



MANAGEMENT OF MULTIDRUG RESISTANT TB: DIAGNOSIS AND TREATMENT

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MRC

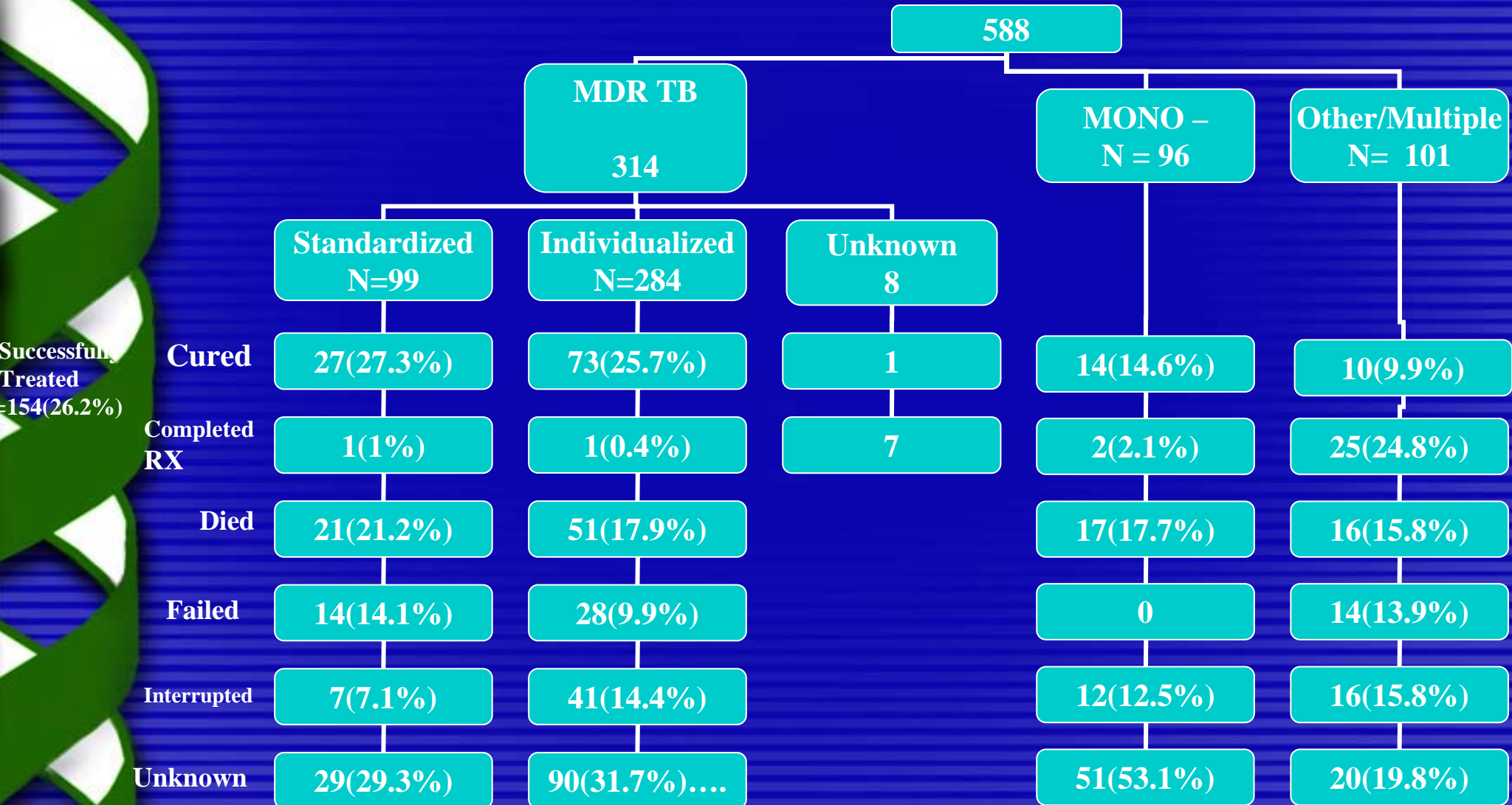
September 29th

XDR TB Symposium

PRESENTATION OVERVIEW

- Background
- Case-finding and diagnosis
- Treatment strategies and regimens
- Patient contacts
- Healthcare workers
- Management of patients with MDR TB Treatment Failure
- HIV and MDR TB treatment

Treatment outcomes for MDR TB and non-MDR drug-resistant TB by treatment given (97-2000)





MDR Patterns (referral hosp- KZN)

Year	INH & RIF + 3 other (≥ 5)	Kanamycin Ciprofloxacin	Other: (XDR)
2000	45	1	2
2001	70	3	6
2002	85	3	11
2003	119	2	13
2004	129	1	27
2005	109	17	18
2006	36	14	5
Total	593 (4.5 %)	41	82



