
**IMPROVING THE SENSITIVITY AND
EFFICIENCY OF AFB MICROSCOPY
SHOULD START BY IMPROVING
THE TESTING STRATEGY**

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AFB-microscopy

- “Most appropriate diagnostic tool for TB-control in high-burden”
- But widespread dissatisfaction:
 - lesser sensitivity
 - tedious and cumbersome
- Sensitivity difficult to improve
- Streamline its use: guidelines

Spot-morning-spot

- Compromise
 - patient convenience
 - non-integrated setting
- Recent review: third sample adds about 3%
 - remarkably constant over a wide variety of settings & study designs
 - no doubt some confusion and cheating, but reality!

YIELD OF THREE SPUTUM SMEARS: % SM+

REFERENCE/ COUNTRY	TECHNIQUE	% POSITIVE ON FIRST	INCREMENT ON SECOND	THIRD
Andrews, India 1959	spot-morning-spot	79%	18%	3%
Blair, USA 1973		81%	10%	9%
Nelson, USA 1998	fluorescence, conc.	77%	15%	8%
Urbanczik 1985		80-82%	10-14%	5-8%
Ipuge, Tanzania 1996	3 morning	88%	9%	3%
Harries, Malawi 1996	spot-morning-spot	83%	13%	4%
Finch, USA 1997	fluorescence, HIV-	89%	10%	1%
	fluorescence, HIV+	79%	21%	-
Salim, Bangladesh 1998	spot-morning-spot	85%	14%	1%
Van Deun, Bdesb 2002	morning- morning - morning	95%	4%	1%

Inefficiency of the third (spot)

- At 10% pos. rate: +/- 900 tests for 3 cases
 - equals 2-3 months of work
 - possibly serious adverse effect on quality
- Never shown that less cases would be detected using a 2 sputum strategy
 - only 1 study, historical comparison: same detection
 - could even bring more positives
 - better quality of examination
 - alternative strategy: 2 morning sputa? 2 smears from 1 morning sputum?

YIELD OF DUPLICATE SMEARS FROM THE SAME SPUTUM

Study	Positive with the least sensitive technique only		Any positive
	n	%	n
Cameroon	16	5%	303
Bangladesh	68	12%	567
Peru	15	15%	100
Average		11%	

Spot or morning sputa ?

- Morning sputa clearly superior
 - Urbanczik 1985: 10 - 100% more positives
 - Bangladesh study:
 - morning: ~ 10% more positives
 - 3 morning: 94% positive on first, 1% on third
- 2 morning samples, patient returning once?
 - Bangladesh study:
 - 10% non-return (1.5% of positive cases) & refusing
 - finally more cases on treatment

Incompatible with increased detection?

- No: screening versus complete strategy
 - repeat series of two as required
 - continuing complaints / suspicion
 - 1-2 weeks intervals
- Zimbabwe study with 83% HIV+

(Munyati et al., Clin Inf Dis 2005; 40: 1818-27)

 - 90% SM+/CU+ in HIV+, 91% in HIV-
 - repeated series, concentration + fluorescence
 - yield third sputa << first two from repeat series

Two smear-positive results to declare a case ?

- Can still be done with 2-sputum strategy
 - additional sputum eventually
- But justified and useful?
 - rationale??
 - delays start of treatment: early deaths, default
 - for which gain?

