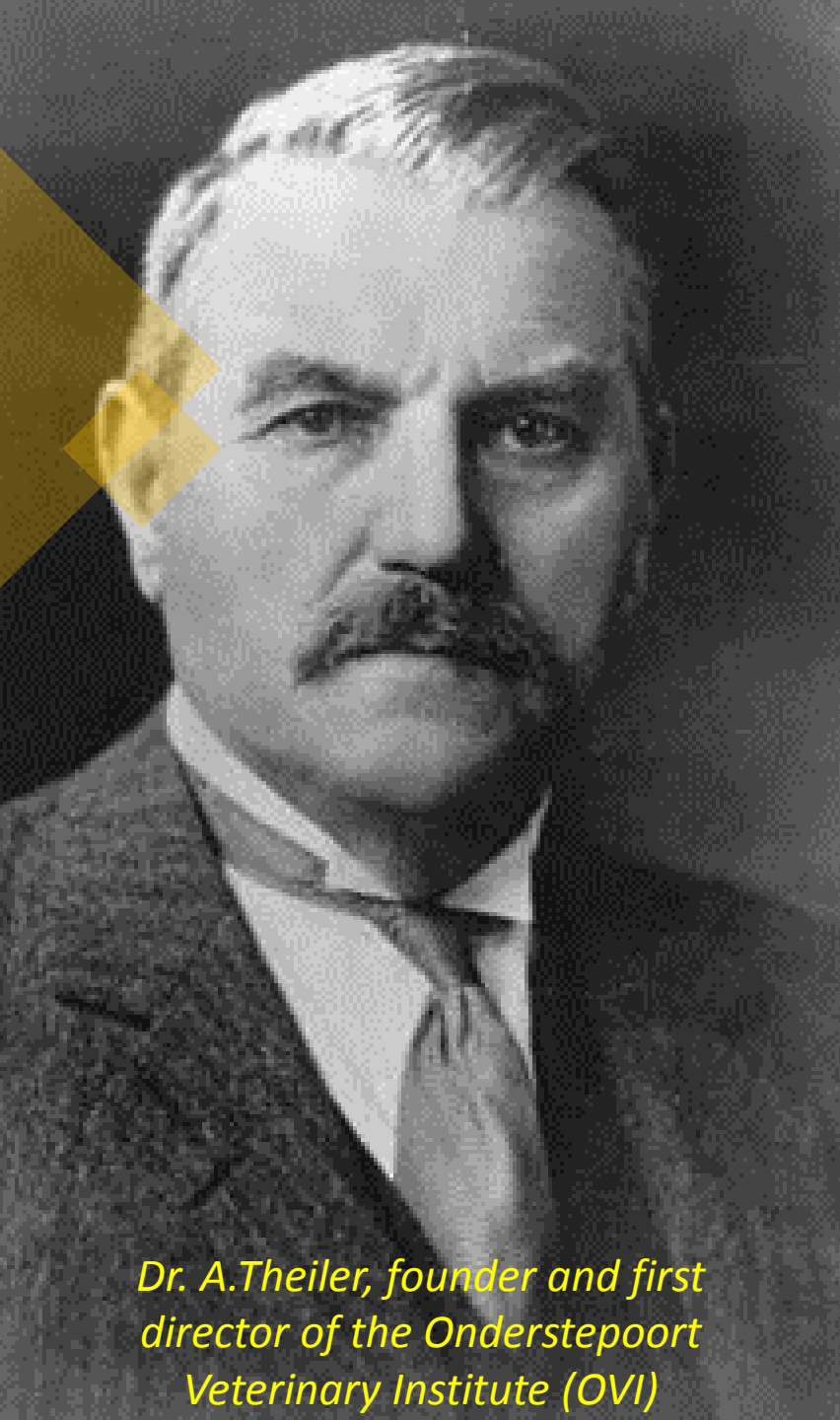


Eminent South African Veterinary Virologists

Daan W. Verwoerd, DVSc, DSc.