MDR OUTCOMES

Outcome	KC	Other
ABSCONDED	10* (?died)	6
CURED	4	24
DIED	11	11
FAILED	1	21
SURVIVED	0	2
UNKNOWN	0	8
HOSPITAL	11	0
TOTAL	37	97

Case-finding Strategies : target high risk groups for susceptibility testing

- Failure of re-treatment & Chronic TB cases
- Exposure to known MDR TB case
- Failure of first line regimen
- Smear + at 2 & 3 mths of SCC
- Relapse and return after default
- Smear negative but no clinical response
- Exposure in institutions
- Other: poor drug quality and supply, co-morbidity, HIV etc.
- Chronic case = smear + at the end of re-treatment – have highest MDR rate (>80%)
- Most studies show close contacts – high rates
- Smear + at month 5 or later – not all patients but depends on adherence and Rif in continuation
- Culture and DST
- Not majority but if early relapse and poor adherence

Diagnosis

- Laboratory diagnosis in suspected cases (MCSS)
- NALC/NaOH decontamination
- Smears → direct from sputum or decontaminated sputa
- Stained → Auramine O
- Middlebrook 7H11 agar and automated MGIT culture.



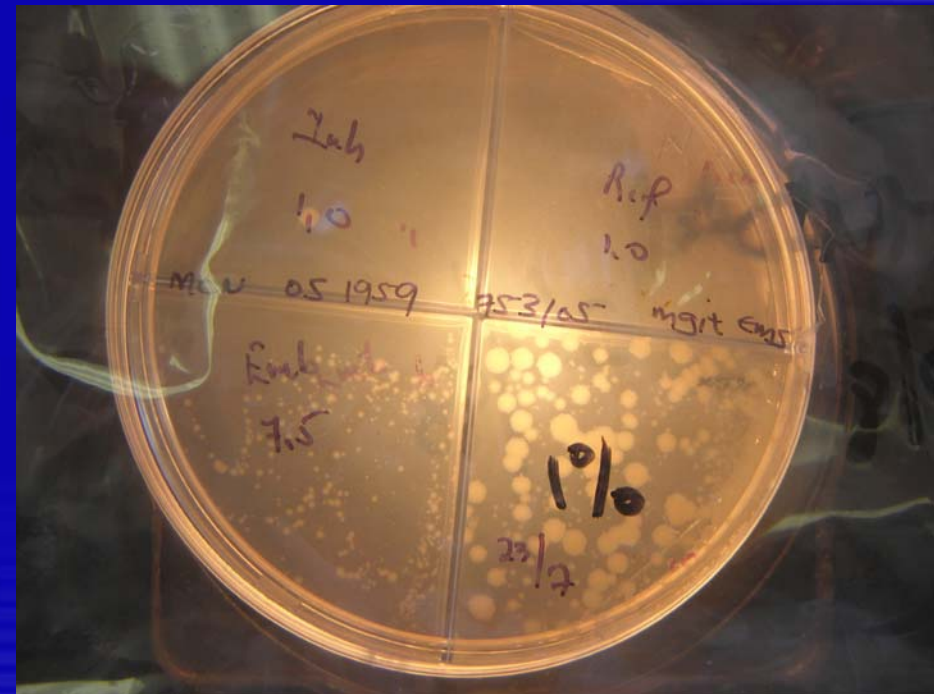
TB Culture

- Colonial morphology checked → Niacin and Nitrate tests → confirm *M. tuberculosis*. (Genprobe)
- Negative cultures → 6 weeks incubation
- Positive MGIT → ZN and blood agar, 7H10 Middlebrook agar susceptibilities
- Negative MGIT → 42 days incubation



