Genital TB
&
Our Experience

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Director :- LifeCare center

LifeCare A unit of Lifecare centre IVF

Chairman PCH OBST/ Gynae Dpt.

Genital TB in Infertility History

Ancient Indian Text – 3000 BC by Charak

Morgagni 1744 - autopsy , 20 years with Genital TB
Ut + Tubes – filled with caseous material

Robert Koch 1882 - **Discovered M. Tuberculosis**

Sutherland 1949, Schaefer 1970

1/3 of words population is affected by TB

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India

TB

No. 1 cause of death of women in India - Till 2012

2013 - it is 3rd cause

Active 10% V/s latent 90%

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Latent Genital TB is Big Diagnostic Dilemma

Biggest Cause - Infertility, Rec. Miscarriage , AUB, PMB,

Pain in abdomen

Grossly Under Reported

- Due to lack of good tests in virtually symptomless patients - Latent GTB - Remains undiagnosed
- No Case Definition

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Genital Tuberculosis

INCIDENCE

- 2-10% infertility (western Data)
- 9-50% infertility (Indian Data)

ETIOLOGY

- Secondary to primary focus elsewhere (most common- lung)

MODE OF INFECTION

- Hematogenous spread – most common
- From adjacent structures – few cases
- Ascending structure – rare
- Age : 16-53 years (Max: 25-35 years)

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Genital Tuberculosis

Pathology

Tube – Involved in 90% cases

Endosalpingitis

Patency may be present

Secondary infection with pyogenic organism

Exosalpingitis interstitial salpingitis

Uterus : Involves in 60-70% cases

Ovaries : Involves in 30% cases

Vulva / Vagina – ulcerative or hypertrophic growth

Cervix – very rare

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GTB-Effects on genital organs

- **Tubes** (95-100%)
  - Peri-tubal adhesions
  - Tubal blocks (PTO, mid-segment, distal)
  - hydrosalpinges
- **Endometrium** (50-75%)
  - IU adhesions, tubular cavity
  - ↓Sub-endometrial blood flow
  - Implantation failures
- **Ovary** (20-30%)
  - Reduced ovarian reserves
  - **Peritoneum**
  - Adhesions
- **Immunological**

*(**Malhotra N** et al , 2012,IJGO)*

Genital Tuberculosis
Clinical Picture

- Asymptomatic 10%
- Infertility 35 – 60%
- Menstrual Disorder 40-50%
  Initial menorrhagia
  Later oligo / amenorhoea
- Pain in lower abdomen -40%
- Lower grade fever, malaise, weight loss
  mass, encysted ascites, doughy feel)
- Pelvic mass – usually non – tender , unless superadded
  infection
- Post coital bleeding / irregular bleeding PV – local lesion

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Diagnostic Challenges

- "GOLD STANDARD"-Conventional methods
  - Histopathology (epitheloid granuloma)
  - Microbiology (AFB, positive culture)
- Conventional detect only 15-20%
- Difficult, Dilemma when conventional negative
- **Case definition for FGTB in absence of conventional?**

Combination - bacteriology, histopathology, molecular methods and laparoscopy/Hysteroscopy

Challenges in managing GTB

Diagnostic Dilemma

- When conventional tests are negative?
- How to diagnose Latent TB
- Is there a role of endoscopy?

Treatment Dilemma

– **When only TB PCR / MTBC + ?**

Tests after ATT

- AFB culture ?

- HSG/ hysteroscopy

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Our Current Practice of Investigations for Genital Tuberculosis

- USG – TVS
- TLC, DLC
- ESR & Mantoux test
- Interferone gamma tes
- Pre- menstrual EB – Granulomas/ tuberculoma

  MTBS/PCR
- HSG - rigid, lead – pipe appearance , bleeding of tobacco pouch appearance – pyosalpinx
- Hysteroscopy Laparoscopy in selective cases

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SEROLOGY ? IgG,IgM

NOT To BE USED

Policy statement, WHO 2011

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Did not Pick up TB

Mx Test

- ESR
- Rapid Culture for AFB
- HPE – for Koch's
- X-ray chest

Did not pick up TB

In our Experience

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We know that **Conventional methods diagnose only 15-23% cases**

PAUCI-BACILLARY INFECTION

- **AFB staining**-1-3%
  - At-least 10,000 bacilli/ml
- **LJ culture** 3-5%
  - At-least 100 bacilli/ml
- **HPE**-Granuloma-3-20%
  - Granuloma take up to 3 wks to develop
  - Periodic shedding of endometrium

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Interferon –γ release assay(IGRA)

- Immune based test indicate cellular response to recent or remote sensitization to M.tuberculosis
- Quantiferon Gold, Quantiferon Gold – in tube and T-spot test
- Alternative to TST/Mantoux
- Results unaffected y BCG vaccination status
- High specificity(96%) even in BCG vaccinated individuals
- Detection of latent TB

Widely Used Now

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Rapid culture methods

- Radiometric culture **BACTEC 460** :
  - Based on generation of radioactive CO_2 from palmitic acid
  - Problem with disposal of radioactive compounds
- MGIT(mycobacteria growth indicator tube system)
  - Uses a fluorochrome marker

- **Advantage**
  - higher sensitivity -80–90% (30-35% with LJ)
  - Higher detection rate-7-10% (3-5% with LJ)
  - quicker results -5–10 days (6weeks with LJ)
  - Useful for drug susceptibility testing
- **Disadvantage**-Cost

