Primary TB

First TB infection → Hilar area → Ghons focus + Lymph nodes → Ghons complex ⇒ Non-infective & ≈ 40% of Indian population infected

- **Healed TB (95%)** [Non infective]
- **Latent TB (3-5%)** — Immunocompromised / Immunodeficient / External stressor (STRESSORS) → [<1%] **Secondary TB [Reactivated TB]** [↑ V/Q ratio]
  Hilar → Apex as O2 low perfusion → Cavitation (central caseous necrosis & surrounding polymorphonuclear cells) → Infective → DOTS regimen given
  - Disseminated TB
  - Miliary TB
  - Cryptic TB
- **Primary progressive TB (1-2%)** [Children]
  - TB like feature (fever, cough, pleural effusion, bronchitis)
  - Hypersensitivity reactions (Erythema nodosum, Phlyctenular conjunctivitis)
  - Treatment needed

*] **Epidemiology** :- a) Barometer for social welfare & 1 TB case can give rise to 10-15 new TB cases/year

b) If annual TB infec" rate (annual risk of TB infection) is 1% ⇒ 50 new sputum +ve cases/year/1,00,000 population

c) TB stats
- Incidence = 204/1,00,000 population
- Incidence of MDR TB = 10/1,00,000 population
- Mortality rate = 32/1,00,000 population
- Case fatality rate = 0.16/1,00,000
- Among new TB cases
  - Known HIV status = 64%
  - Pulmonary TB = 85-87%
  - MDR TB cases = 6.19% of all TB cases
  - 2.18% Antibiotic resistant
- Previously treated pt c TB → 11.2% Antibiotic resistant

M/C resistance → Isoniazid (H)

1] **Agent factor** → M. tuberculosis [Incubation period → weeks to yrs ; Receipt of infection → +Tuberculin test :- 3 to 6 weeks]
[Transmission → Droplet (airborne) or Bovine (milk) but NOT by fomites or fingers]

2] **Host factor** → M/C age → 15-54 yrs while due to Household contacts M/C affected are children ; Males > Females ; Malnutrition predisposes to TB

3] **Environmental factors** → Poor socioeconomic status, lack of excercise.

*] **Diagnosis** → a) **Sputum Microscopy** :- i) M/C used investigation & Investigation of choice for Diagnosis & Screening under RNTCP [↑ sensitivity & specificity] (ZN stain)

ii) > 5ml ; Can be mucoid, mucopurulent or purulent & should have < 10% Squamous epithelial cells

iii) min > 10,000 living M.TB/ml of sputum to call it positive

iv) No bacilli → Sputum -ve
- 1-9/100 OIF → Scanty
- 10-99/100 OIF → +1
- 1-10/OIF → +2
- >10/OIF → +3

One +ve specimen out of the two is enough to declare a pt as smear +ve for TB

day 1	sample 1	Patient provides an "on-the-spot" sample under supervision when presenting to the health facility. Give the patient a sputum container to take home for an early morning sample the following morning.
day 2	sample 2	Patient brings an early morning sample.

b) Fluorescence microscopy (faster ; uses Auramine stain)

c) Light emitting diode fluorescence microscopy (alternative to ZN stain light microscopy)

d) Chest X-ray (↓ sensitivity & specificity) :- To diagnose Smear -ve, Children, Miliary TB, pleural/pericardial effusion, hemoptysis (to exclude B.trasis, Aspergilloma)

c) Sputum culture (LJ medium (egg), Middle brook (Agar), Choice of RNTCP → Kirchners media / middle brook (Liquid & results <48 hrs)

f) BACTEC 460 TB diagnostic method [Carbon labelled palmitic acid → checking the amount of CO_2 excreted by live bacilli [Growth Index]] + DST

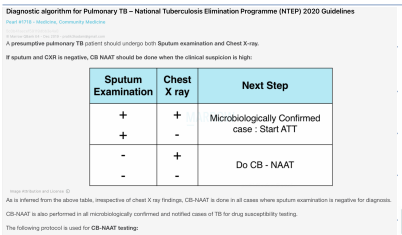
g) MGIT 960 TB diagnostic method [O_2 consumption by live bacilli] [960 coz it can incubate & monitor 960 MGIT tubes/hr for ↑ in fluorescence]

h) Identification of bacilli from clinical samples → Genotypic → a) PCR (↑ sensitivity & specificity ⇒ min. 10 bacteria should be present)

b) Cartridge based Nucleic acid amplification test (CBNAAT) (RNTCP used)

→ Machine which performs it is called Gene xpert → Rapid method & Gold standard for Diagnosis of TB & provides rifampin status of the pt & results ∈ in 90 min but expensive

→ It's cheaper version = TruNAAT


Diagnostic algorithm for Pulmonary TB – National Tuberculosis Elimination Programme (NTEP) 2020 Guidelines

A presumptive pulmonary TB patient should undergo both Sputum examination and Chest X-ray.

