The KZN “outbreak”

The Tugela Ferry event

- In Tugela Ferry HIV/TB co-infected patients, responding to ARV but **not** to ATT, were identified early 2005
- This prompted culture and susceptibility testing
- Infection with highly resistant *M.tuberculosis*

Susceptibility pattern

• Isoniazide	R
• Rifampicine	R
• Pyrazinamide	R
• Ethambutol	R
• Streptomycin	R
• Kanamycin/amikacin	R
• Ciprofloxacin/ofloxacin/gatifloxacin/moxifloxacin	R
• Ethionamide	S
• Cycloserine	S
• Capreomycin	?
• PAS	?

In Tugela Ferry

- 53 cases of XDR-TB in 1 year
  - largest cluster ever reported from one site
  - ± 20-25 % of all cases world-wide

Definitions (WHO/CDC 2006)

- MDR-TB: resistance to isoniazid and rifampicin, independent on any other resistance
- HDR-TB: MDR with resistance to 2 of the 6 classes of second-line drugs
- XDR-TB: MDR with resistance to 3 of the 6 classes of second-line drugs

Anti-TB drug classes

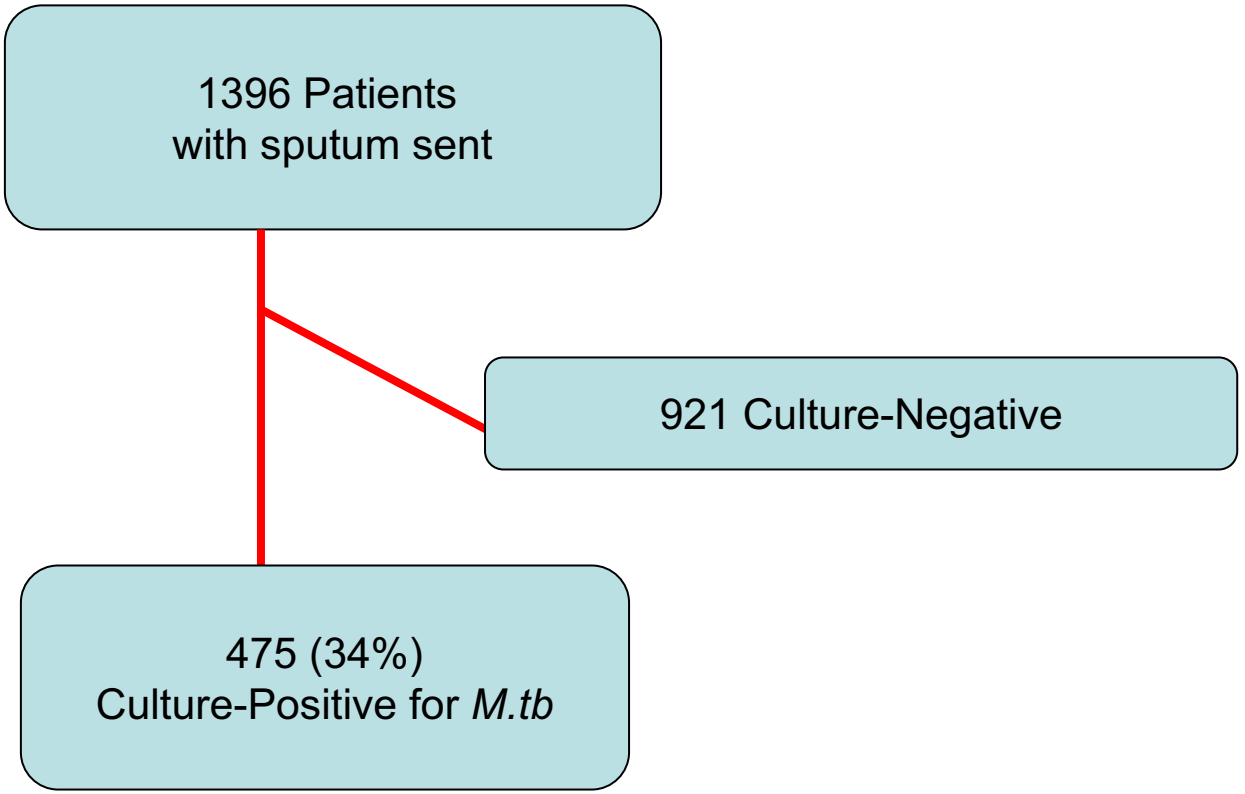
First line

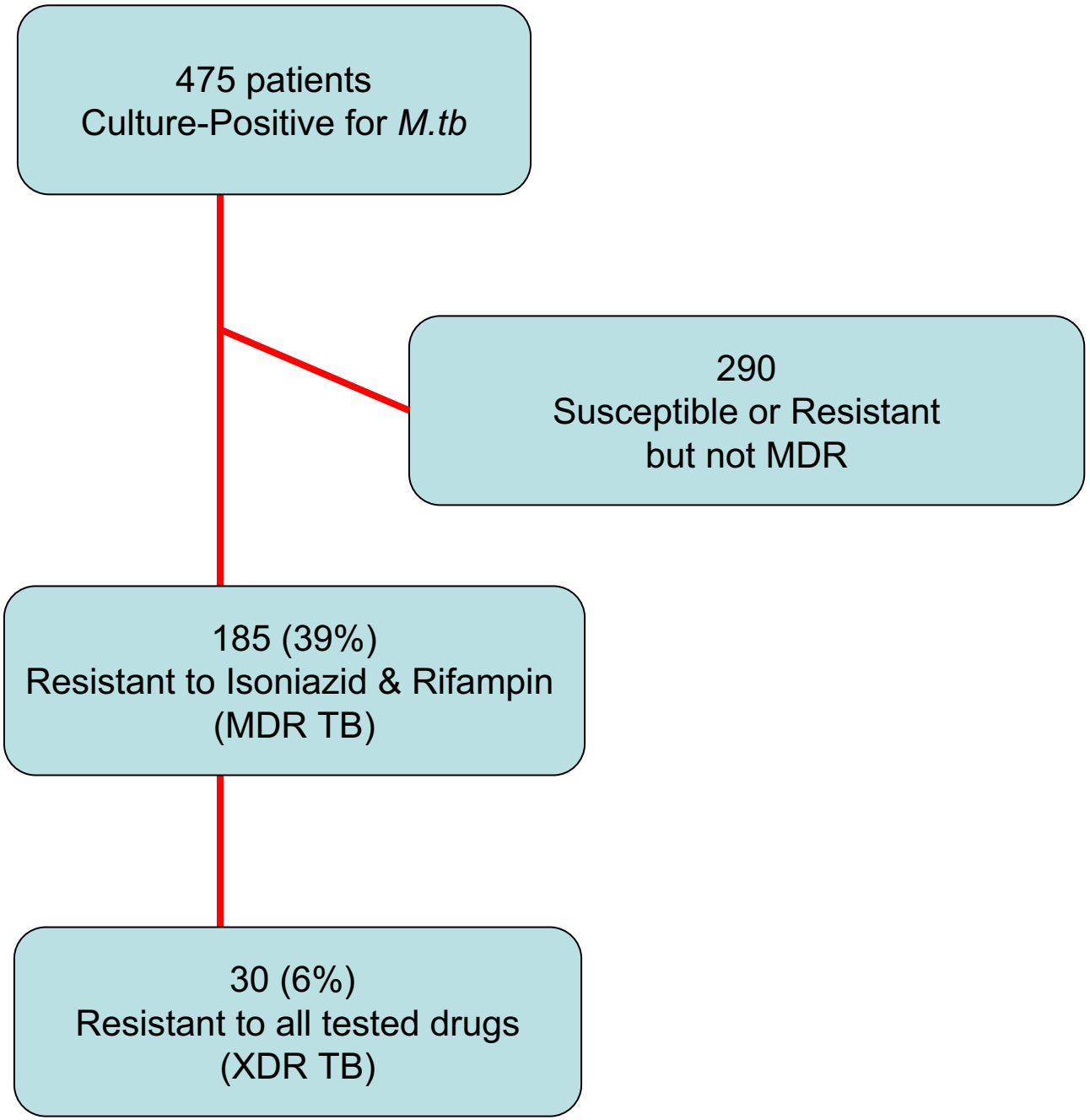
- isoniazid
- rifampicin
- pyrazinamide
- ethambutol
- streptomycin

Second line

- kanamycine/amikacin
- fluoro-quinolones
- cycloserine
- ethionamide
- capreomycin
- p-amino-salicylic acid

Results


1396 Patients
with sputum sent
921 Culture-Negative
475 (34%)
Culture-Positive for *M.tb*


475 patients
Culture-Positive for *M.tb*
290
Susceptible or Resistant
but not MDR
185 (39%)
Resistant to Isoniazid & Rifampin
(MDR TB)
30 (6%)
Resistant to all tested drugs
(XDR TB)

Prior TB Treatment or Hospitalization

Characteristic	XDR TB patients n (%)
Prior TB Treatment:	
No prior TB treatment	26 (51%)
Cure or Completed treatment	14 (28%)
Default or Treatment Failure	7 (14%)
Prior Hospitalization:	32 (64%)