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Now we have accepted Molecular methods-PCR

- **PCR-DNA**
  - Detection rates 22-44%

    (Jindal UN, 2006, Rana T, 2011,Thangappah 2012)
  - False positive-10-12% *(Thangappah et al, 2012)*
  - Positive even after full course ATT

- **RT-PCR (m-RNA)**
  - Detection rates 2-8% *(Rana T, 2011)*
  - Available in few labs
  - Technically challenging

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MTBC

HISTOCHEMISTRY BASED TEST

- Patented By Dr. Ghosh
- Potent *monoclonal TB* is tagged to MTB complex
- Sensitively specificity for MTBC is very high

Used at LifeCare center

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we have recently Associated that **Cell mediated immune** markers i.e

- **TNF*a***
- ***Interferon Gamma are raised in* patient of**

Genital Koch's

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Laparoscopy-Why?

- Tubal and peritoneal status
- Peritoneal spillage avoided in latent/early disease
- When PCR alone positive- Multiple samples-PW from POD/biopsies
- PCR positivity in PF-bacillary spill in peritoneum early in disease even before fibrosis sets

<u>Diagnostic Accuracy</u>

– Lap diagnosis in 33-60%

(Sharma JB et al, 2008, Jindal U 2006)

– Lap findings in 59% vs 7.4% by HSG to diagnose FGTB

Kulshrestha. V et al. IJGO, 2011

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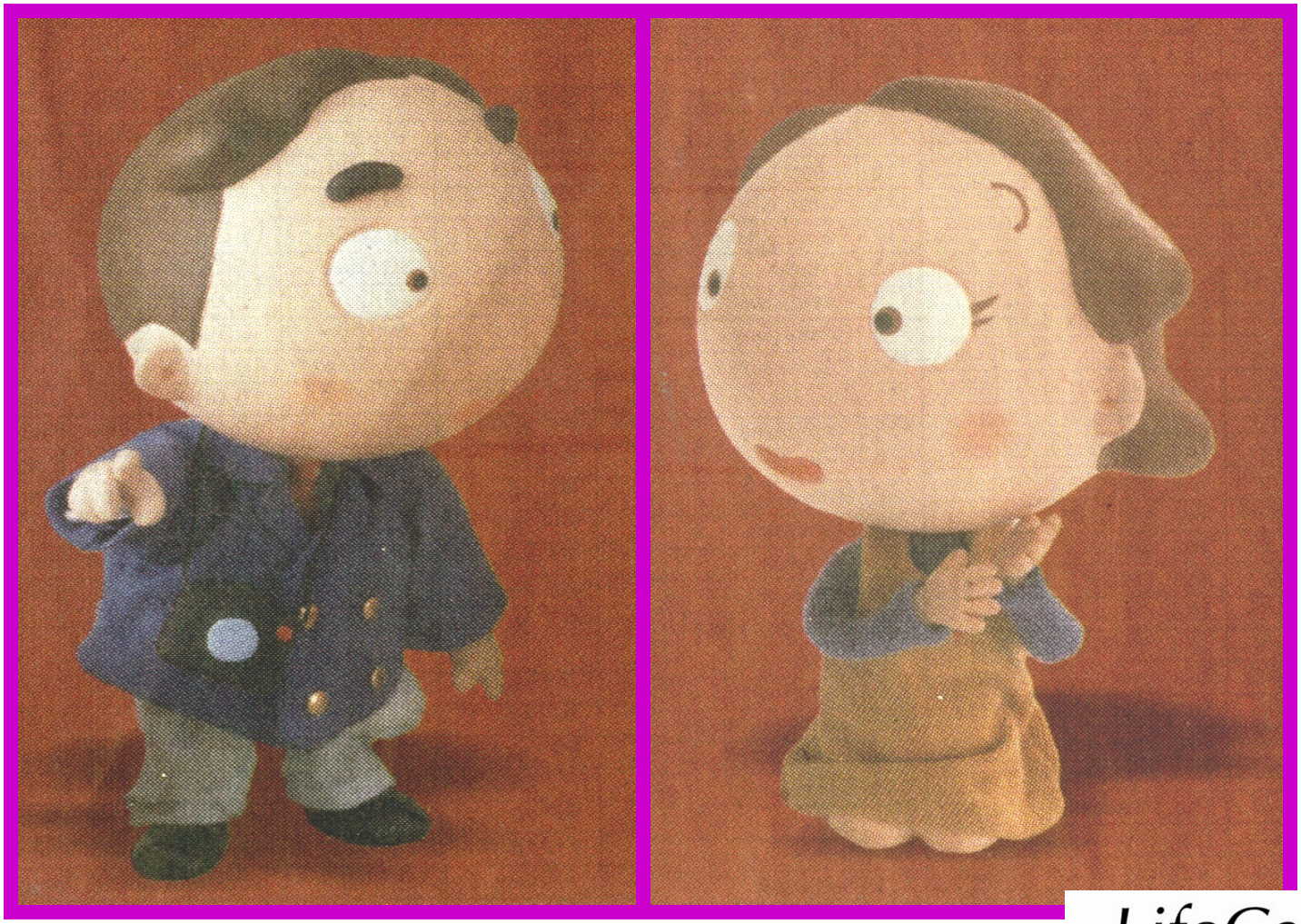
Clarifying Role of Tubercular Endometritis in infertility