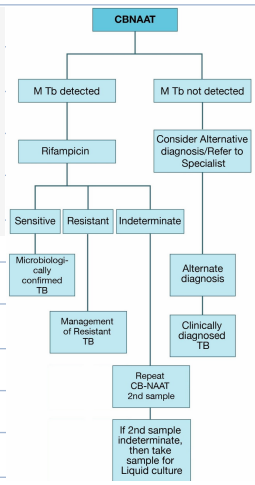
If sputum and CXR is negative, CB NAAT should be done when the clinical suspicion is high:

Sputum Examination	Chest X ray	Next Step
+	+	Microbiologically Confirmed case : Start ATT
+	-	
-	+	Do CB - NAAT
-	-	

As is inferred from the above table, irrespective of chest X ray findings, CB-NAAT is done in all cases where sputum examination is negative for diagnosis.

CB-NAAT is also performed in all microbiologically confirmed and notified cases of TB for drug susceptibility testing.

The following protocol is used for CB-NAAT testing:



→ Phenotypic → a) FAST plaque TB :- phage mediated test to detect TB

b) Serological → ↑ False positive & detects infection and not disease

→ High Negative predictive value (-ve then almost nahihe)

c) TB stat PAK → Immunochromatographic test for TB antibody

d) IGRA (Interferon gamma release assay) → WHO / FDA approved invest. of choice in low TB incidence countries while in India it is aka Quantiferon test & is Banned ⇒ coz it detects TB infection → ↑ India → prevent panic

c) Tuberculin test → Purified protein derivative (RT 23 ∈ Tween 80) 0.1ml = STU

→ Test read after 48-72 hrs

→ +ve → >15mm [No risk factor]

→ >5mm [HIV pt, prior TB, CXray +ve, Recent Organ transplant]

→ >10mm [Recent immigrants, HIV ⊖ but drug abusers, Health care workers, Chronic debilitating diseases, child <4yrs]

In people who are routinely checked they have ↑↑ ← 2-step tuberculin test ← chance of being false -ve first TST :-

→ 1st TST (check ∈ in 48-72 hrs) → +ve → ∴ TST +ve

→ -ve → Do 2nd TST

→ 2nd TST after 3 wks → +ve → ∴ TST +ve

→ -ve → ∴ TST -ve (uninfective)

RNTCP (targets, Plan or strategy, Organisation & Monitoring/evaluation indicators)

1] TARGETS :- a) 90-90-90 [90% of total cases diagnosed → Rx to 90% of diagnosed ones → 90% of Rx should achieve adequate cure]

b) WHO → End TB by 2035

Sustainable dev. goals (SDG in 2015) → to end TB by 2030 } GLOBALLY

c) Gov. of India under National health policy (2017) → End TB by 2025 for this Ministry of Health & Family welfare started End TB mission in 2017 :- to control & achieve zero TB by 2020

d) Target under RNTCP (short term targets of the prog.) → >85% cure rate & >70% case detection rate (in not achieved states) but if achieved then new target is 90% Cure rate & 90% Case detection rate

INDICATORS	MILESTONES		TARGETS	
	2020	2025	SDG 2030	End TB 2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	80% (<20/100 000)	90% (<10/100 000)
TB-affected families facing catastrophic expenditures due to TB (%)	Zero	Zero	Zero	Zero

2] STRATERGY :- Approach is to Detect → Treat → Prevent → Build

a) Detect via ↑ Case detection model (2018) → by ACD (active case detection) which involves House to House survey

i) Presumptive TB case (earlier k.a suspect) ⇒ Any person having fever >14d, cough >14d, night sweats >14d, Wt of >10% body wt in last 1 month

