INTRADERMAL APPLICATION OF FMD VACCINES

Erwin van den Born

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Background intradermal vaccination

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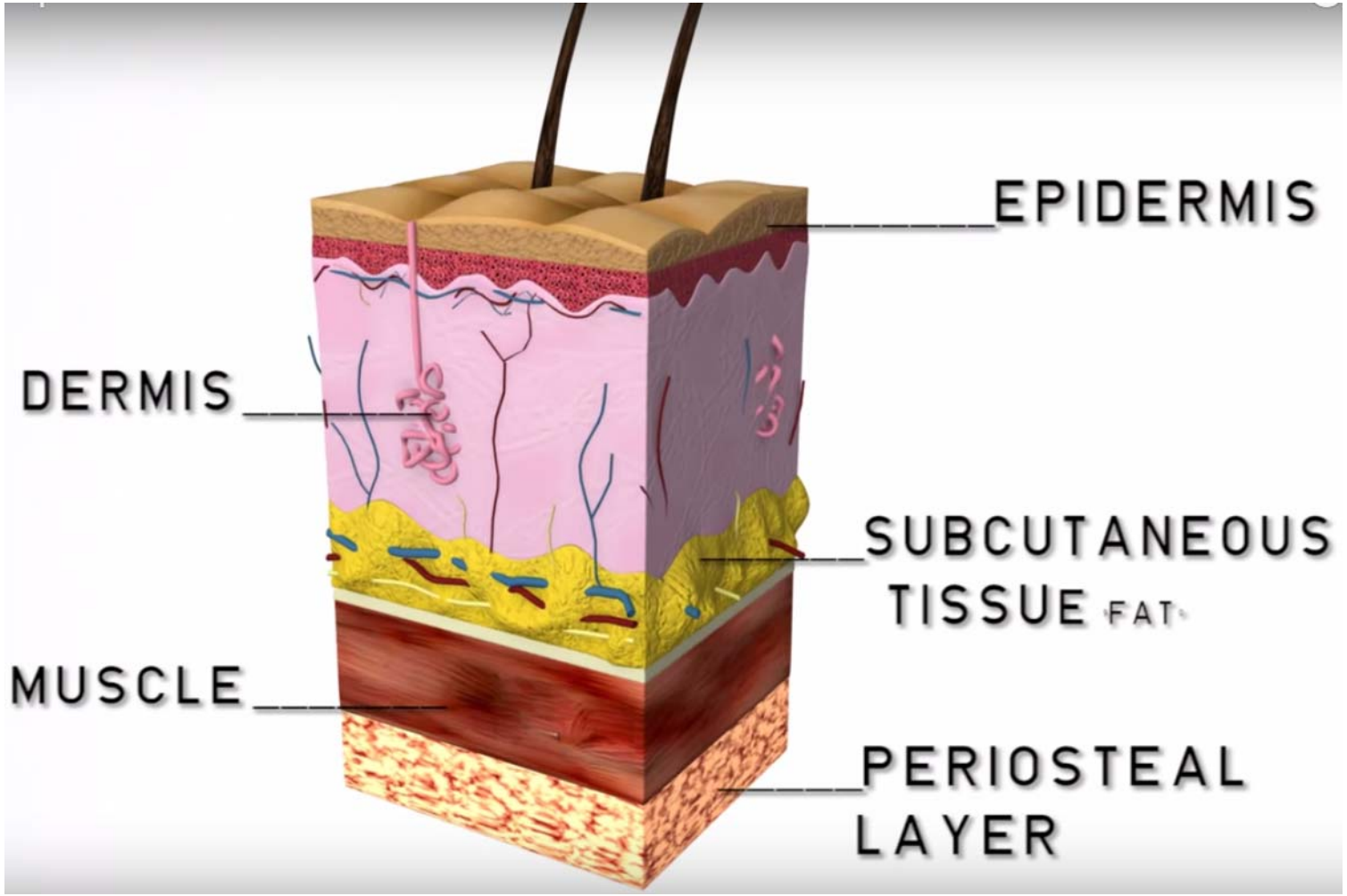
Schematic representation of the skin