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We Run Dedicated

Infertility Clinic

since 1990

Our Obsession with TB started in 2005

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at LifeCare center We Introduced

- **TB Gold test**

  (inferferone Gamma Test,)

- **MTBC in E. Biopsy/ Fluids**

  (Dr. Reita ghosh)

- **TB PCR, E. Biopsy Fluids**

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Greatest Wonders

Happened in 2005

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2005 - IVF Failure -13

7 Cases positive for MBTC (EB)
4 Cases Conceived on their own
3 required Lit Therapy
All had Threatened Abortion

Incidence of TB in Infertility

Markedly ↑ since 2005

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Experience

since 2005

June 2013 **36%**

(N- 1440)

Prior to 2005 - 11% only

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Detection of Latent Genital Koch's

ESR **HPE** **AFB culture** **X-ray chest**	**TVS** **Mx Test** **MTBC Test** **TB PCR** **Interferon gamma Test**
Prior < 2005 – 11%	**After 2005 till June 2013 - 36%**
X	✓

Pick up Rate

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Counseling
Genital Koch's

Diagnosis

(TB gold /MTBC/TB- PCR)

Plays

Major Role

Immunology - ↑ TNF is invariably associated

Association of
Cell mediated immune marker

TNF*a*

Interferone Gamma

Latent Genital

Koch's

TH – type I cytokine production -

Causing infertility & Rec. Miscarriage

TH – Type I

↓

Reproductive Disaster

↓

- **Infertility**
- **Rec. Miscarriage**

TH – Type II

↓

Successful Pregnancy

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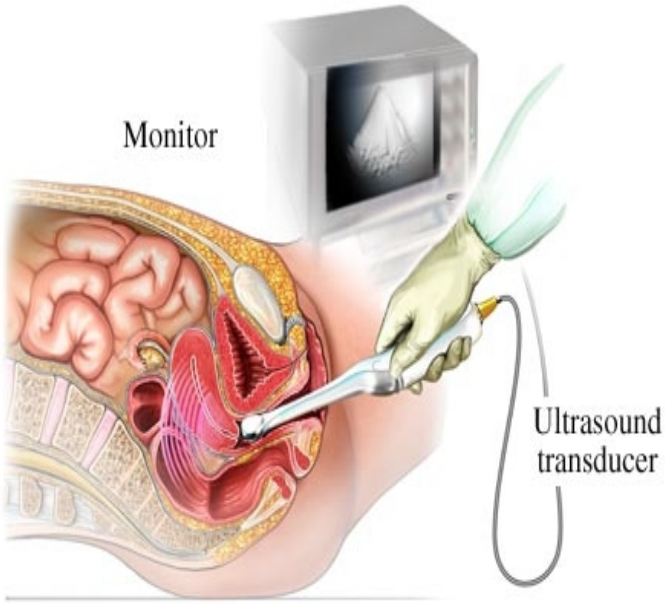
DILEMMAS

TVS in TB has big role



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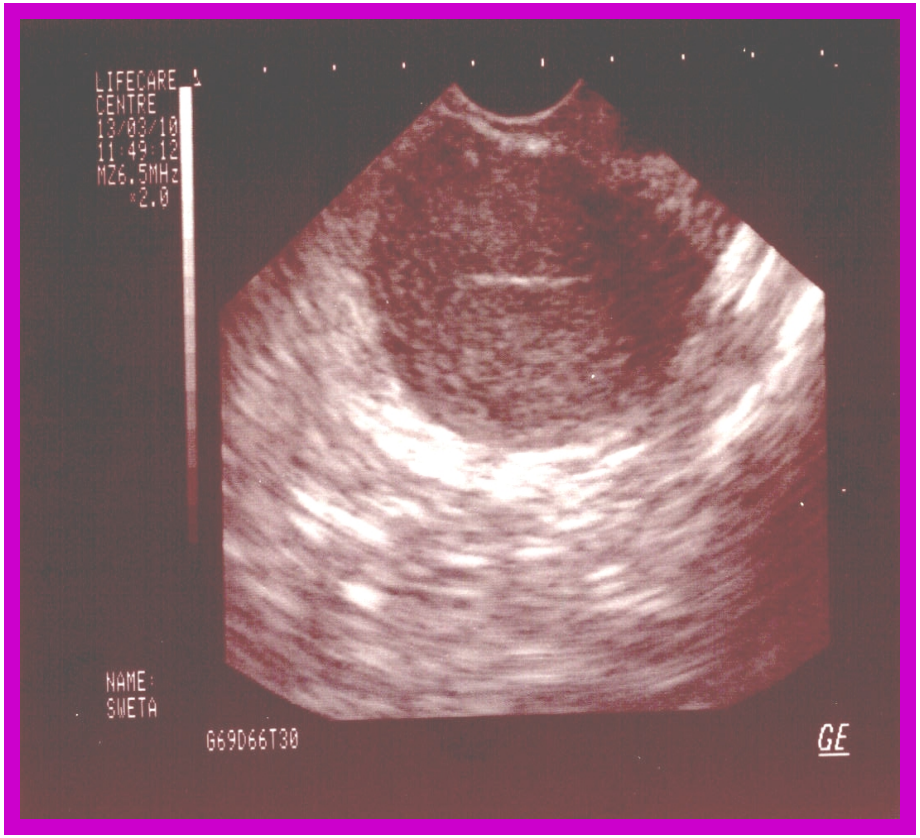
In TB