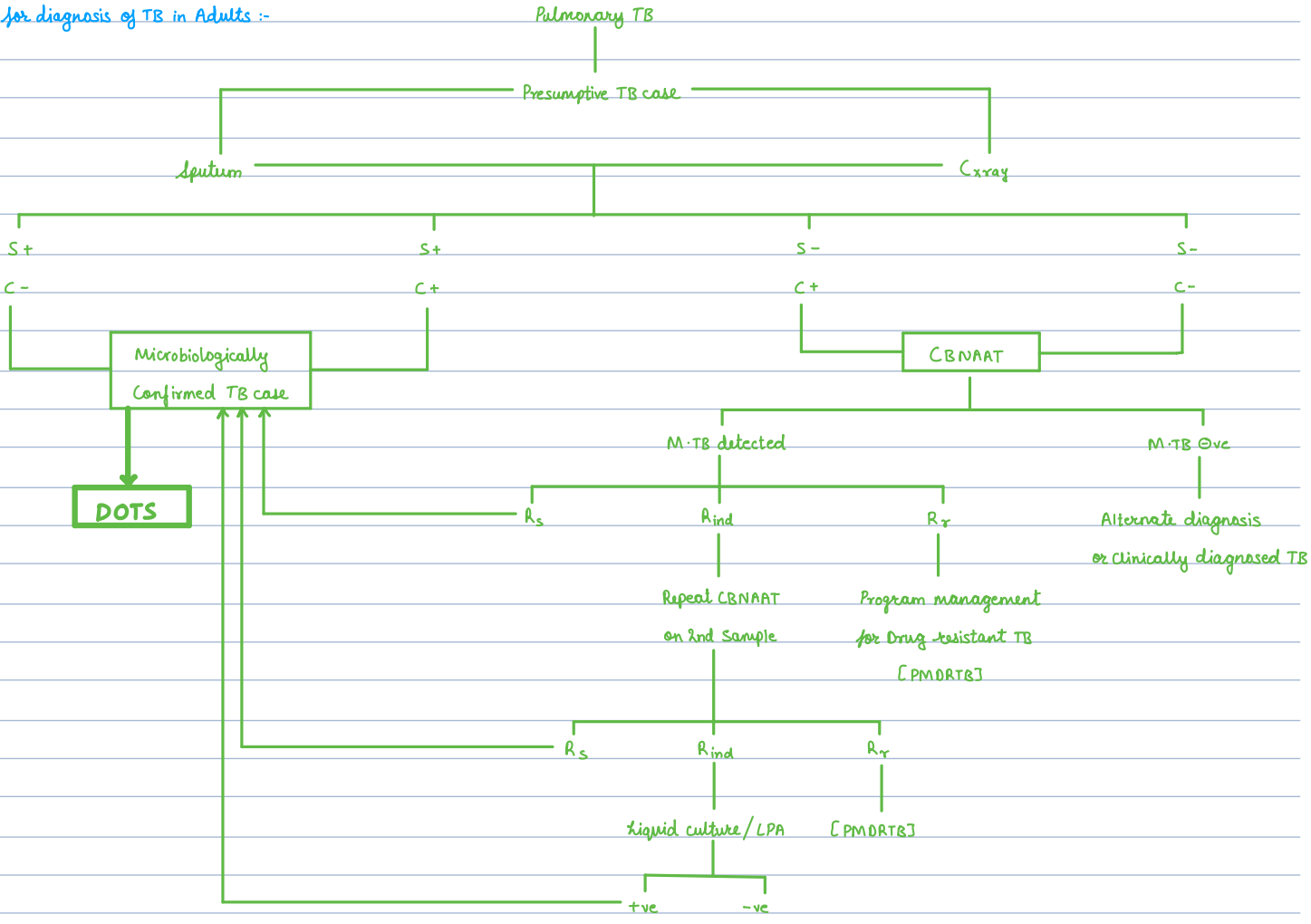
IC0 children → fever >14d, cough >14d, wt. loss >5% ∈ in last 3 months

ii) Bacteriologically confirmed TB case (earlier ka sputum +ve); Clinically Confirmed TB case (earlier k.a sputum -ve)

