Rabies monoclonal antibodies
WHO Perspective

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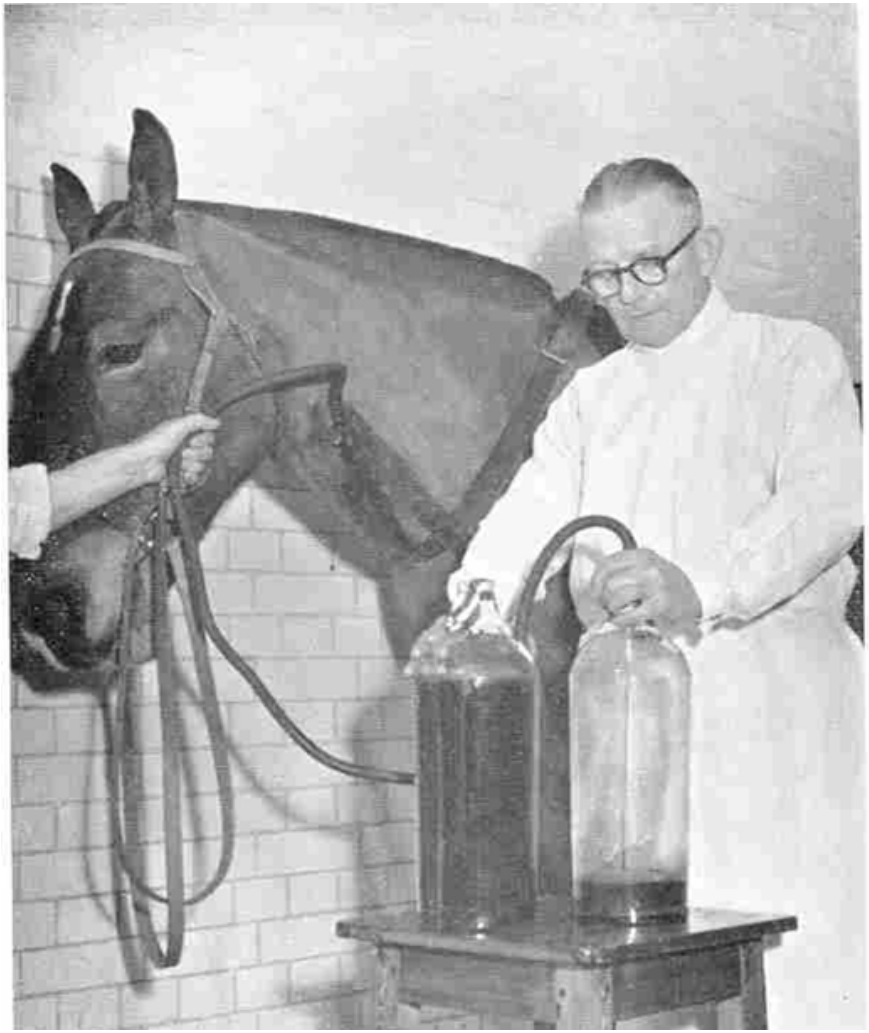
World Health Organization

Limitations of blood-derived RIG

- **Availability** (limited supply)
- **Affordability** (expensive, often paid out of pocket)
- **Safety** (ERIG: adverse reactions can occur; varying purity)



The promise of monoclonal antibodies

Recombinant DNA technology

- Adequate supply (easier to produce, mass production, QC easier)
- Reduced production costs
- Reduces risks of adverse reactions
- Advantage of concentrated neutralizing mAbs

Rabies mAbs development on the WHO radar since 1990

- 6th WHO consultation on monoclonal antibodies in rabies diagnosis and research, Philadelphia, April 1990
  - Recommendations/steps for development mapped out
  - apps.who.int/iris/bitstream/10665/61437/1/WHO_Rab.Res_90.34.pdf
- WHO Consultation on a Rabies Monoclonal Antibody Cocktail for Rabies Post Exposure Treatment, Geneva, May 2002
  - Plan for evaluation & selection of candidate mAbs and technology transfer plan with WHO CCs.
  - www.who.int/rabies/resources/mabs_final_report_WHO_consultation_2002.pdf

WHO initiative to develop rabies mAbs 2002-present

- **Goal**: To make monoclonal antibody products to replace RIG which are available at the lowest possible price to the public sector of developing countries.
- **Phase 1**, 2002-2006: Select and evaluate potential mAbs – donated to WHO by Collaborating Centres for further evaluation
- **Phase 2,** 2008-present – transfer the mAbs to developing country manufacturers (Zydus India, CSIR South Africa, Span Biotherapeutics India)

Advanced candidates

Product Name	Manufacturer	Stage/Registration No.	Comment
CL184	Crucell, Johnson & Johnson	Phase I (USA) completed ISRCTN18660493	Further clinical trials not planned (communication from Crucell 2016).
		Phase I/II (India) completed ISRCTN12693237	
		Phase II (USA) completed NCT00656097	
		Phase II (India) completed NCT01228383	
		Phase II (Philippines) completed NCT00708084	
RMAb	Partnership between MassBiologics and Serum Institute of India	Phase I (India) completed CTRI/2009/091/000465	**Product was licensed in India in August 2016**
		Phase II/III (India) completed CTRI/2012/05/002709	
Rabimabs	Zydus Cadila	Phase I/II (India) completed CTRI/2012/12/003225 CTRI/2015/06/005838	Phase III to be initiated in 2017
SYN 023	Synermore Inc.	Phase II (currently recruiting) NCT02956746	Expected completion of phase II in Q2 2017
Human Anti-Rabies MAb	M.T.T.I and NCPC (US & China)	Phase II ongoing www.mtarget.com/mm5/pdfs/pipeline/RabiesMonoclonalAnti.pdf	

The challenges?

Challenges of development

- Funding
  - Costly preclinical and clinical studies
  - Return on investment?
- Phase III efficacy challenging
  - Not clear what is required
  - Sample size
  - Confirmed rabies exposure?
- Registering the product in other countries?
  - Differing data requirements?

Challenges of uptake/use

- Decision by policy makers to include mAbs in PEP?
  - Inclusion in the WHO essential medicines list
  - SAGE recommendation
- Cost effectiveness needed
- Treatment guidelines needed
- Training of HCWs
- Procurement/supply
  - UN procurement / bulk purchase?
  - WHO Prequalification?
  - Shelf-life and stockpiling?

SAGE working group on rabies vaccines and immunoglobulins

- Established in July 2016. Among other tasks the WG is:
  - Reviewing the evidence and revisiting the current WHO position for RIG and monoclonal antibody use with the view to improve access to care and increase public health impact.
  - Their recommendation will be presented to the next SAGE meeting on 17-19 October 2017.
  - www.who.int/immunization/policy/sage/sage_wg_rabies_jul2016

Thank you