- **Persistently**

THIN

Endometrium

Is a common finding

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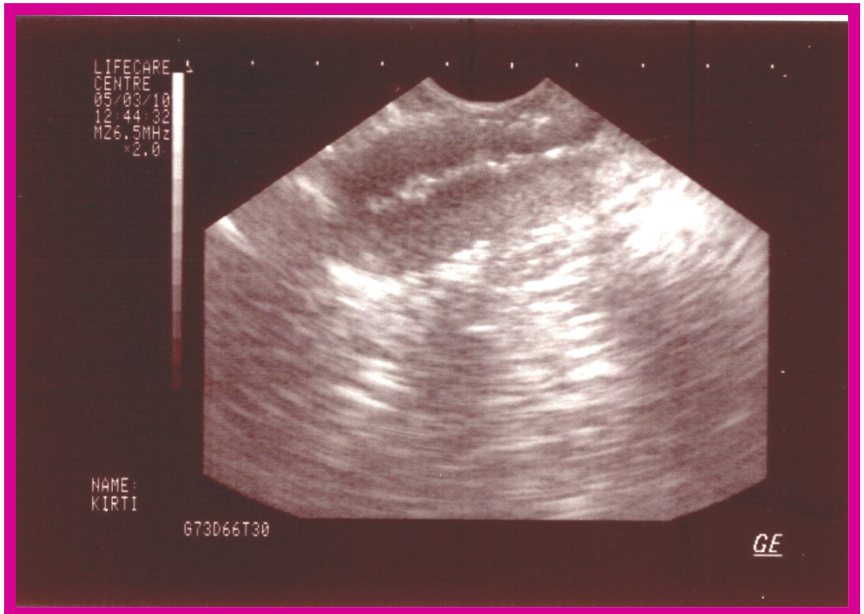
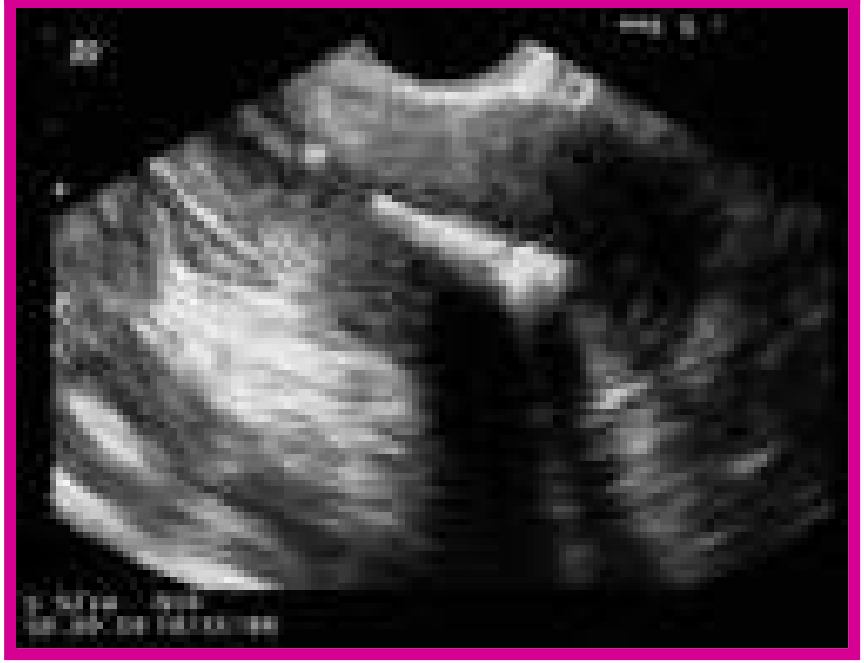
In TB





- ***Endometrium hardly 2-3 mm.***
- ***Endometrial lining appears broken, bright echog***

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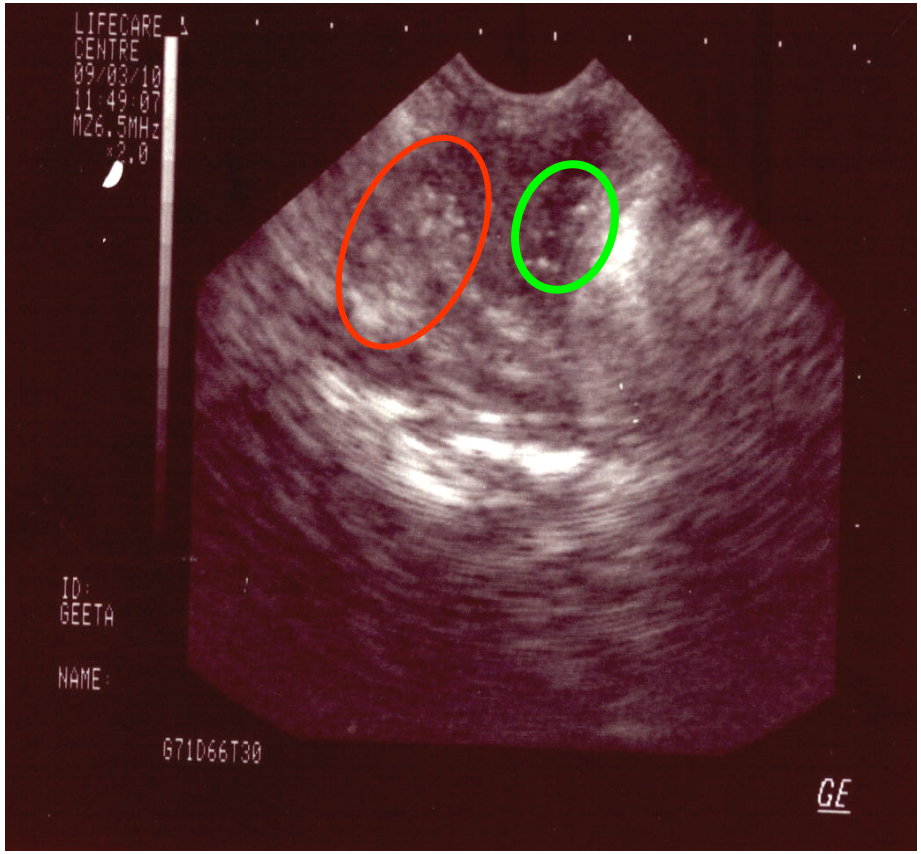
In TB