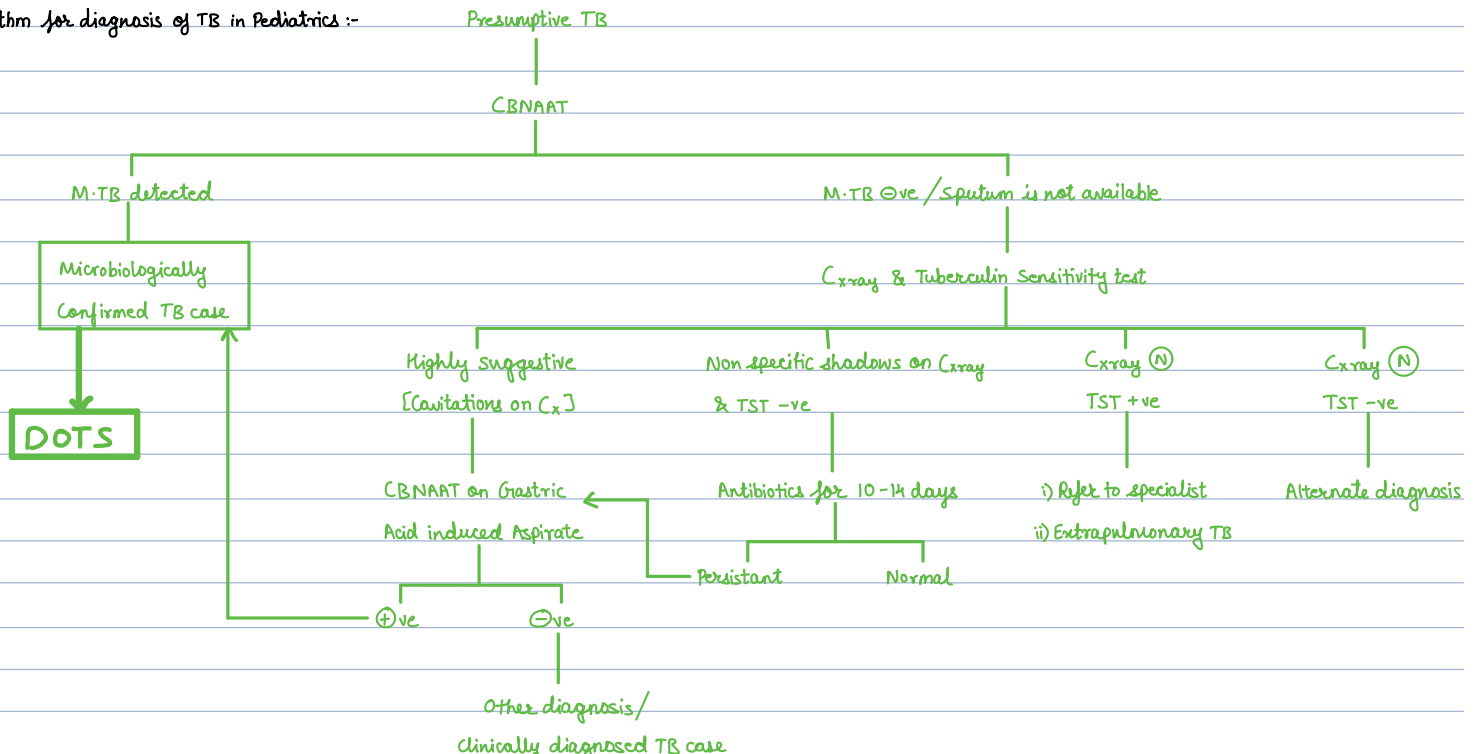
iii) New case ⇒ Any person who has never taken ATT or taken for <4 wks [Category I]

Old case ⇒ Any person who has taken ATT for >4 wks [Category II]
- → Failure
  - → Any person who is sputum +ve even at 5th month of Rx
  - → Anytime sputum +ve in previously sputum −ve case
- → Recurrent (earlier relapse) → Anytime sputum +ve after treatment completion
- → Defaulter → Any person who has taken ATT for >4 wks & has discontinued Rx for >2 months