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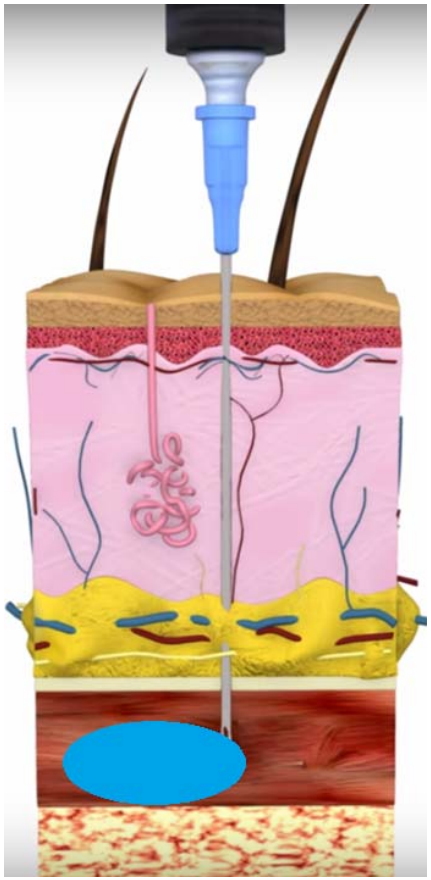
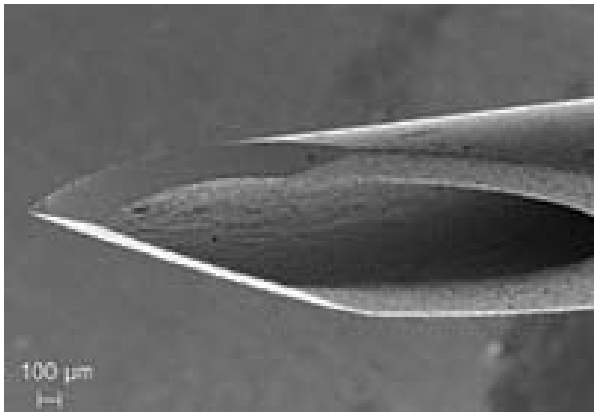
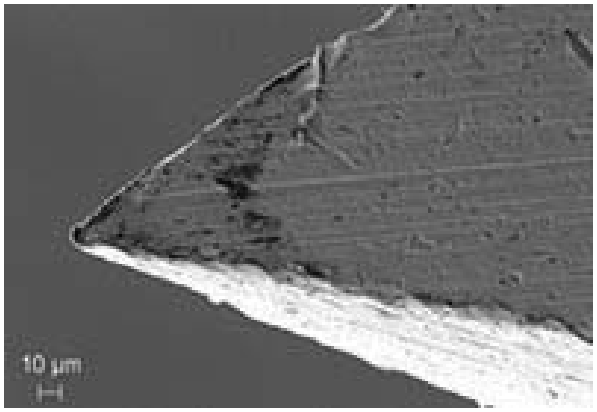
Intramuscular (IM) vaccination

