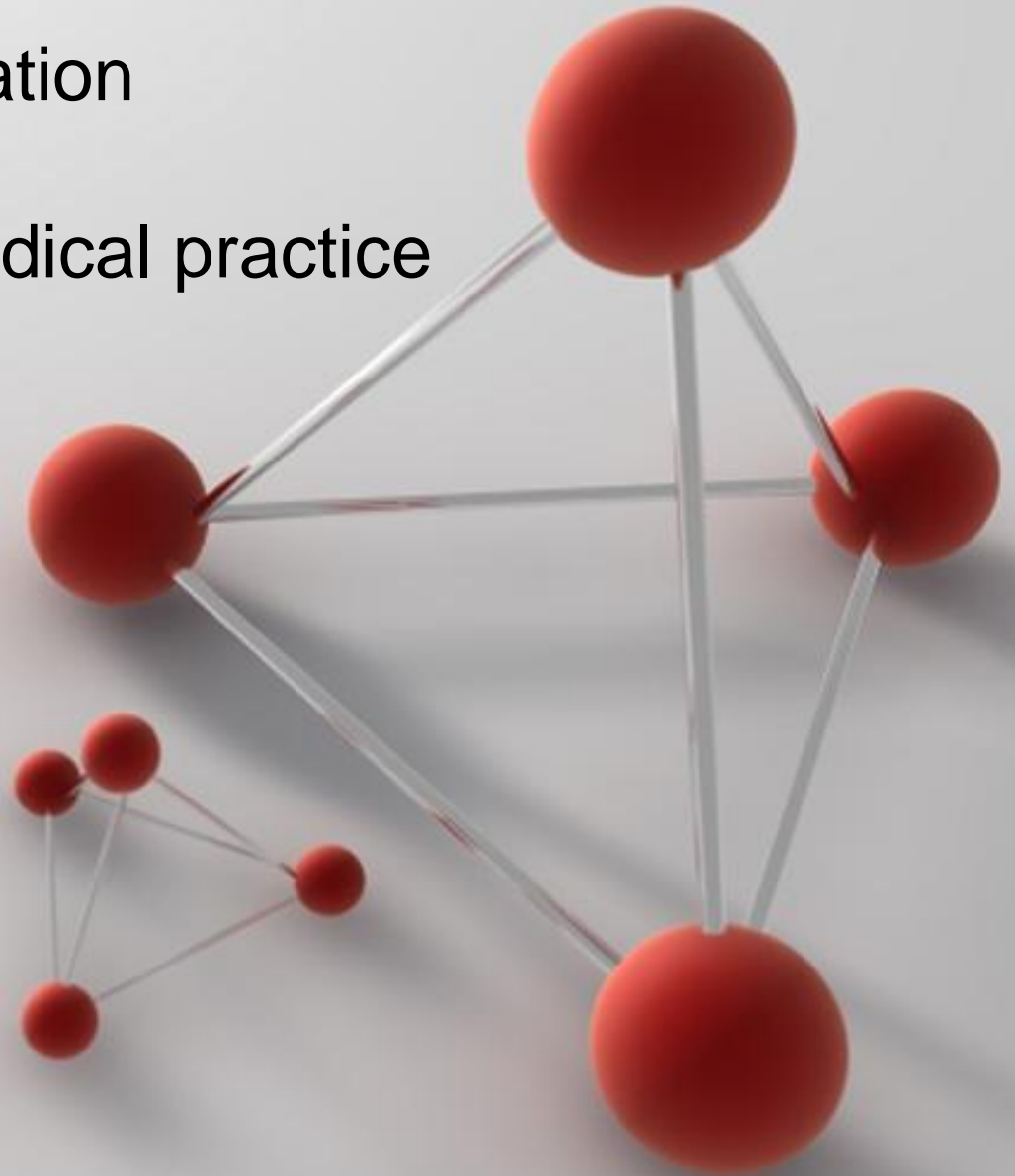


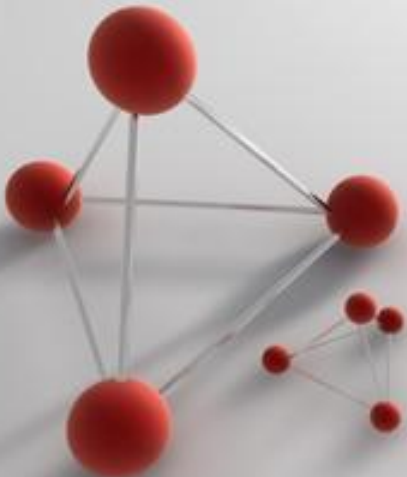
# Presentation on Gene Xpert in medical practice

