

MGIT 2nd LINE DRUG SUSCEPTIBILITY TESTING

“A personal experience”

Dr Johan Van Wyk
MB.Ch.B, M.Med (Clin Path)
Clinical Pathologist – iBhayi Region,
Eastern Cape



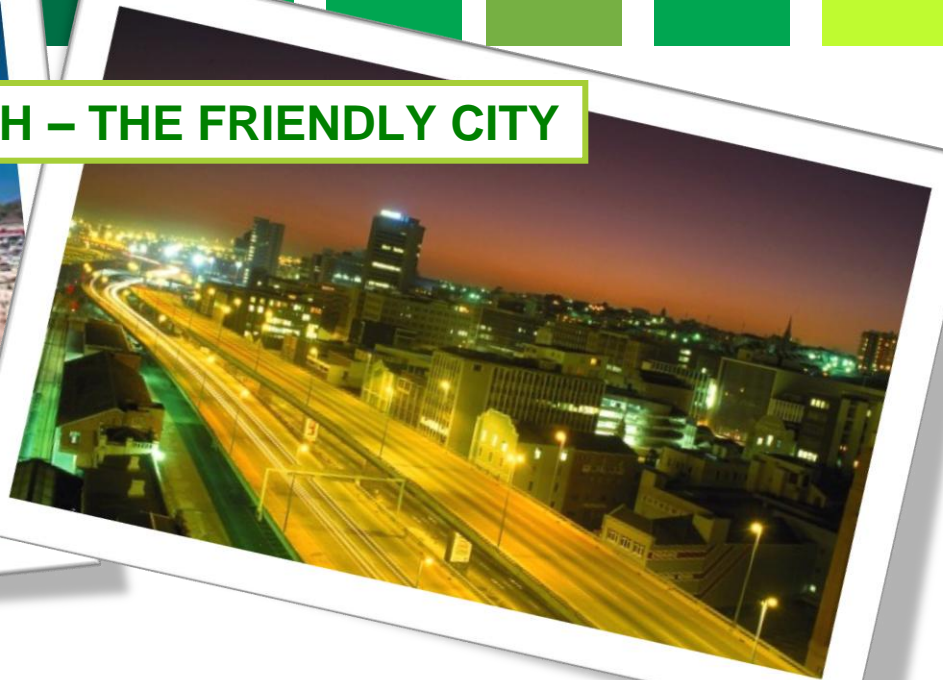


GWYNETH PALTROW "SHAKESPEARE IN LOVE – 1998"





PORT ELIZABETH – THE FRIENDLY CITY



- Staffed by 24 dedicated personnel
- TB-laboratory located at Port Elizabeth Main Branch Laboratory
- Offer 24 hour service



PORT ELIZABETH – THE ACID FAST CITY

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- Process on average 13 000 cultures each month (April 2011-March 2012: 156 059)
 - 2nd Line testing: ± 300/month
 - Instrumentation: 22 MGITs
 - Limited by space!
 - Routine cultures incubated up to 35 days



INDIAN OCEAN



How we got here...

- Up to 2003/2004: DST was done on MGIT system
 - RIF, INH, Streptomycin and Ethambutol
 - No second line testing done: incidence of drug resistance was small
- Due to cost: decision at Business Management level decided to change platform to Middlebrook 7H11 solid media DST
 - Same repertoire: RIF, INH, Streptomycin and Ethambutol
 - No processing problems reported
 - Still low incidence of drug resistance reported