Intramuscular

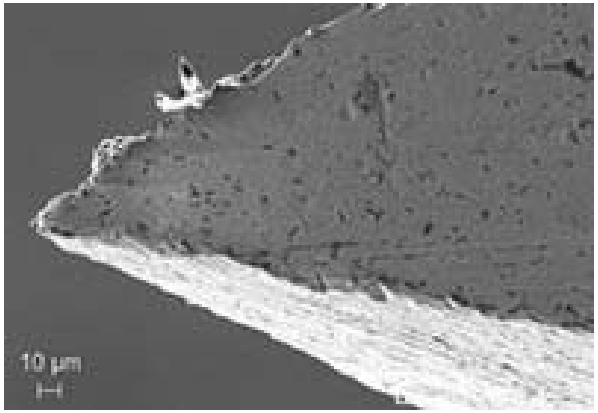




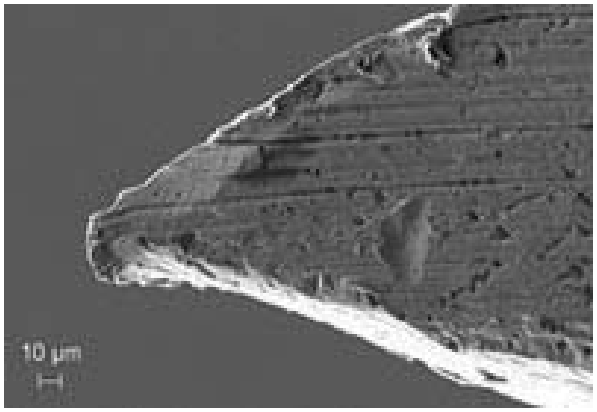
Unused needle



Needle used once



Needle used twice



Needle used 12 times

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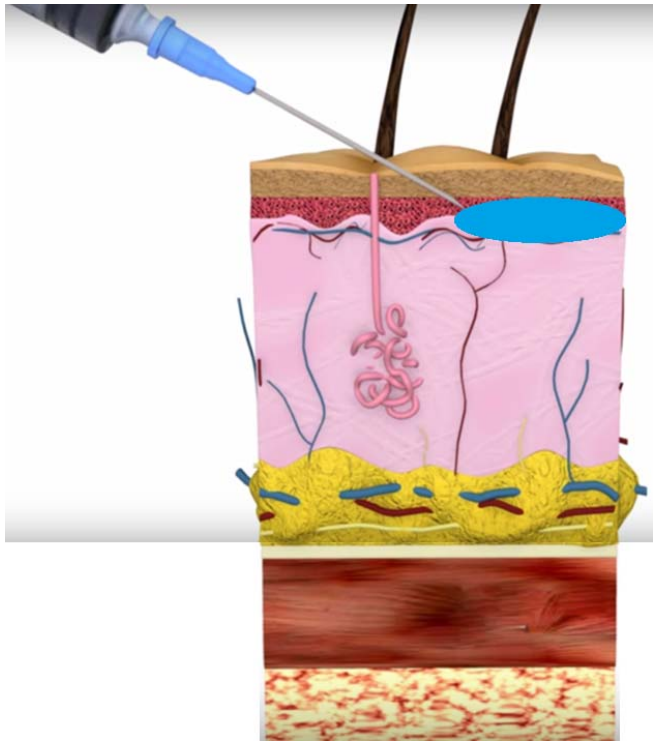
Intradermal (ID) vaccination

Intradermal
with needle



Intradermal with
Jet Injector (IDAL)