HIV Characteristics

HIV Characteristics	XDR TB Patients
Previously Tested: n (%)	44 (86%)
HIV positive (if tested): n (%)	44 (100%)
Recent CD4 count: mean	72.7
median (range)	63 (9 - 283)
On Antiretroviral Therapy: n (%)	15 (34%)

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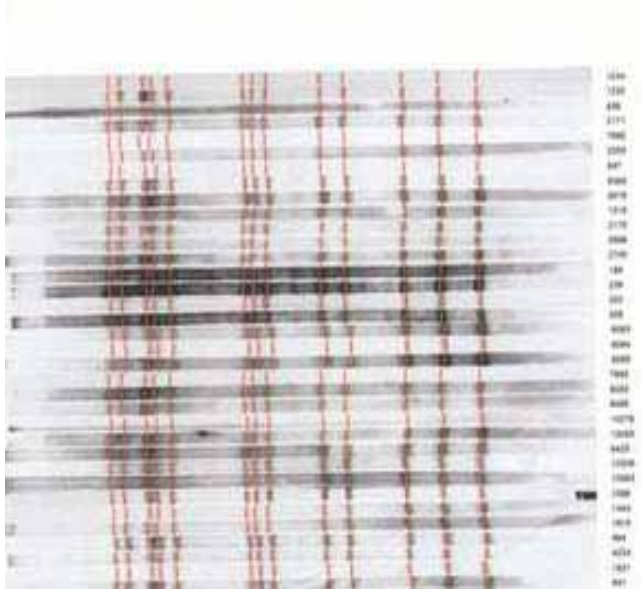
- This prompted culture and susceptibility testing
- Infection with highly resistant *M.tuberculosis*
- IS 6110 genotyping:
  - 13/16: one strain with known pattern
  - KZN strain

What is the KZN strain ?