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Dhaka National Medical College



# Case Scenario 1

A 35 years old female was diagnosed as a case of pulmonary TB on the basis of clinical feature, chest X-ray and positive AFB in sputum. During follow up, two months after getting anti TB category 1, her sputum was again positive for AFB.



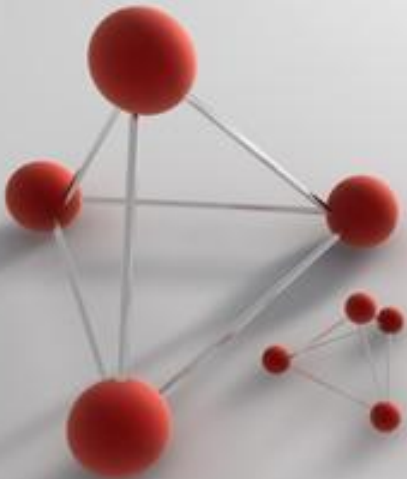
# Case Scenario 2

A 40 years old man diagnosed case of HIV on anti retro viral treatment, developed cough and hemoptysis for 7 days. His CXR shows patchy opacity suggestive of pulmonary tuberculosis and sputum is positive for AFB.

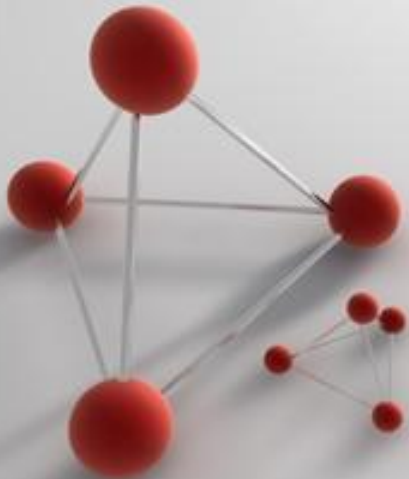


# Case Scenario 3

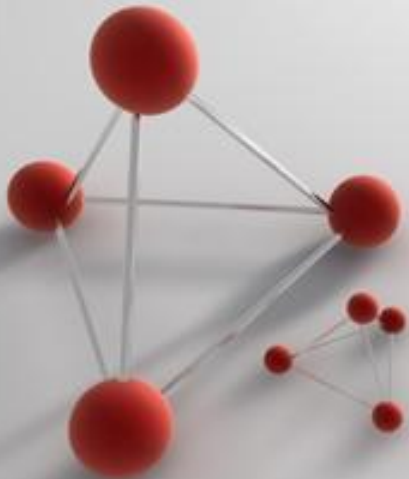
A 15 years old boy presented with low grade fever, weight loss and anorexia for two months. His CXR shows bilateral patchy opacity. Sputum AFB was negative.



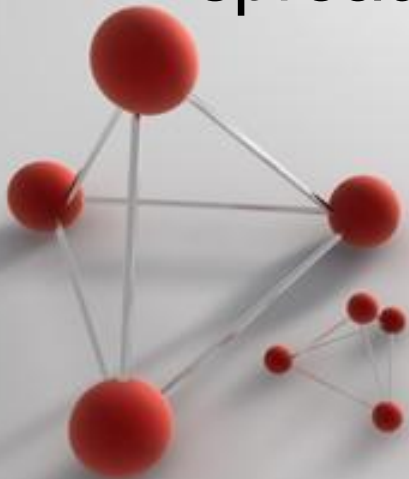
# Gene Xpert



The most widely use method to detect TB is the 125 years old **sputum smear microscopy test**, which has a number of drawbacks including low sensitivity (especially in HIV +ve individuals and children) and inability to determine drug resistance.