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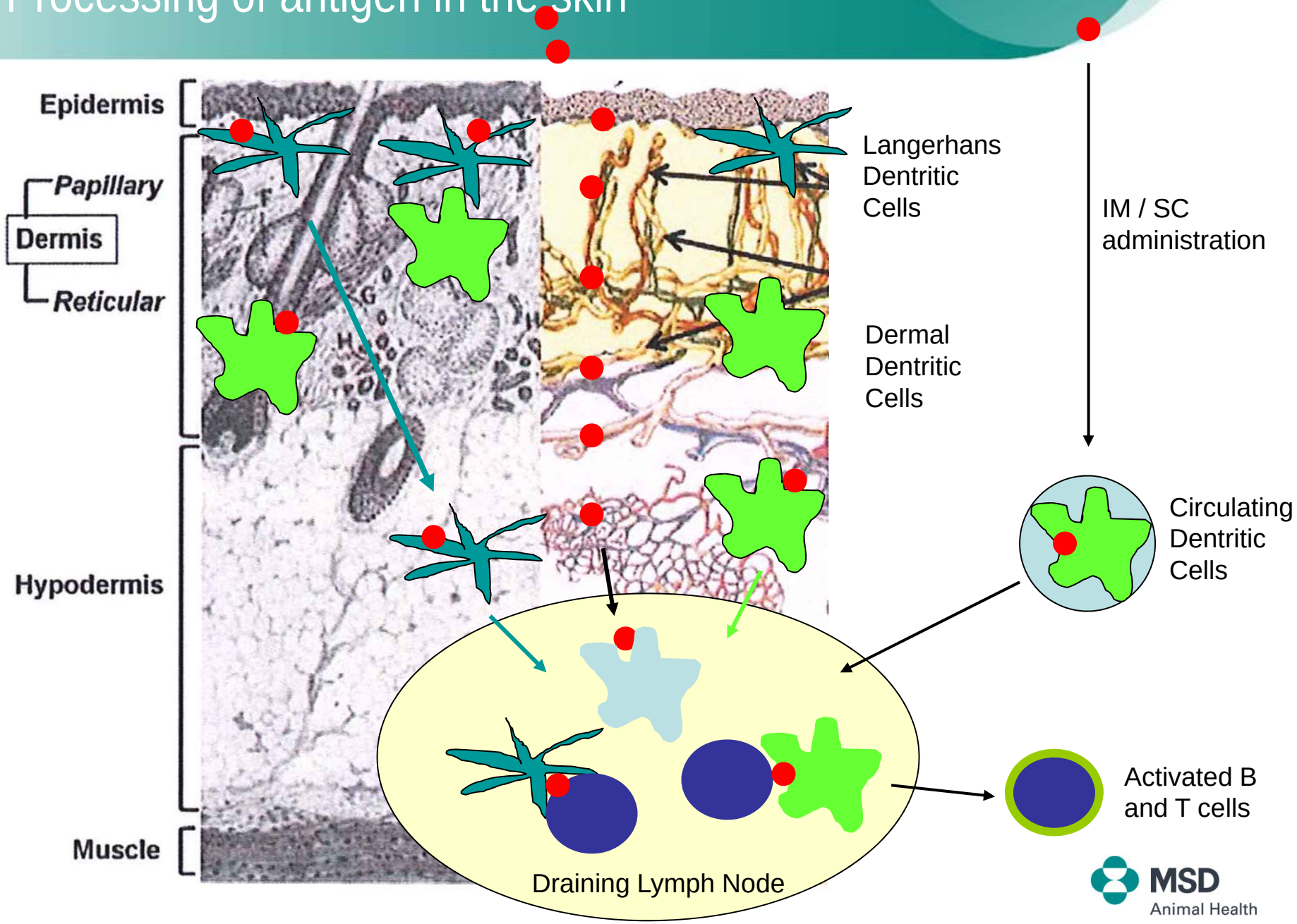
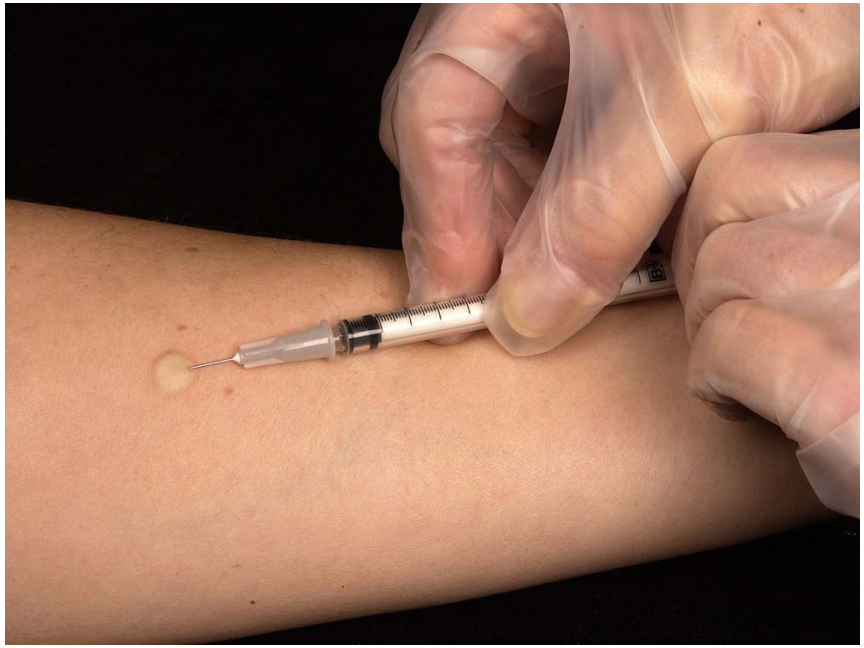
Processing of antigen in the skin