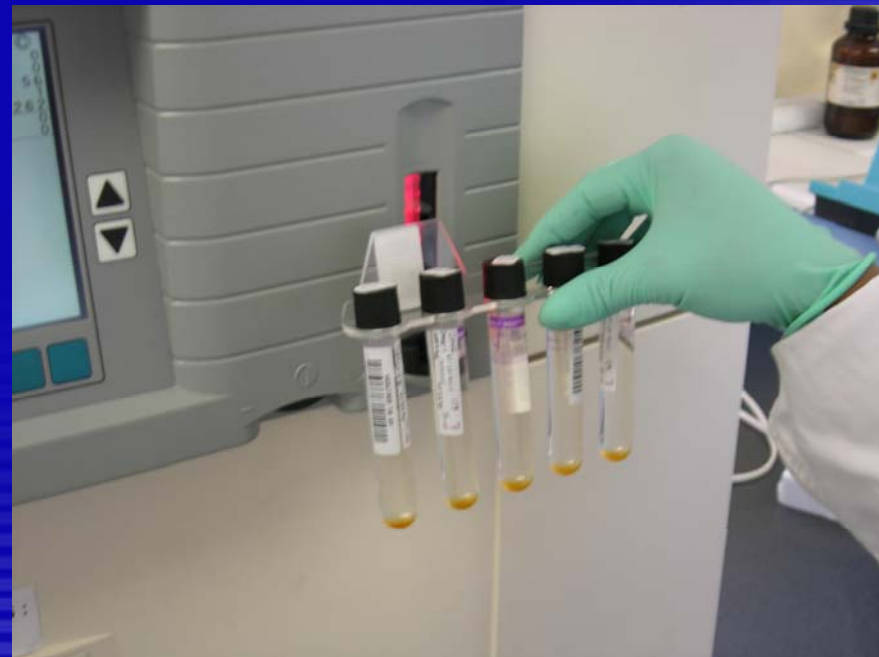
Susceptibility

- Middlebrook 7H10 susceptibilities/LJ → 1% Proportion method. (Resistance ratio and absolute concentration)
- Susceptibility turn around time from MGIT culture improved by 3 weeks
- Study specific drugs:
 - H (1ug/ml)
 - E (7,5ug/ml),
 - R (1ug/ml),
 - S (2 ug/ml),
 - and
 - Ofloxacin (1ug/ml),
 - Cirpofloxacin
 - Kanamycin (5ug/ml)
 - Thiacetazone
 - Cyclocerine



MGIT SIRE

- MGIT SIRE susceptibility tests →
 - ◆ S (1ug/ml), H (0.1ug/ml), R (1ug/ml), E (5ug/ml)
- Turn around time is 4-12 days
- Limitations – slow growing strains rejected by instrument and 1st line only
- Cost of the SIRE kit R1178 → 40 tests (R29 /SIRE)
- Tubes Cost R35x5 → R175 per test



Treatment

- Specialized facility & team with continuous supply of 2nd line drugs
- Individual holistic treatment plan
- In-patient and supervised (outpatient –exception)
- Discharge (3 neg culture) but continue Rx
- High quality recording and reporting
- Strict adherence monitoring and recourse
- Tracing and evaluating contacts
- HIV status

Treatment Guidelines

- Standardized/ Individualized but similar because of limited number of reserve drugs
- Dosing and duration: at least 5X/week; 4mnths intensive (5 drugs); 12-18 mnth continuation
- Cultures monthly, until 3 neg then 3 monthly
- Shorten treatment if at least 12 months of TX after 3 consecutively negative cultures (1mnth apart)
- Option of surgery (unilaterally confined disease)
 - ◆ Relapse or no rx response (6mnths),
 - ◆ Conversion but XDR, residual cavitations

Treatment Regimens

- **Moderately bactericidal:** Aminoglycosides (IM) (streptomycin, kanamycin^S, amikasin, capreomycin*) ; Thioamides (Ethionamide^S; Prothionamide*) ; Pyrazinamide^S
- **Low Bactericidal:** Fluoroquinolones (ofloxacin^S/ ciprofoxacin)
- **Bacteriostatic:** Ethambutol^S/ Cycloserine^S, PAS*
(*not available in SA); part of std regimen^S continuation phase

Patient Contacts

- Effectiveness of preventive therapy in exposed or infected persons is unknown
- Factors to consider: infectiousness of case, closeness and intensity of exposure
- As for drug susceptible TB (if smear negative)
 - < 5yrs – preventive TX (as for TB)
 - >5yrs and adults: routine preventive Rx not indicated
- Depends on clinical findings, x-ray, MCSS
- Avoid presumptive MDR TB Rx
- HIV + followed 3 mnthly for early symptoms

Health care workers

- Nosocomial risk – particularly HIV +
- High risk category – prolonged exposure to MDR
- Education, training, awareness of risk, HIV status
- Universal infection control
- Coughing procedures (SOP)
- Wards/Labs – ventilation , negative pressure, extractor fans, masks, UV lights
- Baseline and periodic screening – in high risk
- Recording and reporting (quarterly in high risk)
- COID – compensable

MDR treatment failure

- No improvement after 4 mnths of TX:
 - Indication for suspending TX
 - ◆ Review adherence and px history
 - ◆ Review regimen – design new regimen
 - Indication for suspending Tx
 - ◆ Persistent positive smear and culture (>8mnths Rx)
 - ◆ Progressive extensive disease, bilateral
 - ◆ XDR with no option for 2 additional drugs
 - ◆ Clinical deterioration incl severe respiratory insuffuc
- Palliative supportive and end of life care*

HIV and MDR TB

- Ensure TB and HIV mx is a co-ordinated effort
(routine HIV testing, culture for smear negatives, DST where risk of MDR, prompt HAART, strict infection control)
- Clinical Features and Diagnosis (not different)
Be aware of – smear - & extra pulm
- Concomitant HAART: AE common
avoid thiocetazone

Infection Control