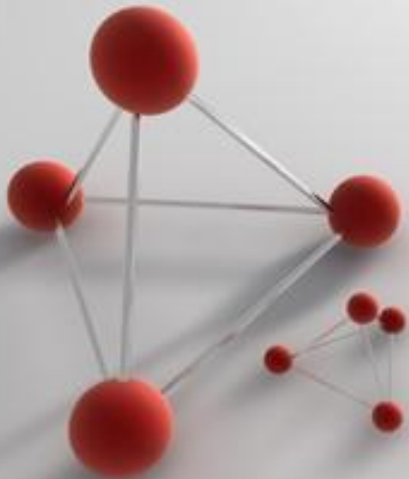


- Conventional diagnosis of drug resistant TB relies on **bacterial culture and drug susceptibility testing**, a slow and cumbersome process.
- During this time patient may be inappropriately treated. Drug resistant strains may continue to spread and resistance may become amplified.



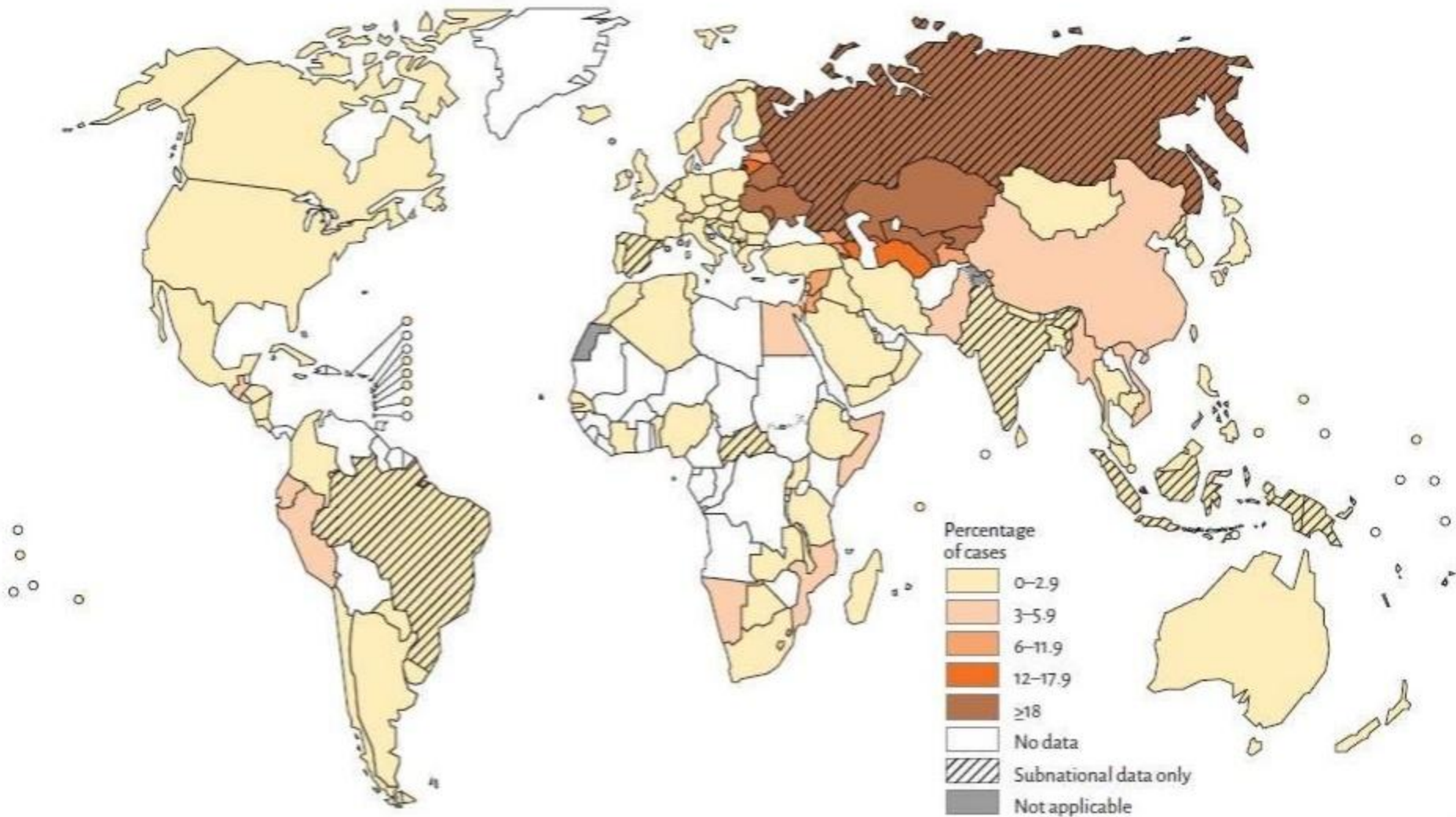