Two smear-positive results: rationale

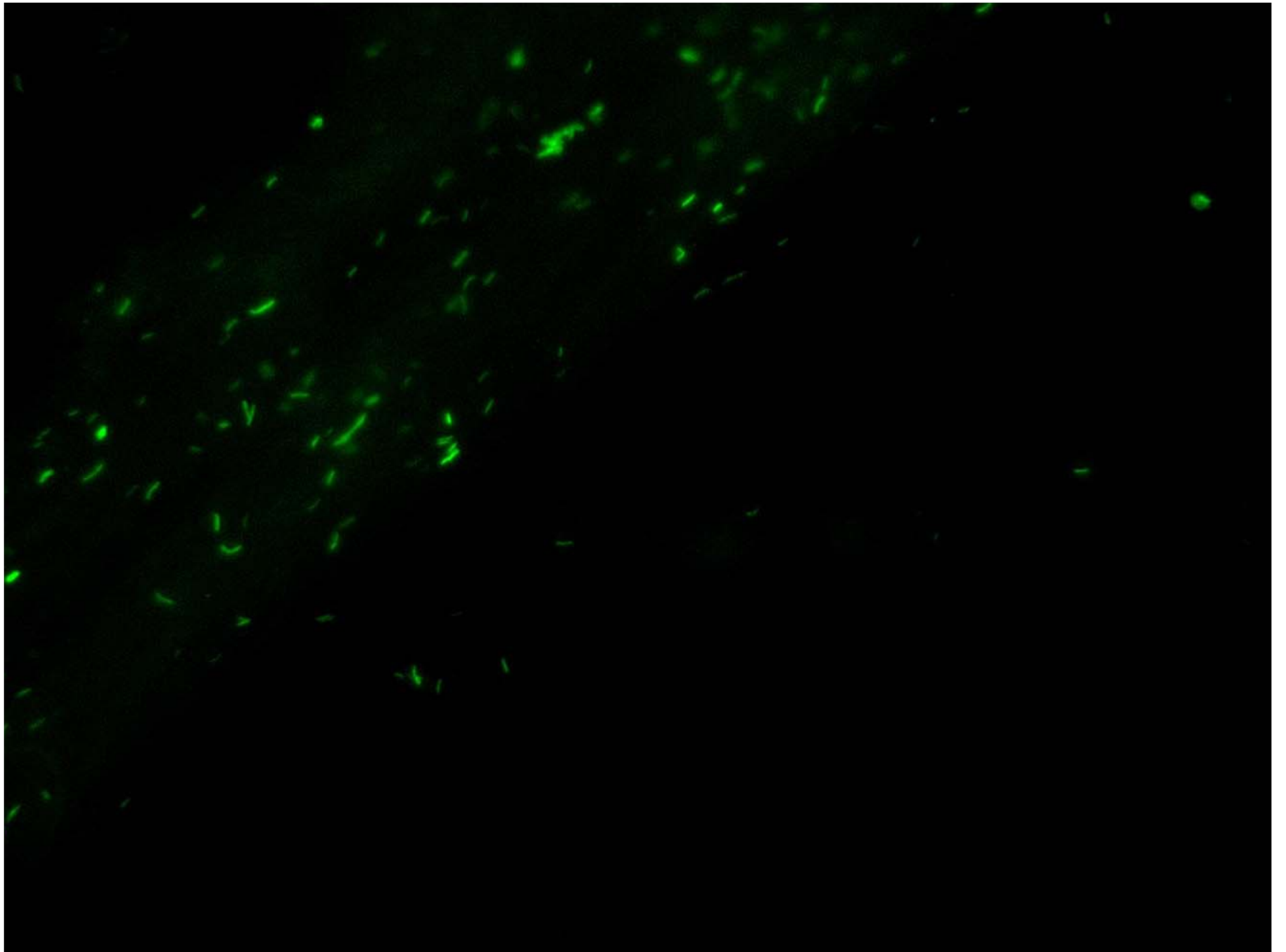
- 2 positive smears, but 1 positive culture?
 - high prevalence: specificity of smear likely to be higher than that of culture
 - while risk of misidentification stays same
- Inconsistency, i.e. X-Ray errors++
- Bangladesh study
 - PPV of single positive smear >99%
 - non-confirmed usually started on treatment anyway