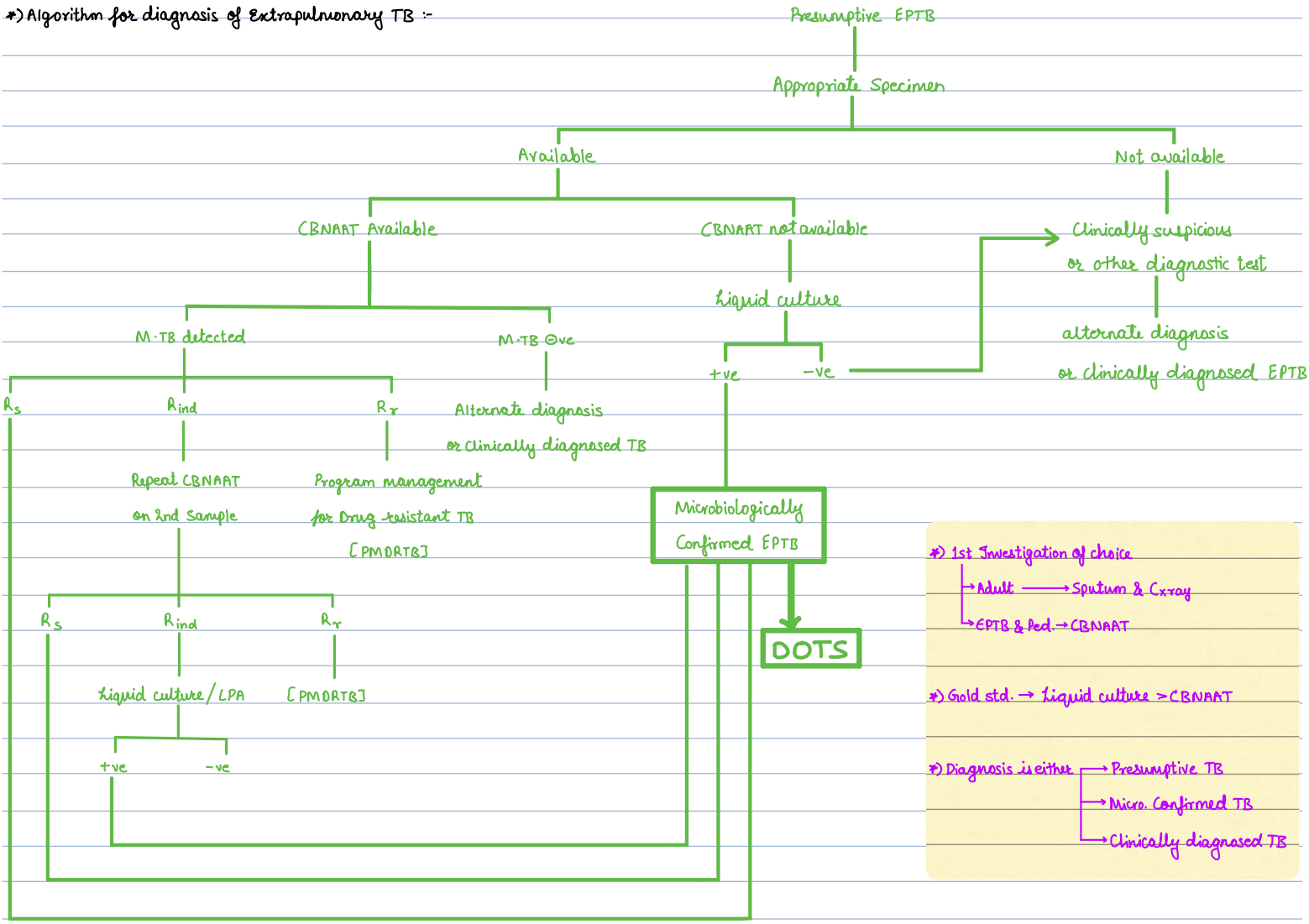
*) Algorithm for diagnosis of TB in Adults :-



*) Algorithm for diagnosis of TB in Pediatrics :-



*) Algorithm for diagnosis of Extrapulmonary TB :-



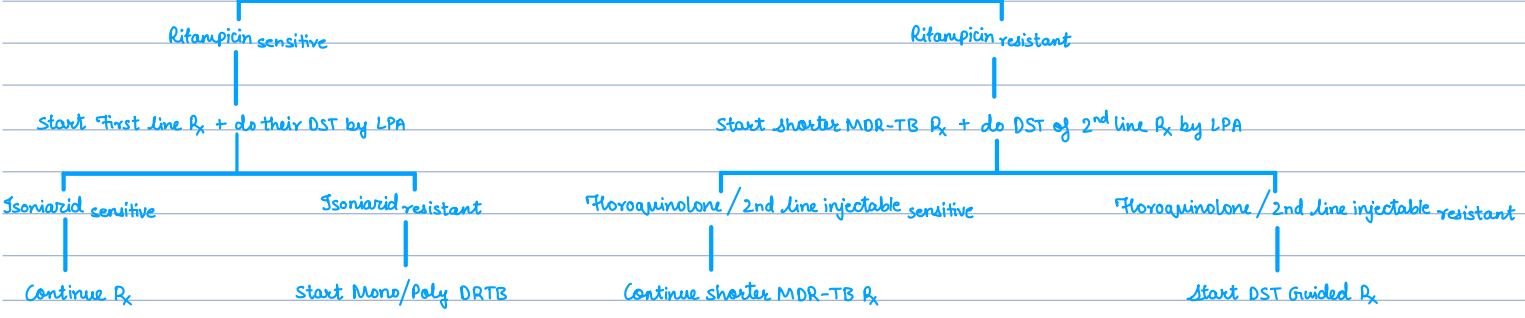
*) 1st Investigation of choice
- Adult → Sputum & Cxray
- EPTB & Ped. → CBNAAT