Human intradermal vaccines

- Mostly inactivated antigen (e.g. Hepatitis B, Influenza, Rabies)
- Antigen dose for ID 5-10x lower than for IM, but similar efficacy
- Many vaccines do not contain adjuvants.
- Local reactions ID often higher than for IM administration, but mostly mild and transient



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The history of ID vaccination in MSD Animal Health

- Two decades of experience
- Low-volume 0.2-mL dose administered intradermally with the needle-free IDAL® System*
- First products developed for live virus vaccines
  - Porcilis® PRRS
  - Porcilis® Begonia
- Followed by inactivated vaccines:
  - Porcilis® M Hyo ID ONCE
  - Porcilis® PCV ID

* IntraDermal Application of Liquids

10 Reasons to go for an intradermal vaccination of pigs

1. Powerful antigen-presenting cells in the epidermis cause an induction of a broad range of immune responses
2. Potential to overcome pre-existing immunity because (maternal) antibodies are not located in the skin
3. Less systemic adverse events because of minimal invasiveness
4. Faster and more convenient than IM administration
5. Limits transmission of pathogens caused by reuse of needles
6. No risk of needle-stick injuries of the farmer/vet
7. Potentially less antigen needed
8. Less stress and pain for the animals
9. Food quality improvement by avoiding muscle lesions, broken needles, infections/abcesses
10. No IM injection in neck muscle, which is most important meet in South-Korea

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Published work by Lelystad group

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journal homepage: www.elsevier.com/locate/vaccine

Intradermal vaccination of pigs against FMD with 1/10 dose results in comparable vaccine efficacy as intramuscular vaccination with a full dose

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- FMDV O/TAW/3/97 vaccination and challenge
- Double-oil-in-water emulsion (DOE) vaccines
- IDAL vaccinated
- Pigs (~6 wks old)

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Published work by Lelystad group

Trial	Group	Route	Dose (µg)*	VN	Protection
1 (n=3)	1	-	-	<0.3	0
	2	IM	3	2.5	100
	3	ID	0.3	1.7	100
	4	ID	3	1.3	66
2 (n=5)	1	-	-	<0.3	0
	2	IM	3	2.1	100
	3	IM	30	2.3	100
	4	ID	0.3	1.7	100
	5	ID	3	1.4	80
3 (n=5)	1	-	-	<0.3	0
	2	IM	3	2.3	100
	3	IM	0.3	1.8	100
	4	IM	4x 0.3	2.1	100
	5	ID	0.3	2.2	100
	6	ID	4x 0.3	2.2	100

∗ 3 µg is standard dose

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Development of an intradermal vaccine for pigs against FMDV

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Going from IM to ID vaccination is not that straightforward...

Adjuvant

Antigen concentration

Local reactions

0.2 ml

Dose

Efficacy

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Animal trial to select adjuvant for FMD ID vaccine

- Pigs (~6 wks old)
- FMDV A22 standard dose
- ID with IDAL
- Adjuvants selected based on previous experience with ID vaccination

Group	Route	Adjuvant	Adjuvant type	Maximum space available in water phase for antigens (% v/v)
1	ID (0.2 ml)	A	water-in-oil	39
2		B	water-in-oil	41
3		C	oil-in-water	79
4		D	oil-in-water	51
5		E	oil-in-water	49
6		F	oil-in-water	50
7		G	water-in-oil	37
8		H	water-in-oil	14
9		I	real double oil emulsion	28
10		J	reversed double oil emulsion	46
11	IM (2 ml)	J	reversed double oil emulsion	46