Dr. A.Theiler, founder and first director of the Onderstepoort Veterinary Institute (OVI)

Introduction

- Virology is a relatively young scientific discipline only recognised at the Onderstepoort institute as a separate science in the mid-1950s.
- Before that, research on viruses was mainly carried out in its Section Protozoology and contributions were made by researchers in various other disciplines.
- For this presentation important contributions to our knowledge of viruses and viral diseases will be discussed and only the main contributors identified.
- The first breakthrough was the proof by Arnold Theiler in 1905, that the agent causing bluetongue in sheep is a virus by means of filterability studies, following in the footsteps of M'Fadyean who similarly proved in 1900 in London that African Horsesickness (AHS) is caused by a virus.

Development and improvement of early vaccines

- Theiler developed the first vaccines for the bluetongue and AHS diseases. He also developed the concept of antigenic multiplicity to explain failures after using the vaccines.
- Both Theiler and his successor P.J. du Toit made various efforts to improve the reliability of the vaccines and they were used for many years, until 1946 in the case of BT.
- The fact that so much effort was spent on their improvement indicates that these two viruses, later called **orbiviruses**, are of great economic importance for animal husbandry in our country.



Dr. P.J. du Toit, Theiler's deputy and later successor

Cultivation of orbiviruses in mouse brains or embryonated eggs

- A key milestone in orbivirus research was the successful propagation of AHSV in the brains of mice by R.A. Alexander in 1932, using the technique developed by Max Theiler, son of Arnold Theiler, in the US for the propagation of human yellow fever virus for which he received the Nobel Prize.
- This led to improved diagnostic techniques for AHSV, confirmation of antigenic multiplicity, the isolation of “attenuated” virus strains and the development of the first live AHSV vaccine in 1934.
- In parallel studies it was found that bluetongue virus could not be adapted to mouse brains but in 1938 cultivation was achieved by Alexander and co-workers in embryonated eggs and used for the production of a vaccine.



Dr R.A. Alexander first head of Virology and later director of the institute

Discovery of *culicoides* vector

- Of major significance was the discovery by René du Toit (entomologist) in 1944 that orbiviruses are transmitted by *Culicoides* biting midges, explaining many of the environmental issues involved in combating the two diseases.



Dr R. du Toit, Entomologist, discovered the transmission of orbiviruses by Culicoides midges

