 90%)
but in other investigations protection
remained at <50% of chickens.

Criterion of protection too rigorous?
Isolation of challenge virus.
Did not look at clinical signs

IBV proteins that induce immunity

- relevant to subunit vaccines & vector vaccines



Spike protein

from purified IBV, baculovirus or fowlpox virus vector
- <50% protection, even with >1 application (baculo).

From single live application of a recombinant fowl adenovirus

- 90% and 100% protection in two experiments.

(Johnson et al., 2003, *Vaccine*, 21, 2730-2736)



Note of caution

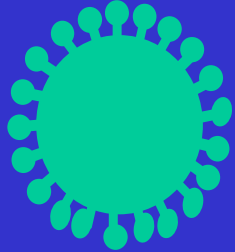
- as little as 5% amino acid difference between spike proteins might result in poor cross-protection.



Experiment with recombinant IBV

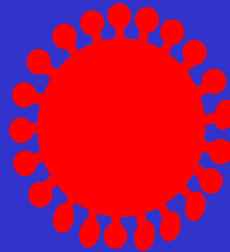
"vaccinated"
with

Beau-R



Challenged with

M41

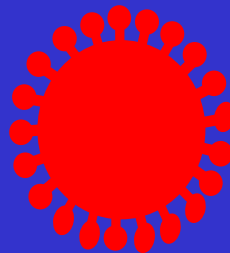
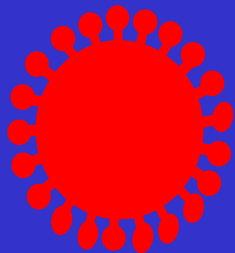


Protection

poor

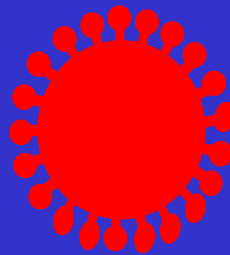
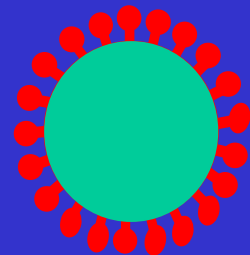
95% identity
in S1

M41



excellent

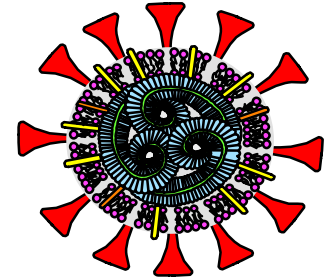
BeauR-M41S



very good



IBV proteins that induce immunity



nucleocapsid protein (N)

Bacterially expressed b-galactosidase fusion protein ([Boots et al., 1992, *Vaccine*, 10, 119-124](#))

- indicated that N protein primed an immune response that improved the response to subsequent inactivated IB vaccination

Two i.m. inoculations with a plasmid expressing N ([Seo et al., 1997, *J. Virol.*, 71, 7889-7894](#)) induced protection. Carboxy-terminal 120 residues formed major immunogen.

Single wing-web inoculation of fowlpox virus expressing N induced some protection against clinical signs ([Yu et al., 2001, *Avian Disease*, 45, 340-348](#)).



Final remarks - 1

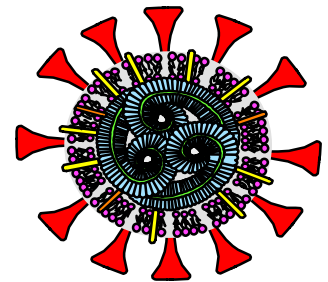
Live IB vaccines more efficacious than inactivated ones.

Inactivated vaccines (and S subunit vaccines).

Single application: max. 50% protection.

Multiple application: <50% or >50%

(in different studies)



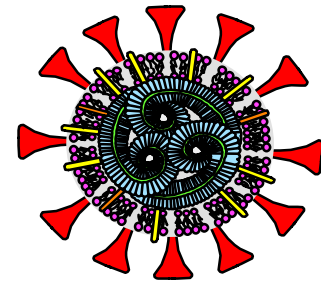
- but criteria for protection too rigorous?
(based on reisolation of challenge virus, not clinical signs)

i.e. protection might have been better than was concluded.



Final remarks - 2

>1 application of inactivated SARS CoV
vaccine
might protect against the worst effects,
even if not perfect?



Keep nucleocapsid protein in mind
as an immunogen.