- *Peri ovarian inflammation and spec's of calcification on ovarian surface.*

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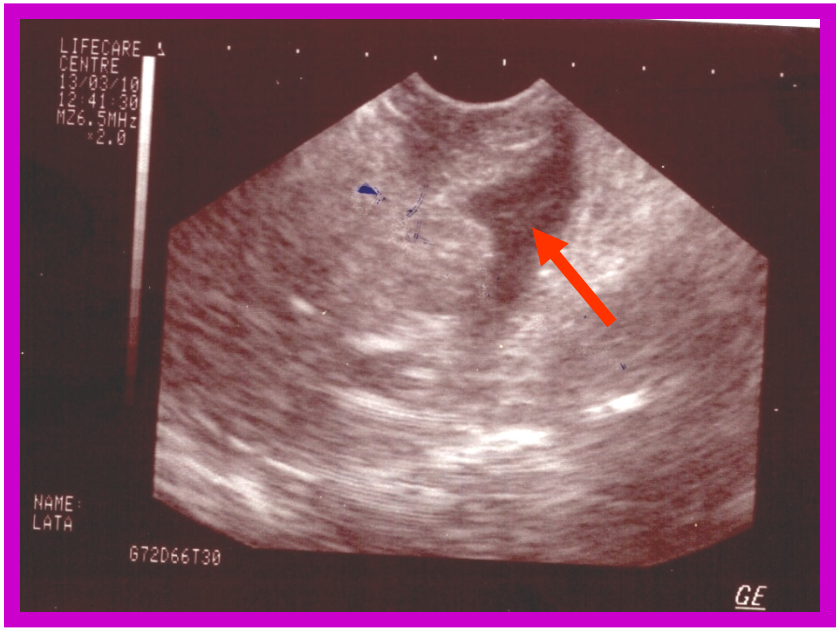
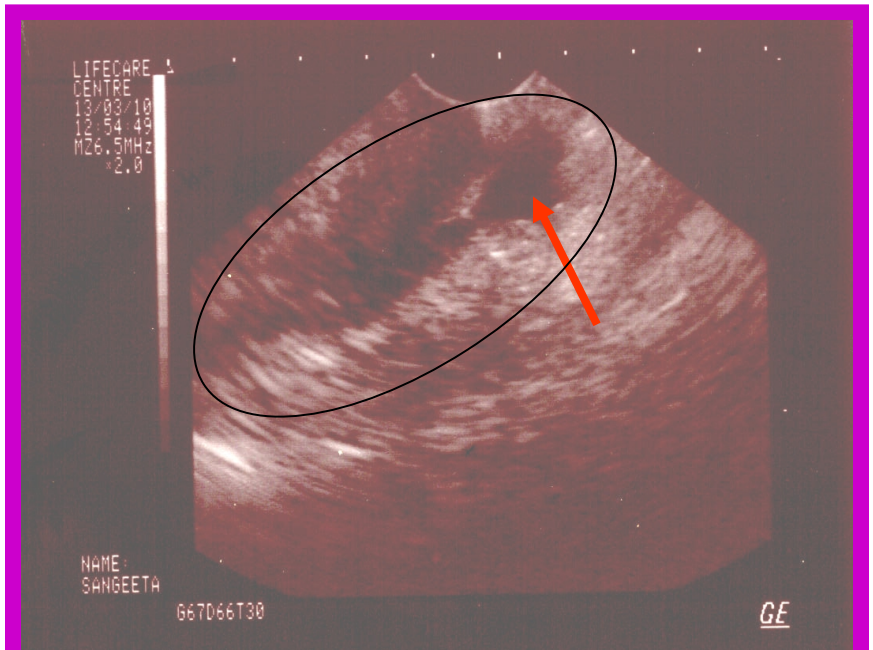
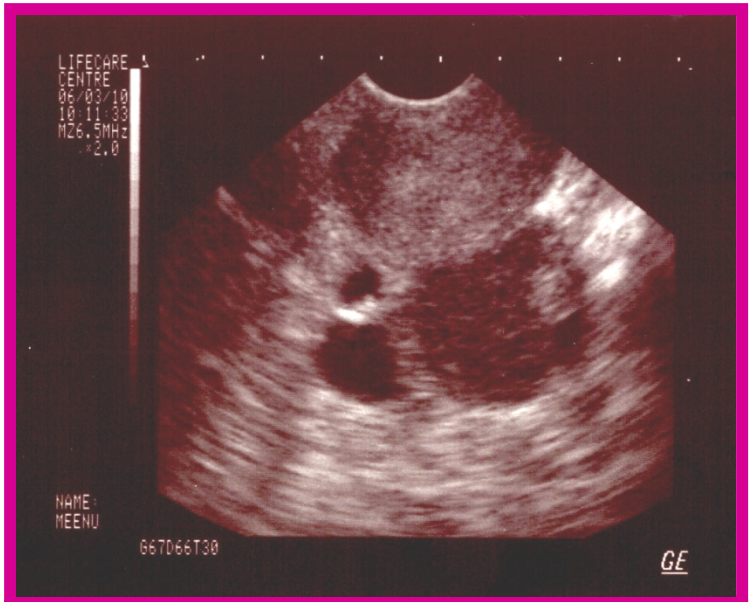
In TB