*) Gold std. → liquid culture > CBNAAT

*) Diagnosis is either
- Presumptive TB
- Micro. Confirmed TB
- Clinically diagnosed TB

*] Treatment guidelines :- Key population Presumptive TB cases & All TB diagnosed cases

*) Key population → Pediatric TB, HIV, EPTB, smear⊖ but Cxray⊕



*] Category I } 2HRZE + 4HRE
Category II }
Category III → ABOLISHED
Category IV → MDR Rx [DOTS plus]
Category V → XDR Rx

Daily dose regimen *(21)*

Type of TB case	Treatment regimen in IP	Treatment regimen CP
New (or Rx < 1 month)	(2) HRZE	(4) HRE
Previously treated	(2) HRZES + (1) HRZE	(5) HRE

Prefix to the drugs stands for number of months, all drugs are given under supervision.

The dose administration *(21)*

Fixed dose combination for adult TB patients (Daily dose regimen)

Weight category	Number of tablets (FDCs)/day		Inj. Streptomycin
	Intensive phase	Continuation phase	
	HRZE	HRE	
mg →	75/150/400/275	75/150/275	gm
25–39 kg	2	2	0.5
40–54 kg	3	3	0.75
55–69 kg	4	4	1
≥ 70 kg	5	5	1

FDCs – Fixed dose combinations.
* Inj. Streptomycin to be added in IP phase for 2 months in the previously treated regimen of drug sensitive patients. In patients above 50 years of age, maximum dose of streptomycin should be 0.75 gm.
Adults weighing less than 25 kg will be given loose drugs as per body weight.

Fixed dose combination for paediatric TB (Daily dose regimen)

Weight category	Number of tablets (dispersible FDCs)			Inj. Streptomycin
	Intensive phase		Continuation phase	
	HRZ	E	HRE	
	50/75/150	100	50/175/100	mg
4–7 kg	1	1	1	100
8–11 kg	2	2	2	150
12–15 kg	3	3	3	200
16–24 kg	4	4	4	300
25–29 kg	3 + 1A*	3	3 + 1A*	400
30–39 kg	2 + 2A*	2	2 + 2A*	500

* A=Adult FDC (HRZE=75/150/400/275; HRE=75/150/275)

*) Along ε 2(HRZE) & 4(HRE) we give these drugs under certain conditions :-

i) Tab Pyridoxine → Alcoholics / Malnourished / Pregnant - lactating mothers / Chronic diseases (HIV & DM)

*] R sensitive & H resistant ⇒ Mono/Poly drug sens. TB [2ERO+K :- Pyrizinamide, Ethambutol, Rif. & Levofloxacin & ~~Kanamycin~~ x 3-6m ; ~~2ERO x 6m~~] → Rx at District DRTB centres & start the Rx without waiting for result of second line - LPA

undivided IP/CP - tot duration 6-9m.

*] MDR regime → Conventional [COKZEE$_t$ + COEE$_t$:- Cycloserine + Levo + Kanamycin + Pyrizinamide + Ethambutol & Ethionamide] (Longer ?)

IP 6-8m. CP 18m

→ Shorter MDR [CHOKZEE$_t$ + COZE :- Clofazamine, High dose Isoniazide, Moxi, Kana, Pyriz, Ethionamide & Ethambutol]

IP 4-6m CP 5m

↓ ethan

*] XDR → DST guided Rx

Longer - 18-20m
Bedaquiline (24wks)
+
Levoflox
+
Linezolid
+
Clofazimine
+
Cycloserine

*] Organisation :-

CTD (Central TB division)

↓

State TB Cell

↓

District TB Centre ⇒ Administrative Unit

↓

[One/Block or 1/1 to 1·5 lac in Urban] Tuberculosis Unit [Senior TB lab Supervisor, Senior Rx Supervisor & MO] ⇒ Functional Unit

↓ ← supervising →

[DMC :- 1/1Lac in Urban & 0·5 lac in tribal, hilly etc. areas] → Designated Microscopy Centres [DMC]

→ DOTS Centre ←

A Good Politician Understands dc v.

Accounting & systematic monitoring

Good sputum smear micro

Political will & Admin commitment

Uninterrupted supply of short course chemo Rx drugs

Directly obs. Rx