# Prevalence of MDR TB

- Drug-resistant TB poses a major threat to control of TB worldwide.
- Among notified pulmonary TB patients in 2014, an estimated 300 000 (range: 220 000–370 000) had MDR-TB.
- Globally in 2014, 123 000 patients with MDR -TB or rifampicin resistant tuberculosis (RR-TB) were notified.





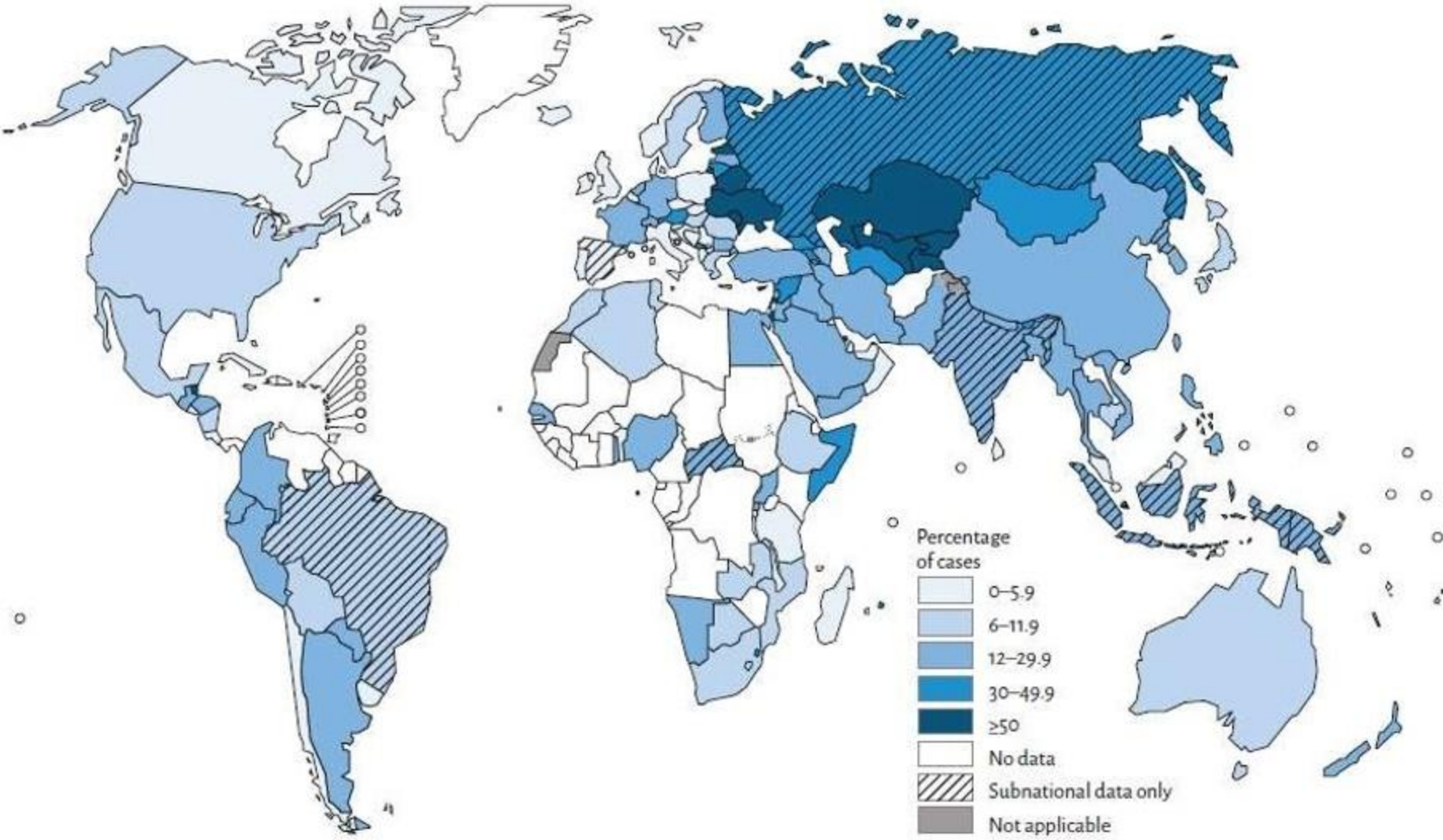
## Percentage of new TB cases with MDR-TB<sup>a</sup>