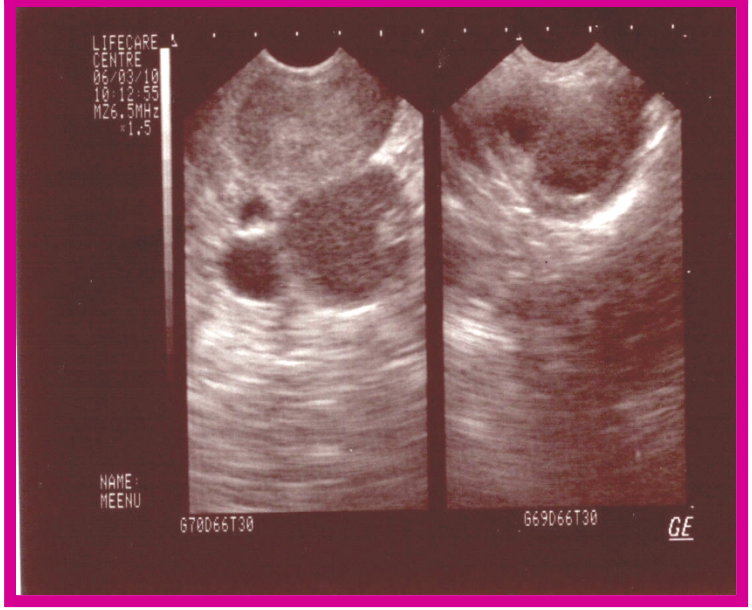




- **PID with no pain is most important symptom/sign.**
- **It may present as -**
- **Fluid collection in cul-de-sac**
- **Fluid collection in endometrial cavity.**
- **Fluid collection inside the tubes (if adhesions at fimbrial end, fluid**

In TB





- *T-O mass are seen as unilocular or multilocular thick walled mass with diffuse internal echoes.*
- *Layering effect seen when debri settles down.*
- *Outer margins poorly delineated if adhesions present*
- *Restricted mobility (Frozen pe*

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Laparoscopic classification

- **Definitive**
  - Tubercles, caseation, beaded tubes
- **Probable**
  - Encysted fluid collection, dense pelvic and peri-tubal/peri-ovarian adhesions, hydrosalpinx, TO masses, thick fibrosed tubes, mid-tubal blocks, extravasation of dye on chromopertubation
- **Possible**
  - Mild/flimsy adhesions, dilated tortuous tubes, cornual/fimbrial bloks, fimbrial agglutination/phimosis
- **Incidental**
  - Fibroid, endometriosis, PCOS
- **Normal findings**

(Rattan A, Tub Lung Ds 1993, Bhanu NV et al. J Med microbiol, 2005)

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Experience

LAPAROSCOPY – 250 cases

- No pathology - 28%
- Acitic Fluid POD – 16%
- One side block Tube 20%
- B/L block Tubes – 20%
  - Pelvic Adhesions
  - Peritoneal Tubercles
- TO-masses – 14%
  - Caseous Tubes -3%
- Frozen pelvic 18%
- Endometriosis – 28%