Vaccine production in cell cultures

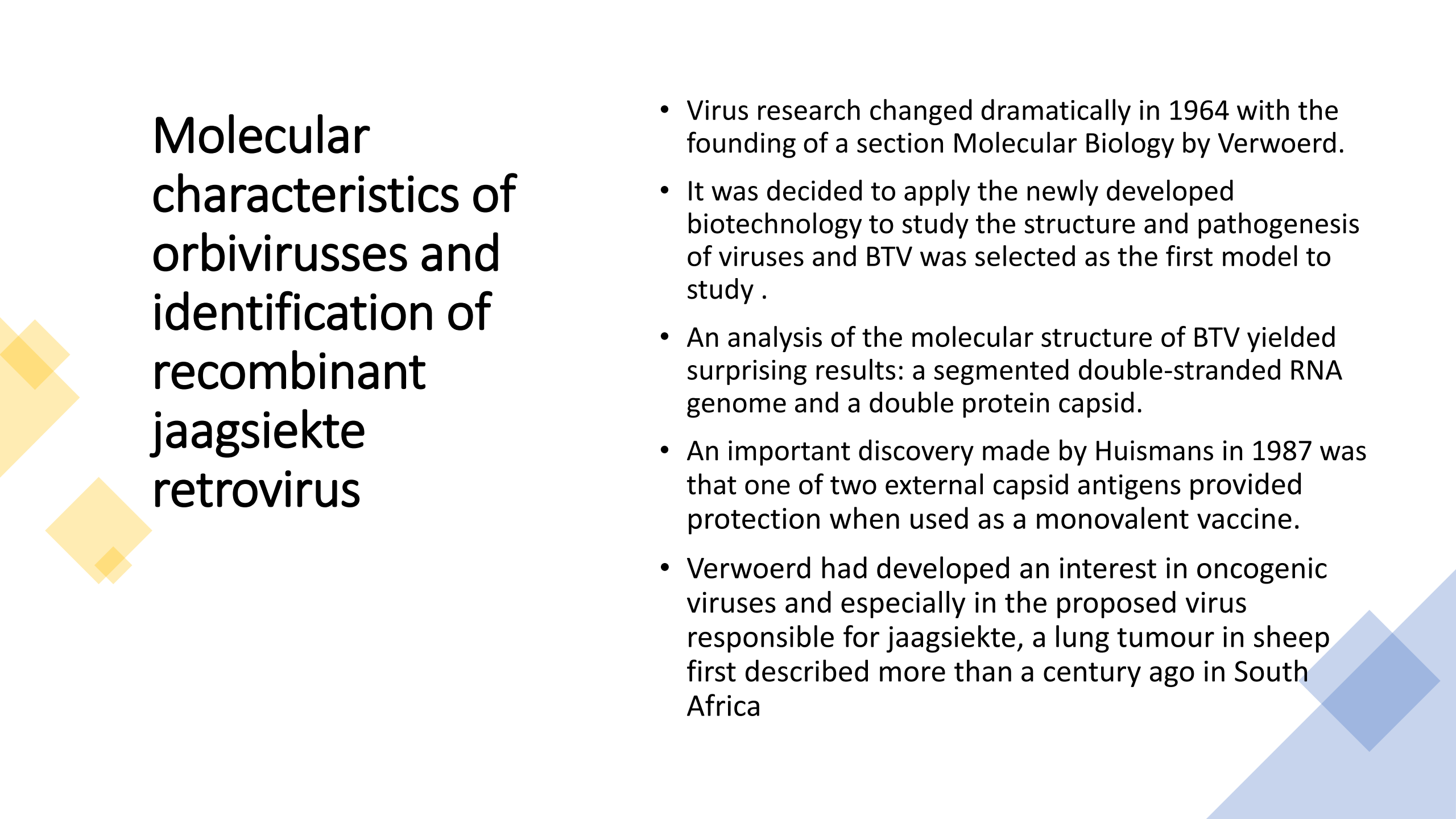
- As head of the new Section Virology, Alexander and Haig was involved in 1956 in the cultivation of BT virus in lamb kidney cell cultures and Haig received international recognition for the development in 1953 of a safe and very effective vaccine against canine distemper which has been used worldwide for many decades.
- In the following years many improvements were made in the serotyping of both orbiviruses by Weiss, Erasmus, Howell, Barnard and others.