WHO Global tuberculosis report 2015

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Go to PC settin

# Percentage of previously treated TB cases with MDR-TB<sup>a</sup>

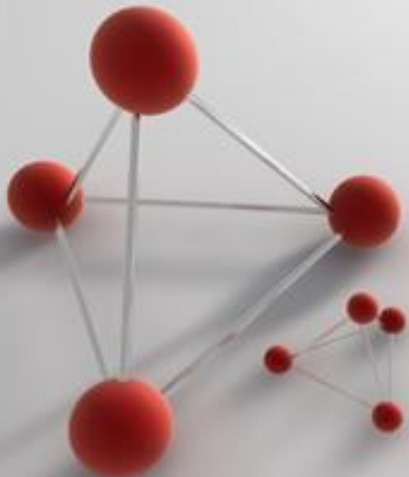


WHO Global tuberculosis report 2015

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# MDR TB

- Globally, 3.3% of new cases (95% CI: 2.2–4.4%) and 20% of previously treated cases (95%CI: 14–27%) have MDR-TB.
- In India (2014), an estimated 2.2% of new cases (95% CI: 1.9– 2.6%) and 15% of previously treated cases (95%CI: 11–19%) have MDR-TB.

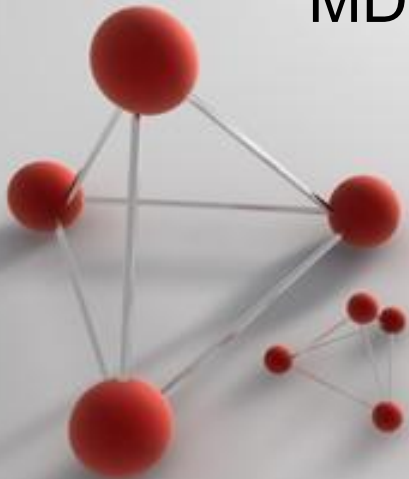


# Annual estimated number of MDR-TB cases in Bangladesh (2011-2015)

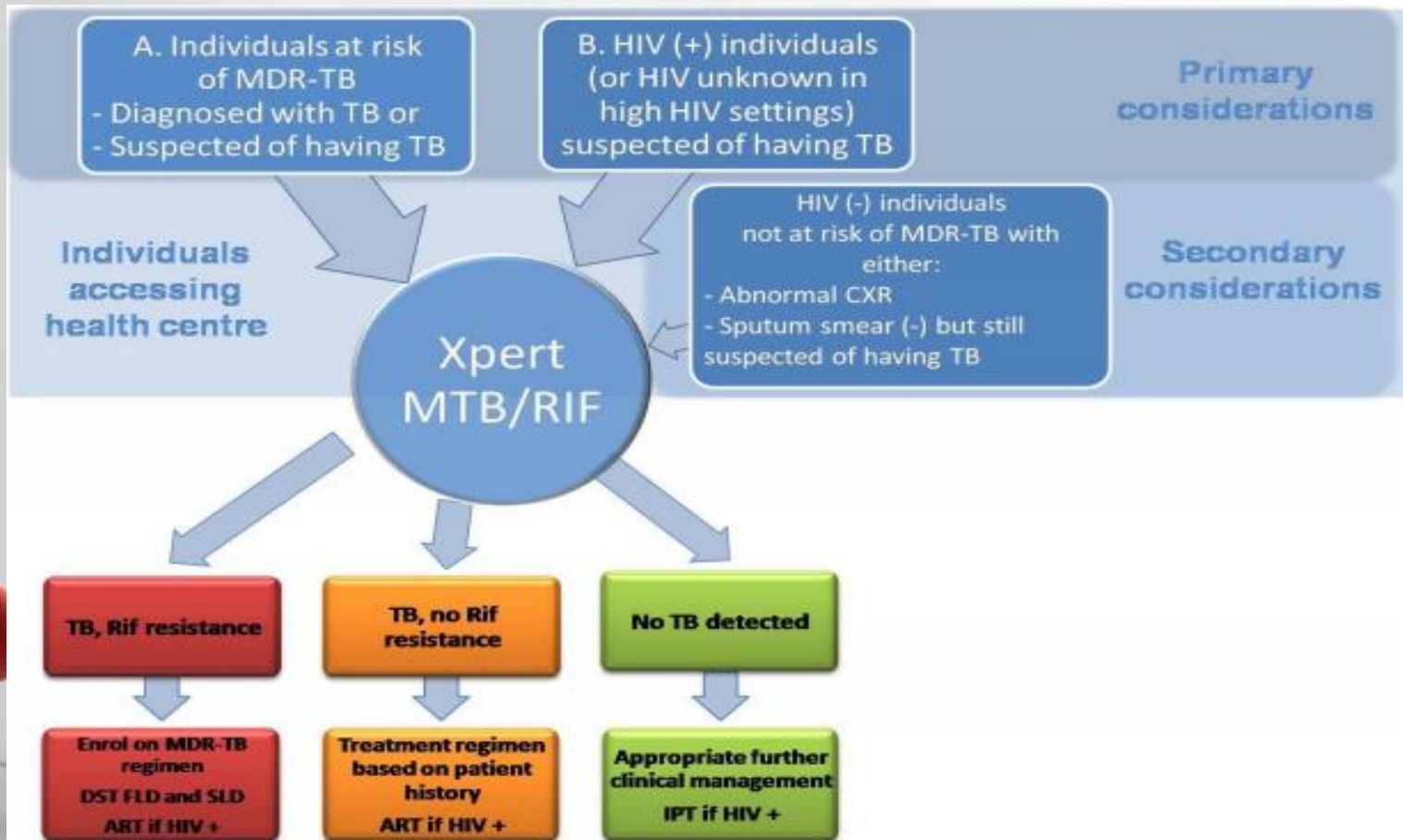