2007: Gloves came off... Tugela Ferry Outbreak

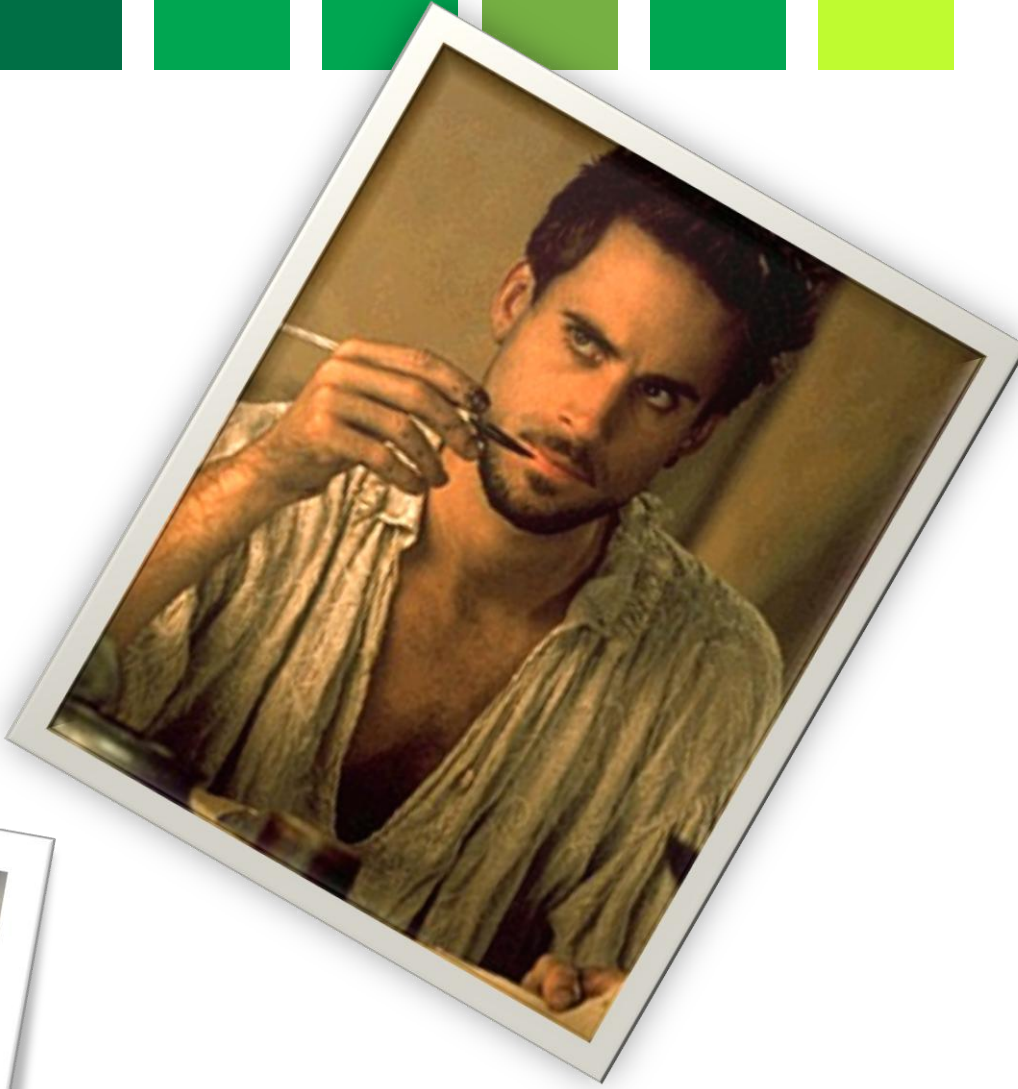




- 2007
 - Started routine 2nd line testing on Middlebrook 7H11 along with first line DST
 - 1st Line: RIF and INH
- 2009
 - First line testing changed to Line Probe LPA Hain Method
 - Second line on Middlebrook:
 - Streptomycin
 - Capreomycin
 - Amikacin
 - Ofloxacin
 - Ethambutol and Ethionamide



EVERY STORY NEEDS A HERO...



FACULTY OF HEALTH SCIENCES, STELLENBOSCH UNIVERSITY



FACULTY OF HEALTH SCIENCES
HEALTH PROMOTION AND COMMUNITY SERVICE



- 2009/2010: Stellenbosch University
 - DST/NRF Centre of Excellence for Biomedical Tuberculosis Research/MRC Centre for Molecular and Cellular Biology asked PE TB Laboratory to provide specimens for their research
- Strain difference in different provinces specifically relating to MDR-TB
- US repeated 2nd Line DST on MGIT platform
- Showed discrepancies with PE TB Laboratory
 - Capreomycin initially reported as sensitive found to be resistant
 - Results at US confirmed by gene sequencing





DST GOLD STANDARD

Second-line DST

- Automated liquid systems for second-line DST are recommended as the current gold standard
- Aminoglycosides, polypeptides and fluoroquinolones have been shown to have relatively good reliability and reproducibility, allowing a quality-assured diagnosis of XDR-TB
- Routine DST for other second-line drugs is not recommended, as the reliability and reproducibility of laboratory testing cannot be guaranteed



Why the discrepancy in our findings?

- Never investigated...
- Own media production at PE (SABS approved) – media produced in accordance with NHLS Diagnostic Media Production guidelines
- Drug concentration of Capreomycin in:
 - Middelbrook 7H11 10ug/mL
 - MGIT 2,5 ug/mL
- Drug concentration too strong in Middlebrook 7H11?



Capreomycin Critical Concentrations ug/mL

	7H10 (Agar)	7H11
CDC Recommendations Middlebrook 7H10 medium only	10 ug/mL	
	7H10 (Agar)	7H11
NCCLS (CLSI) Proportion Method Middlebrook	10 ug/mL	10 ug/mL
	7H10	BACTEC 12B (7H12)
BACTEC 460	10 ug/mL	5 ug/mL
	MGIT 960 (modified 7H9)	BACTEC 12B (7H12)
MGIT 960*	2,5 ug/mL	5 ug/mL

*Rush-Gerdes, et al. J.Clin Microbiol. 2006, 44:688

In response to these findings...