Dr K.E.Weiss, Successor of Alexander and later Director of the institute

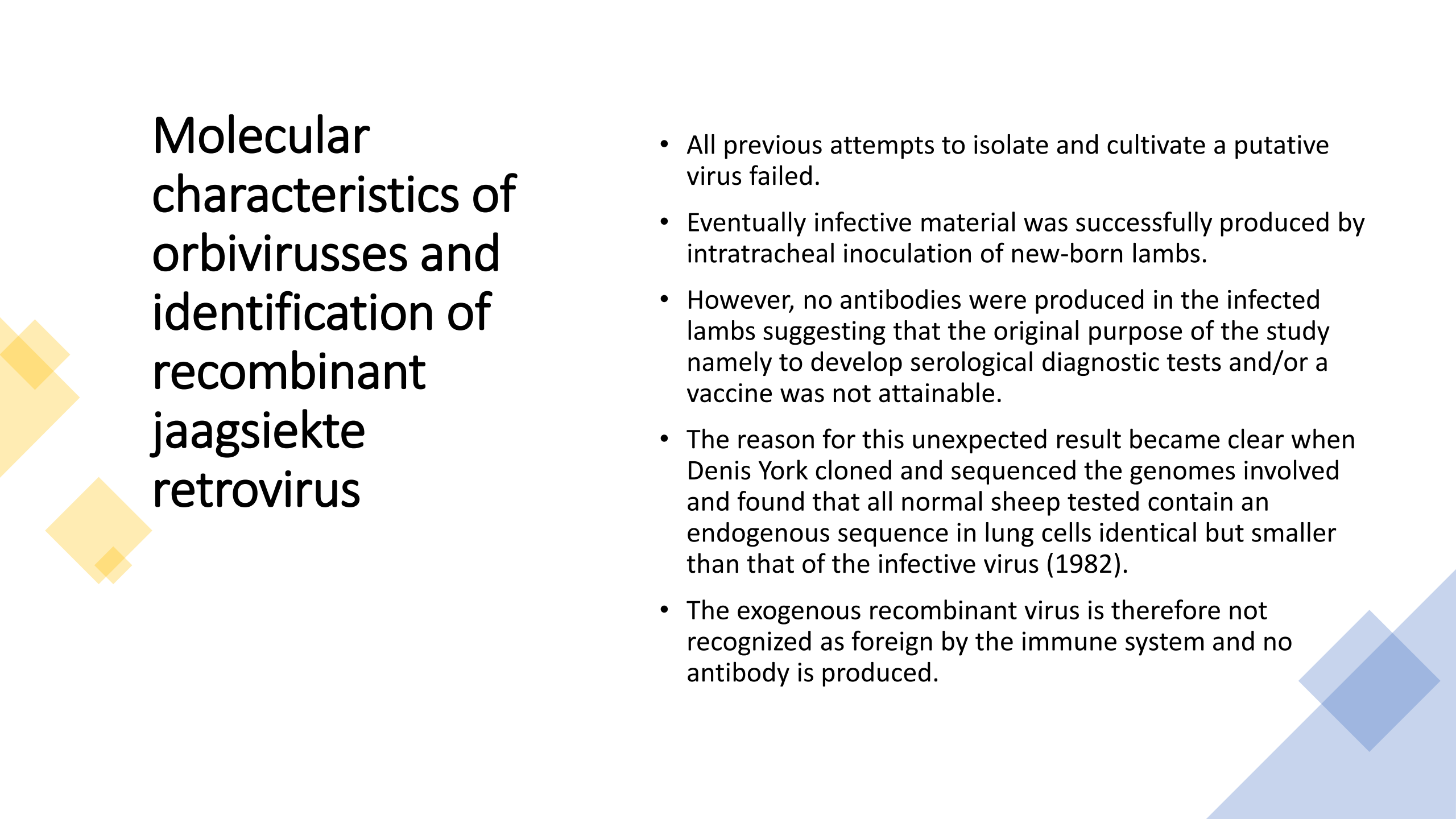


Dr D.A.Haig, virologist responsible for the development of canine distemper vaccine



Molecular characteristics of orbiviruses and identification of recombinant jaagsiekte retrovirus

- Virus research changed dramatically in 1964 with the founding of a section Molecular Biology by Verwoerd.
- It was decided to apply the newly developed biotechnology to study the structure and pathogenesis of viruses and BTV was selected as the first model to study .
- An analysis of the molecular structure of BTV yielded surprising results: a segmented double-stranded RNA genome and a double protein capsid.
- An important discovery made by Huismans in 1987 was that one of two external capsid antigens provided protection when used as a monovalent vaccine.
- Verwoerd had developed an interest in oncogenic viruses and especially in the proposed virus responsible for jaagsiekte, a lung tumour in sheep first described more than a century ago in South Africa




Molecular characteristics of orbiviruses and identification of recombinant jaagsiekte retrovirus

- All previous attempts to isolate and cultivate a putative virus failed.
- Eventually infective material was successfully produced by intratracheal inoculation of new-born lambs.
- However, no antibodies were produced in the infected lambs suggesting that the original purpose of the study namely to develop serological diagnostic tests and/or a vaccine was not attainable.
- The reason for this unexpected result became clear when Denis York cloned and sequenced the genomes involved and found that all normal sheep tested contain an endogenous sequence in lung cells identical but smaller than that of the infective virus (1982).
- The exogenous recombinant virus is therefore not recognized as foreign by the immune system and no antibody is produced.



Conclusion

- Virological research at the OVI maintained world standards during the 20th century and often took the lead in the case of tropical animal diseases such as bluetongue and African horsesickness as well as other tropical diseases.
 - In many cases vaccines and diagnostic procedures were developed and made available to countries when confronted by unknown diseases.
 - In the case of jaagsiekte, or ovine pulmonary adenomatosis, the discovery that it is caused by a recombinant virus of endogenous origin excluded such a solution.
 - A number of research groups in several countries took note of this discovery and for example used the recombinant or part of its genome sequence as vehicle to introduce potential drugs into human lung cells.
 - We may therefore still see some practical application of these results in future.
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Thank you

verwoerd.daan@gmail.com