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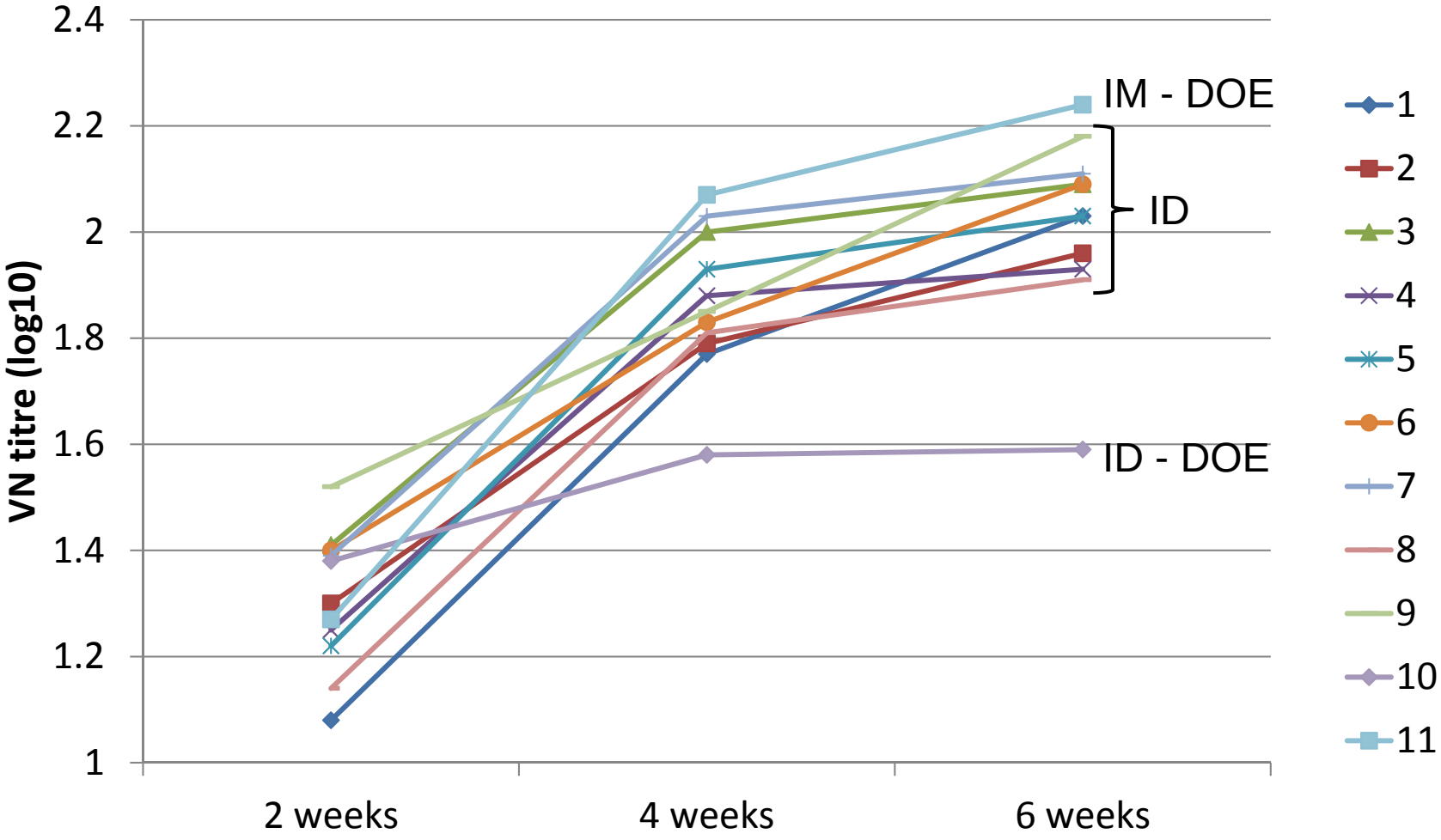
Animal trial to select adjuvant for FMD ID vaccine