Year	Among new PTB cases	Among retreated (including Pulmonary relapse) TB cases	Total
2011	1700	2100	3800
2012	1850	2300	4150
2013	2071	2425	4496
2014	2094	2703	4797
2015	2198	2464	4662

# Importance of detecting drug resistant TB

- Earlier treatment initiation
- Improved patient outcomes
- Reducing transmission
- Reducing the emergence MDR-TB and XDR-TB

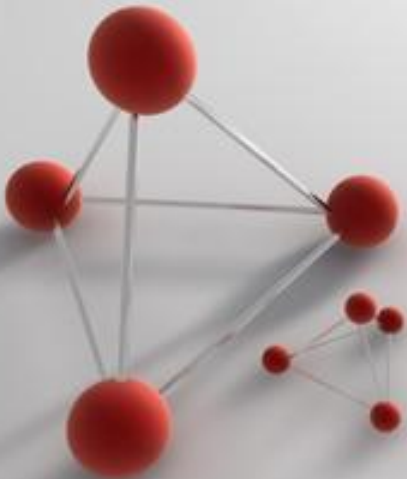


# Selection of individuals to test with Gene xpert MTB/RIF

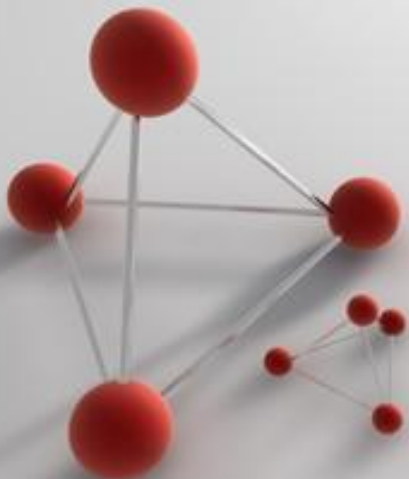


# Xpert MTB/RIF

- Automated, cartridge-based nucleic acid amplification test (NAAT) that uses the multidisease GeneXpert platform.
- Performed directly on sputum, processed sputum sediment and selected extrapulmonary specimens from adults and children.