In endometriosis TB + - 50%

All Cases of TB were not subjected to hysterolaparoscopy

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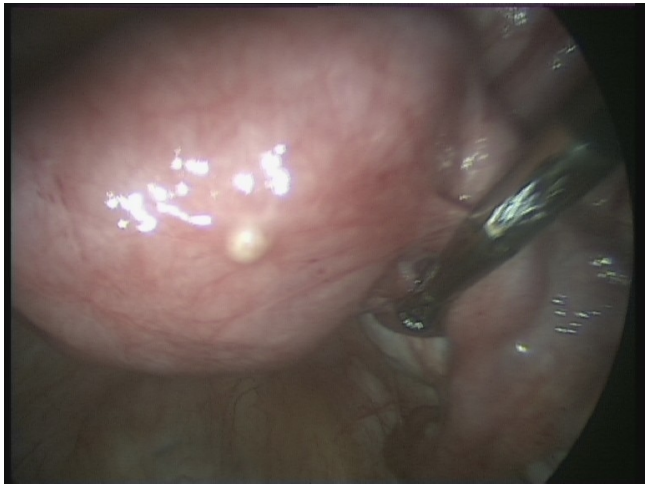
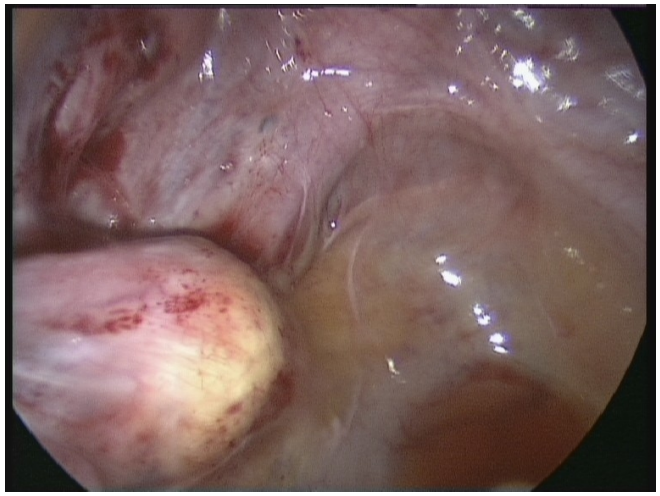
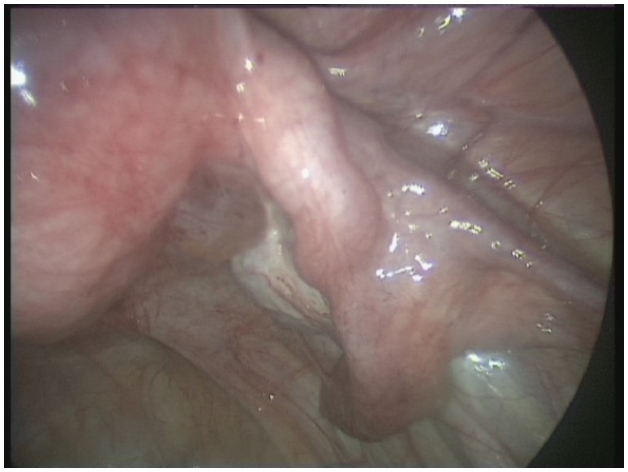
Definitive Diagnosis on Laparoscopy







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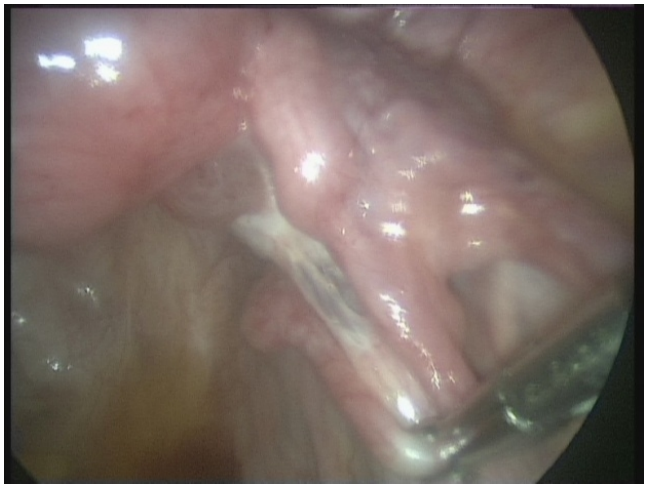
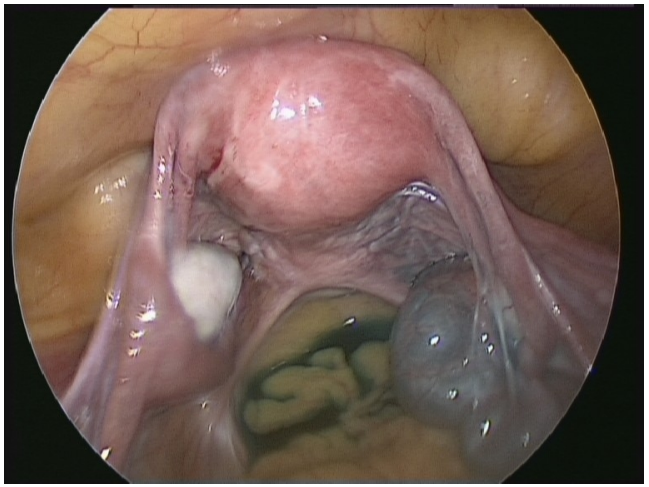
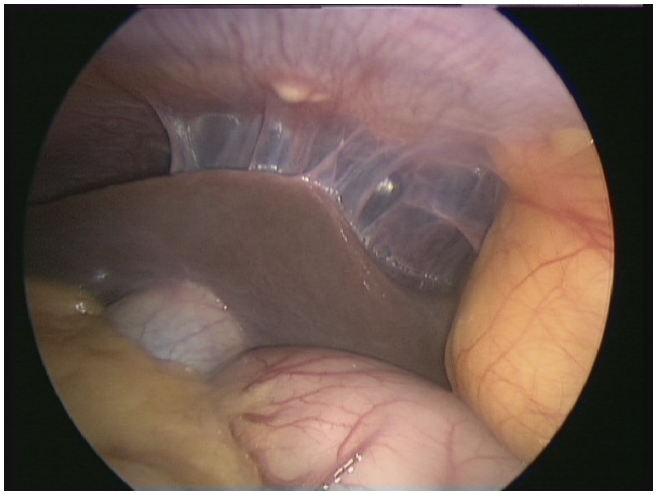
Probable Diagnosis on Laparoscopy