→ *Cannot take standard IM vaccine and use ID*

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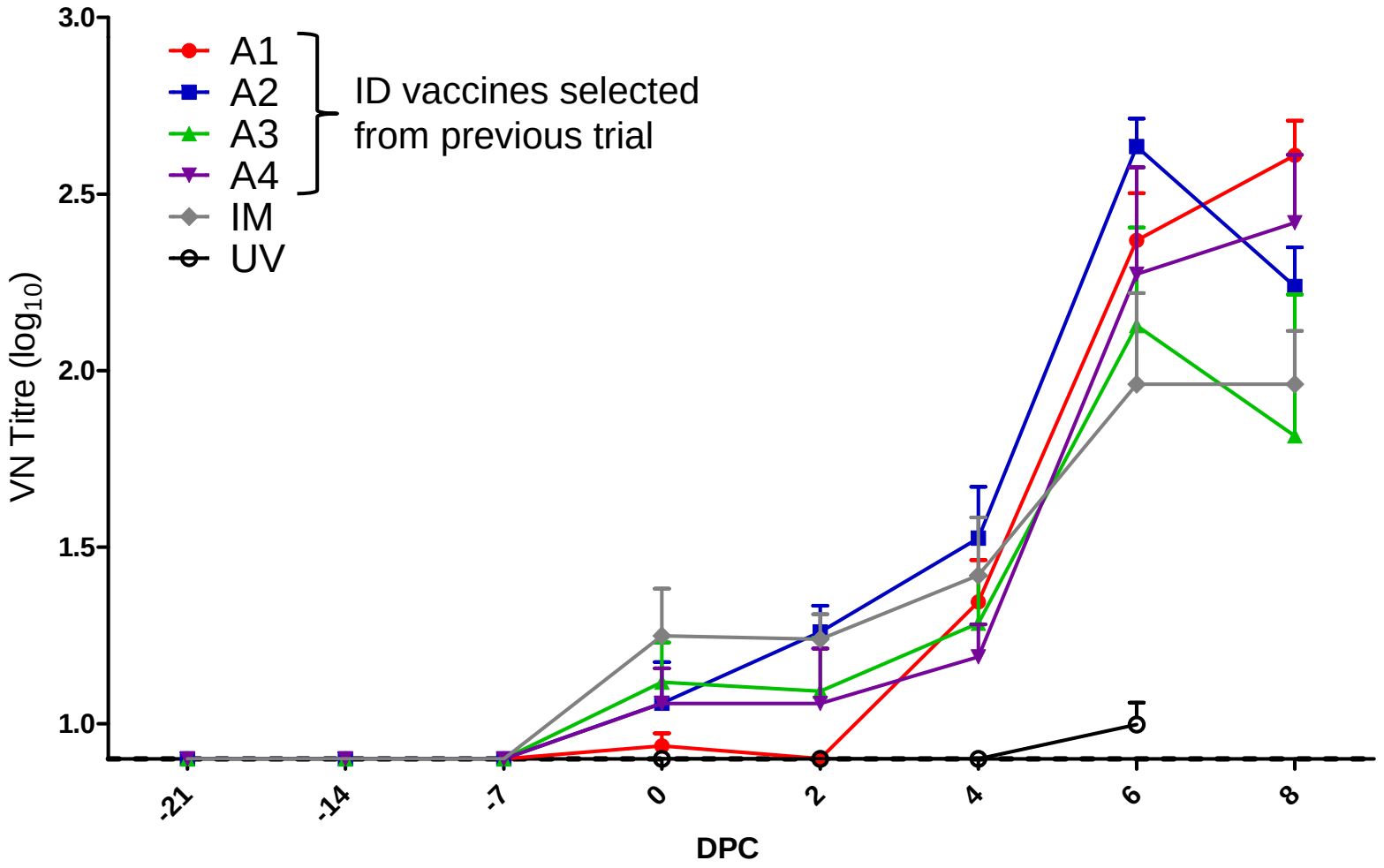
Animal trial to check efficacy of FMD ID vaccines