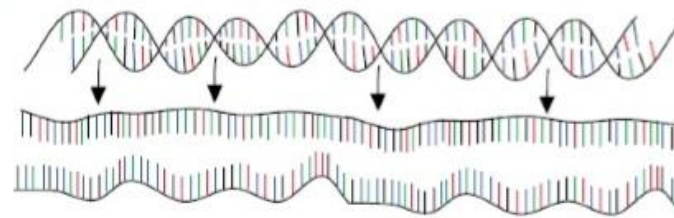


# Gene Xpert Machine



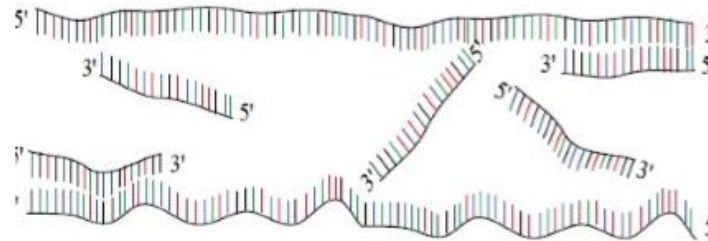


# Three steps of PCR: Denaturation, annealing and extension



Step 1 : denaturation

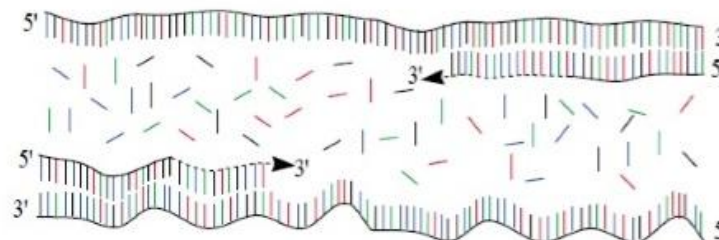
1 minut 94 °C



Step 2 : annealing

45 seconds 54 °C

forward and reverse primers !!!



Step 3 : extension

2 minutes 72 °C

only dNTP's

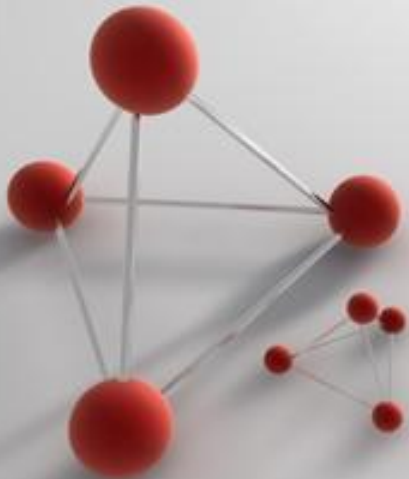
(Andy Vierstraete 1999)

fppt.com

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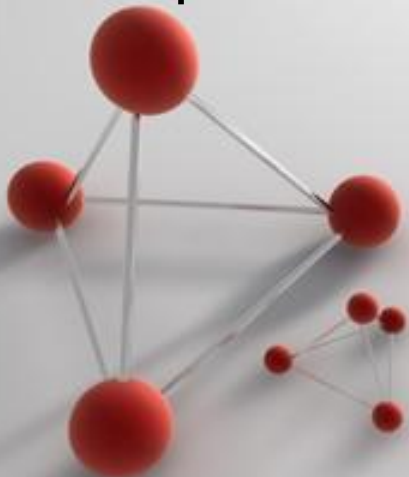
# Advantages - Xpert MTB/RIF

- Simultaneously detects *M. tuberculosis* and rifampicin resistance in less than 2 hours.
- The sensitivity for detecting TB is similar to that of to liquid culture (sensitivity 88%); the specificity is also high (99%).
- The superior performance of Xpert MTB/RIF in detecting TB over that of microscopy makes it a particularly useful tool for case-finding among people living with HIV.