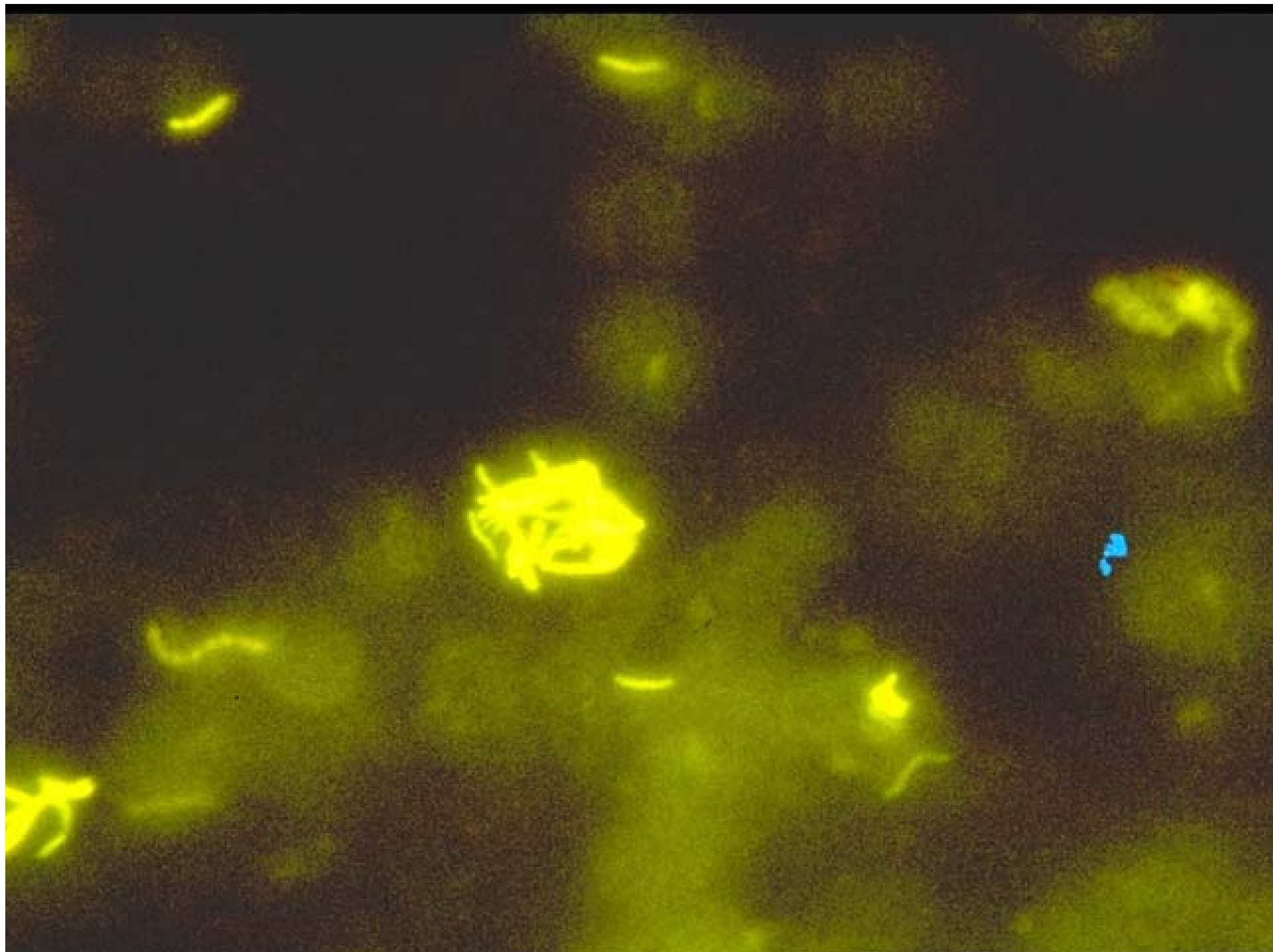
Scanty results, 1-9 AFB/100 fields

- IUATLD/WHO scale: “confirm by further smears”
 - cut-off at 10 AFB per 100 fields : why?
 - correlation with culture positives
 - early studies India, Algeria: cut-off 3-4/100
 - Kubica multi-centre: 1/100, also for fluorescence
- 3-sputa series from detection study:
 - low proportion 1/100 and 2/100 not confirmed
 - total 1-9/100 : 10% of total AFB+

Fluorescence microscopy

- Why confirm fluorescence positives in ZN?
 - advantages of fluorescence undone
 - again more work
 - poor reproducibility of scanty positives
 - using internal controls more important: prevents systematic errors
- Preferably confirm in fluorescence at higher magnification





Conclusions

- Sensitivity of AFB-smear microscopy
 - highly dependent on technical factors
 - quality and number of sputa
 - quality of smear, staining
 - decent microscope
 - number of fields read
 - but also on the human factor
 - motivation
 - fatigue

Conclusions (2)

- Our guidelines should balance:
 - number of sputa & fields versus quality
 - first-line indiscriminate screening guideline
 - further series in selected suspects
 - number/type of sputa and patient-friendliness
 - research questions: spot-morning-spot versus
 - 2 morning sputa delivered together?
 - 2 smears from one morning sputum?
 - pooling morning sputa + concentration method?
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