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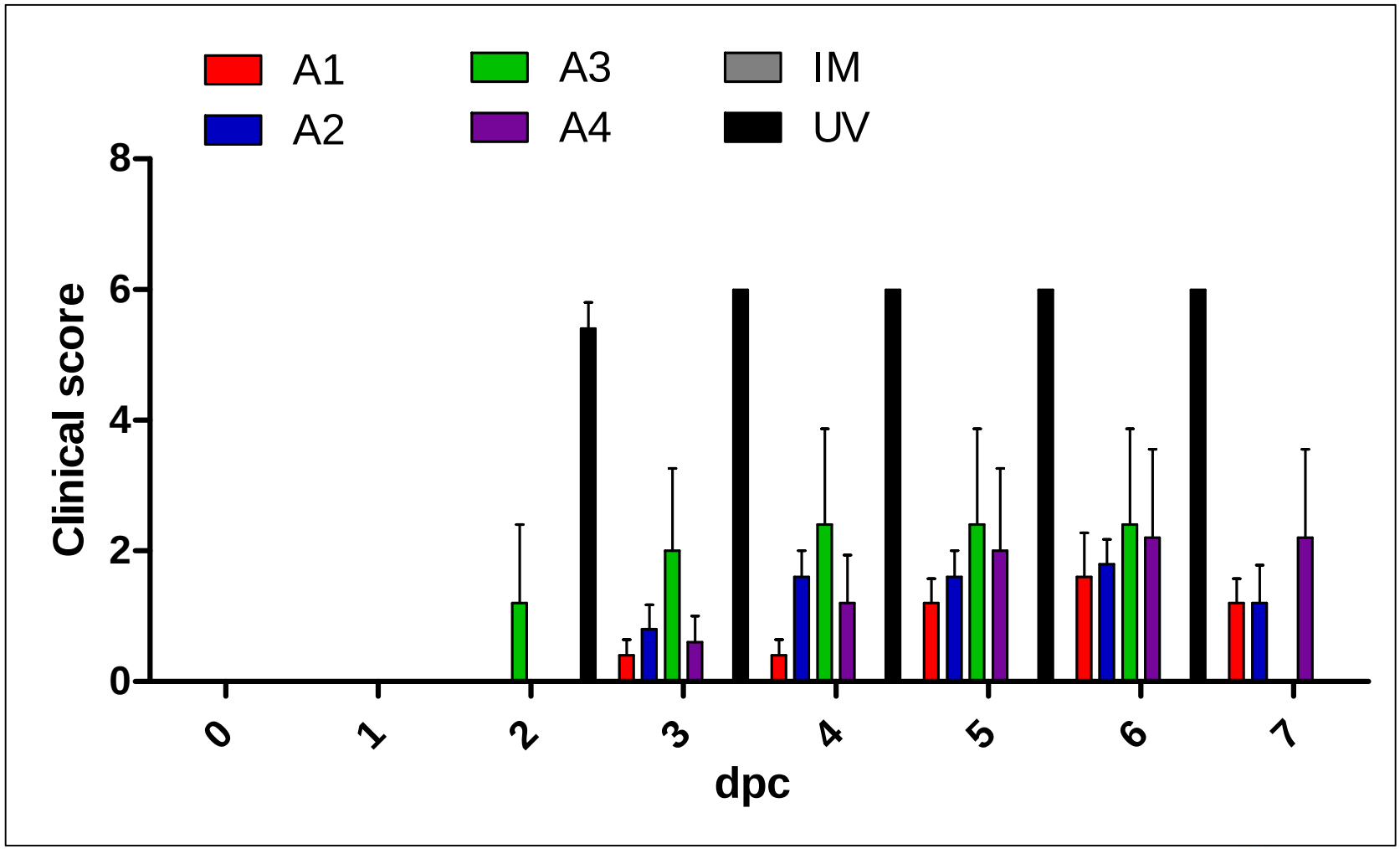
Animal trial to check efficacy of FMD ID vaccine (A22)

None of the ID groups were fully protected (max 75%)



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Summary & Future

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Summary & Future – FMD ID vaccines

- ID vaccines for pigs have several benefits like less stress/pain and increased hygiene, and it is safer and faster.
- Our work demonstrates that several adjuvants can induce higher VN titres in pigs than a typical DOE formulation.
- Published work suggests that for ID vaccines the antigen payload per dose can be lower.
- ID vaccines containing a standard payload formulated with several adjuvants showed suboptimal protection.
- Clearly, there is still uncertainty about efficacy of ID vaccines, and several questions remain to be addressed, e.g.:
  - Is a lower antigen payload more protective?
  - Will different adjuvants improve efficacy?
  - Do VN titers predict protective capacity of ID vaccines?

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