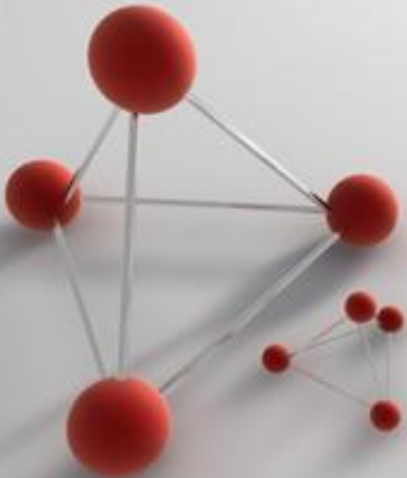
# Disadvantages - Xpert MTB/RIF

- A stable uninterruptable electrical supply is needed
- The ambient operating temperature of the instrument cannot exceed 30 °C, cartridges must be stored at less than 28 °C
- The shelf-life of the cartridges must be monitored to prevent them from expiring before they are used.



# Disadvantages - Xpert MTB/RIF

- The modules require annual calibration.
- Does not eliminate the need for conventional microscopy, culture and DST.
- In patients who are not at risk for drug resistance but tested positive for Rif resistance, a second Xpert MTB/RIF test should be performed to control for preanalytical and postanalytical errors, and to improve the clinician's confidence in the diagnosis.



# Using Xpert MTB/RIF to diagnose pulmonary TB & Rif resistance in adults

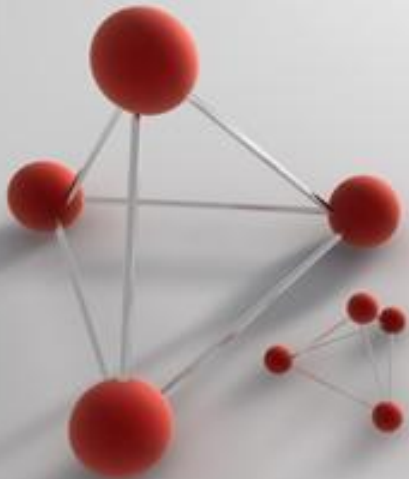
	Pooled Sensitivity	Pooled Specificity	Studies / Population
Initial diagnostic test replacing smear microscopy	(95% credible interval [CrI], 84-92%)	99% (95% CrI, 98-99%)	22 studies, 9008 participants
people living with HIV	79% (95% CrI, 70-86%)	-	7 studies, 1789 participants
for people without HIV infection	86% (95% CrI, 76-92%)	-	7 studies, 1470 participants
to detect rifampicin resistance in adults	95% (95% CrI, 90-97%)	99% (95% CrI, 97-99%)	24 studies, 2414 specimens

# Using Xpert MTB/RIF to diagnose extrapulmonary TB in adults & children

	Pooled sensitivity	Studies/Samples
Lymph node/aspirate	84.9% (95% confidence interval [CI], 72.1-92.4%)	14 studies, 849 samples
Pleural fluid	43.7% (95% CI, 24.8- 64.7%)	17 studies, 1385 specimen
CSF	79.5% (95% CI, 62.0- 90.2%)	90.2%) 16 studies, 709 specimens
Gastric fluid	83.8% (95% CI, 65.9-93.2%)	12 studies, 1258 samples
Other tissue specimens	81.2% (95% CI, 67.7-89.9%)	12 studies, 699 specimens

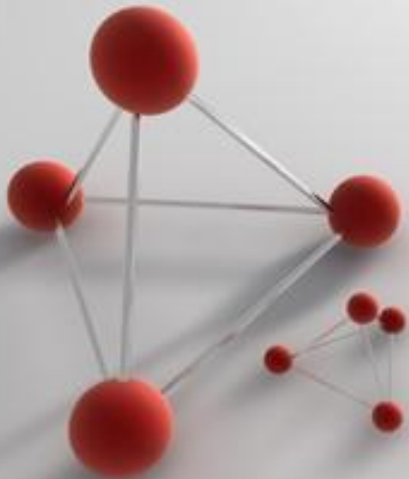
## Point to be Remembered 1

Patient whose diagnosis of TB is confirmed by Xpert MTB/RIF & who have rifampicin susceptible TB disease should be monitored during treatment with sputum smear microscopy.



## Point to be Remembered 2

Patients with TB & rifampicin resistance confirmed by X-pert MTB/RIF and placed on MDR –TB treatment should be monitored by sputum smear and culture as per current WHO guidelines.





# Take Home Message

Gene Xpert should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB. (**Strong recommendation**)

Gene Xpert may be considered as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens.

