“BCG Moreau RDJ basic and clinical research”

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BCG Moreau RDJ

- History
- Oral and Id vaccines
- Adverse effects
- Genomics and proteomics
- Clinical trials
- WHO strain & vaccine
- Future
First BCG immunization
BCG as an oral vaccine

• BCG originally was an oral vaccine
• Used worldwide as an oral vaccine till the Lubeck accident
  ● Mantoux tests were negative in the majority of immunized subjects
  ● Correlated Mantoux test and immunogenicity.
• Strain was developed in Brazil from the thirties
  ● No cervical adenitis
• Used in the National Programme until 1974
**BCG Genealogy**

*Distinct sub strains of BCG developed worldwide*

![Diagram showing the genealogy of BCG strains](image-url)
Genomics BCG Moreau RDJ
Genomics

Size: 4.340.000 pb

% G+C = 65.64
Proteomics

BCG-Moreau

BCG-Pasteur

Mpt70
Mpt83
MPT64
MPB70

3

6

3

6

Proteomics
Genomics BCG Moreau RDJ (FAP/FIOCRUZ)

New tools for:

➤ Quality control

➤ Production control

➤ Traceability

➤ Development of new vaccines
Antibiotic sensitivity of BCG Moreau RDJ

PHLS laboratory in Greenwich, UK

Amikacin SENSITIVE SENSITIVE
Capreomycin SENSITIVE SENSITIVE
Ciprofloxacin SENSITIVE SENSITIVE
Clarithromycin SENSITIVE SENSITIVE
Ethambutol SENSITIVE SENSITIVE
Isoniazid SENSITIVE SENSITIVE
PAS SENSITIVE SENSITIVE
Pyrazinamide RESISTANT RESISTANT *
Rifampicin SENSITIVE SENSITIVE
Streptomycin SENSITIVE SENSITIVE

*This resistance pattern is in keeping with the natural resistance of M.bovis to pyrazinamide.

Therefore the Moreau RDJ strain falls well below the acceptable MICs for the oral agents tested. It was determined that chemoprophylaxis could employ isoniazid +/- rifampcin. Three-drug regimes could add ofloxacin/ciprofloxacin
Clinical Trials

- Largest trial of Id BCG in the world (Barreto et al.)
- Adverse effects were minimal (Dourado et al.)
- BCG Moreau RJ is the only BCG used in babies born to HIV+ mothers
- Phase IV BCG for bladder cancer
71,347 Children 7-14 years old
BCG Moreau RJ from FAP – 100,000 viable bacilli per 0.1 ml.
11,981 (16.8%) no scar
59,360 (83.2%) one scar
25 adverse reactions – no death, permanent injuries or disseminated infections.
2 in no scar students (1 in 5,990, 95% CI 1/1485-1/34,482)
23 in one scar students (1 in 2580, 95%CI 1/1692-1/3984)

“In conclusion, the rate of adverse reactions associated with a second dose of BCG vaccination was found to be roughly twice the rate associated with a first dose but this difference was not statistically significant. As a result, we conclude that adverse reactions to a second dose of BCG are rare, and that these adverse reactions do not represent an important hindrance to the policy of vaccination”.

Brazil is the only country that BCG immunizes babies born to HIV + mothers.

There is no case of disseminated BCG disease amongst HIV-infected children immunised with BCG Moreau RJ.
WHO strain & vaccine

BCG Moreau Rio de Janeiro - Strain certified (RDJ)

Report

WHO Consultation on the characterization of BCG vaccines

WHO, Geneva, Switzerland
8-9 December 2004
WHO strain & vaccine

- Vaccine certified by WHO

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 15 to 19 October 2012

International collaborative study to evaluate and establish the 1st WHO Reference Reagent of BCG vaccine of Moreau-RJ sub-strain

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WHO Reference Reagent
The 1st WHO Reference Reagent for BCG vaccine of Moreau-RJ sub-strain
NIBSC code: 10/272
Instructions for use
(Version 2.0, Dated 22/04/2013)
Quality Control – New Methods

- PCR – Seed lots

- Bioluminescence – Production (+UFCs)
Thank you