- Started the process of changing over to MGIT for 2nd Line DST
- Fully supported by BD team – who also provide onsite training in July 2012
- Successfully validated



2nd Line DST MGIT

- Financial constraints EC DoH and drive towards capitation of services
 - 2nd line: Amikacin, Capreomycin and Ofloxacin
- Other 2nd line drug testing available on request
- Reflect availability and drug use in this region
- Awaiting standardization of 2nd line DST based from National Guidelines
 - should it be standardized
 - or should it be done according to region profiles of organisms seen?





How does it compare?

- Turn-Around-Time
 - No difference between Middlebrook and MGIT - average of three weeks from sub-culturing to final report
- Labor
 - MGIT requires more manual work as it involves more steps
 - Yet managed the same volume of work with same volume of staff
- Robustness of system
 - Middlebrook: Incubator Temperature Control issues – the temperature instability effected results
 - MGIT: more stable temperature control
 - less fluctuations above control limit set points
 - More suitable for our infrastructure



- Cost

- More expensive – but 2nd line smaller portion of our total volume work – dilutes the expense
- Our BUDGET not been effected!
 - Decreased number of drugs used
 - Decreased number of specimens repeated
 - Decreased number of contamination
 - Decreased in samples with lost viability

- Work-Flow

- Not effected
- Currently at 2 day minimum ‘back-log’ once specimens are received
 - Space! – Renovations planned and approved
 - GeneXpert – watch this space (and our space)



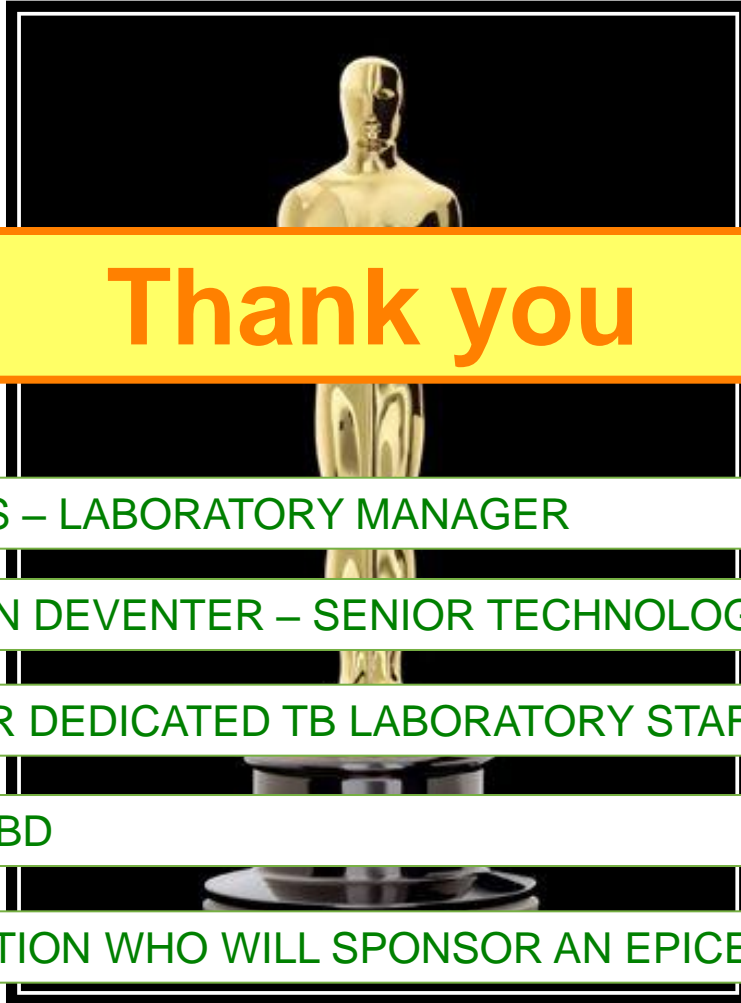
	MIDDELBROOK Initial diagnosis of MDR	MGIT Follow specimen on same pts	CASE #
AMIKACIN	SENS	RESIST	10
CAPREOMYCIN	SENS	RESIST	54
OFLOXACIN	SENS	RESIST	14





“We love it”





Thank you

CINDY HAYES – LABORATORY MANAGER

COLLEEN VAN DEVENTER – SENIOR TECHNOLOGIST

REST OF OUR DEDICATED TB LABORATORY STAFF

TEAM FROM BD

ANY INSTITUTION WHO WILL SPONSOR AN EPICENTRE® FOR OUR LAB!