The KZN IS 6110 fingerprint



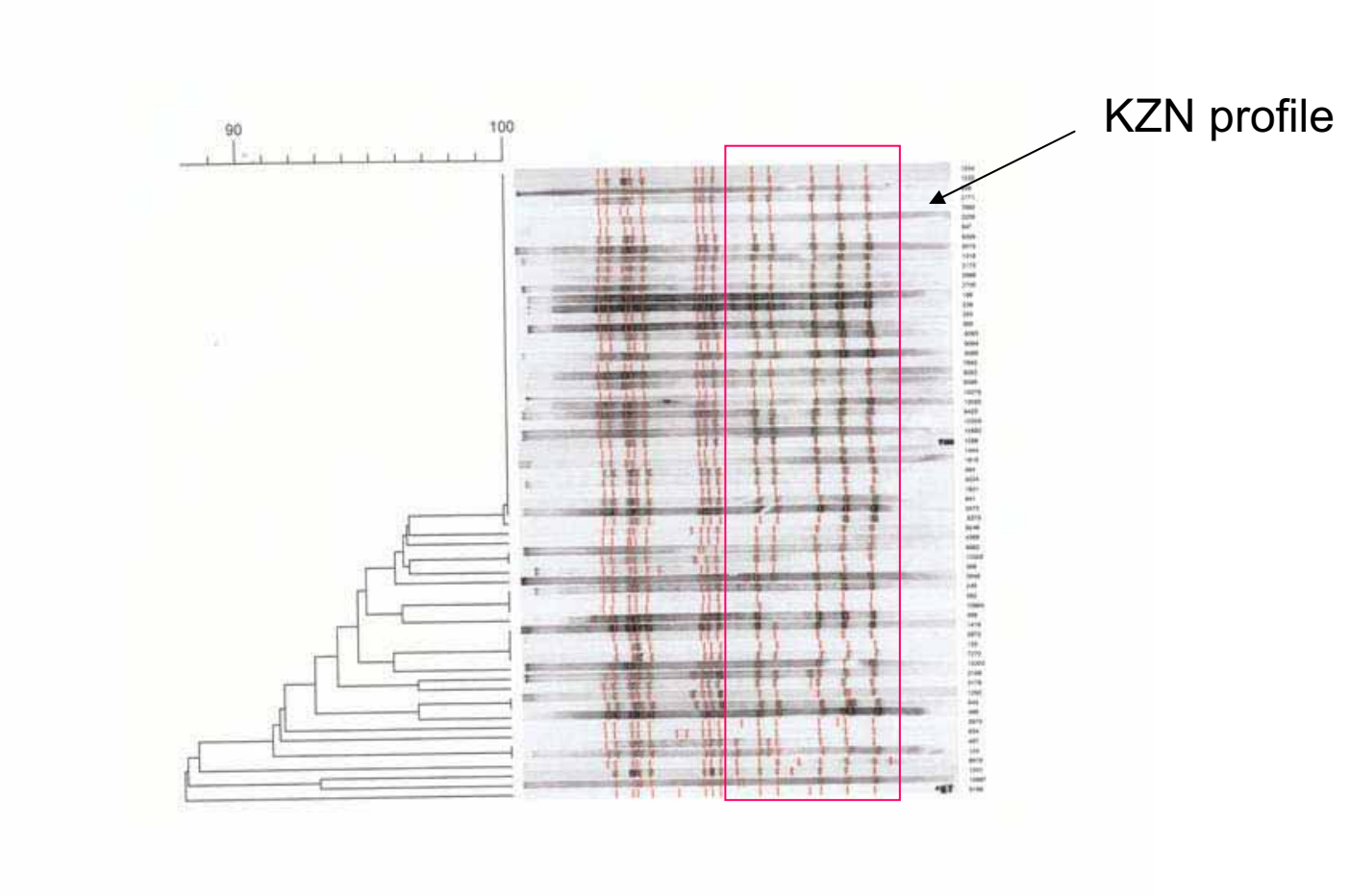
The KZN strain

- 1995
  - IS 6110 RFLP study on MDR cases referred to the provincial MDR referral hospital
    - 40 % one RFLP profile
    - MDR
      - isoniazide R
      - rifampicin R
      - streptomycin R
  - search for organisms with the same profile in a collection of non-MDR isolates:
    - present: fully susceptible
- Conclusion:
  - dominant strain amongst MDR
  - locally developed resistance

After 1995

- RFLP on collection of MDR isolates from each year till 2002
  - present in each year
    - prevalence: 30 – 50 %
  - resistant to a variable number of drugs
    - 2 – 5
    - all quinolone susceptible
    - all kanamycine susceptible
  - province-wide distribution
  - progression into a genotype family

IS 6110 typing: the KZN “family”



2006

- All TB culture and susceptibility testing concentrated in one laboratory at IALCH
  - same methodology
  - **one data-base**
- Data base search for X-DR isolates
  - present in patients from 28 of 67 provincial hospitals (incl. CoSH)
  - even geographical distribution
  - no RFLPs available (yet)

Genotyping July 2005 – June 2006

- 102 MDR (incl. XDR) isolates from Church of Scotland Hospital (CoSH), Tugela Ferry

- spoligotyping

Spoligotyping

MDR		XDR	
Total no.	no. (%) KZN strain	Total no.	no. (%) KZN strain
102	60 (59)	61	52 (85)

remaining 9 isolates:
Beijing strains
or
unique isolates

Conclusion

- HDR TB epidemic in KZN
- 2 strains involved
  - KZN
  - Beijing
- The KZN strain has evolved over a decade
  - family of strains
  - increasingly resistant

Revised definitions (proposal)

- MDR-TB: resistance to isoniazid and rifampicin, independent on any other resistance
- HDR-TB: MDR with resistance to 2 of the 6 classes of second-line drugs
- XDR-TB: MDR with resistance to kanamycin/amikacin and F-quinolones or 3 of the 6 classes of second-line drugs

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Conclusion

- **XDR** TB epidemic in KZN
- 2 strains involved
  - KZN
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Acknowledgements

- TB lab staff
- Medical staff at Church of Scotland Hospital
- Enhanced Care Initiative research group

Action plan

- Survey in 10 of the hospitals in which X-DR patients have been found
  - completed before 31-12-2006
- Continuous analysis of the laboratory data-base
- Spoligotyping immediately on all positive MGIT cultures
  - Isolation of identified cases
  - Intensive contact tracing

- Spoligotyping on a subset of non-MDR isolates
- Procurement of the missing drugs

Protection of our students

- In Medicine blocks:
  - N 95 mask when dealing with patients with chest symptoms with or without TB in the DD
  - surgical mask on all patients with chest problems during small-group bed-side teaching

surgical mask

Protection of our students

- In Medicine blocks:
  - N 95 mask when dealing with patients with chest symptoms with or without TB in the DD
  - surgical mask on all patients with chest problems during small-group bed-side teaching
- In other blocks:
  - surgical mask on coughing patients
  - surgical mask on all patients with chest problems during small-group bed-side teaching

How to protect staff ?

- As students:
  - N95 masks on the staff member when dealing with a possible or proven TB case
  - Surgical masks on coughing patients not expected to have TB while dealing with such patients

Additional measures

- Ventilation of wards
  - How ?
- Open-air waiting areas

- UV light ??????