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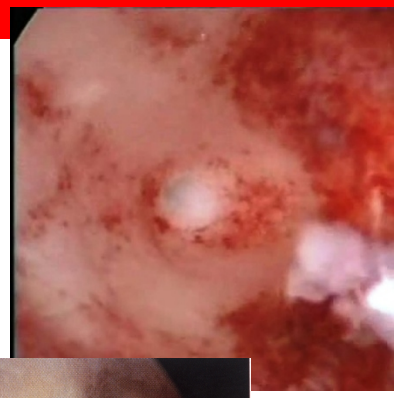
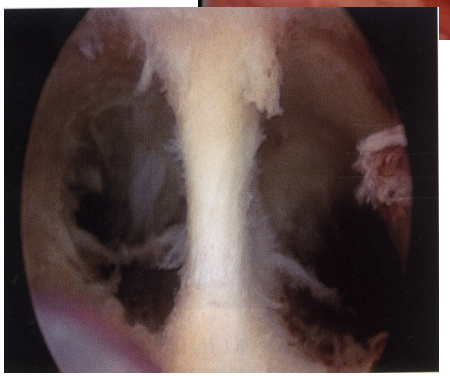
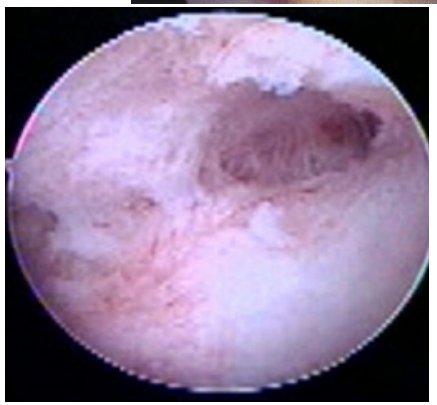
Insight at Hysteroscopy

There is no appearance which can be described as diagnosed of tuberculosis

- Pale endometrium
- Intra-uterine synechiae of varying grade
- Completely obliterated cavity (80%) by adhesions
- Granulomas
- Poor distensibility
- Narrowing of Uterine cavity







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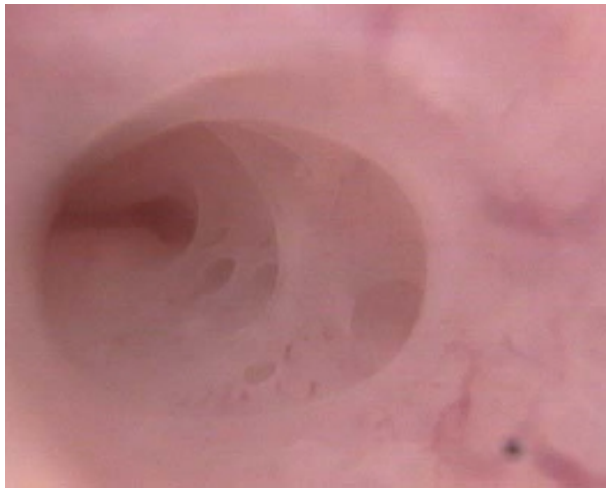
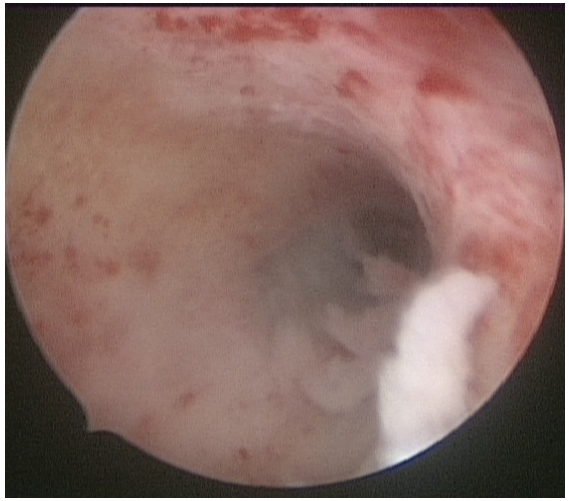
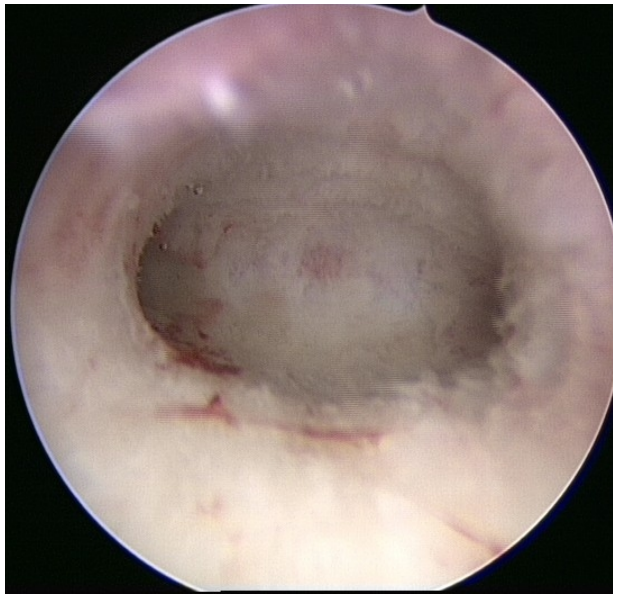
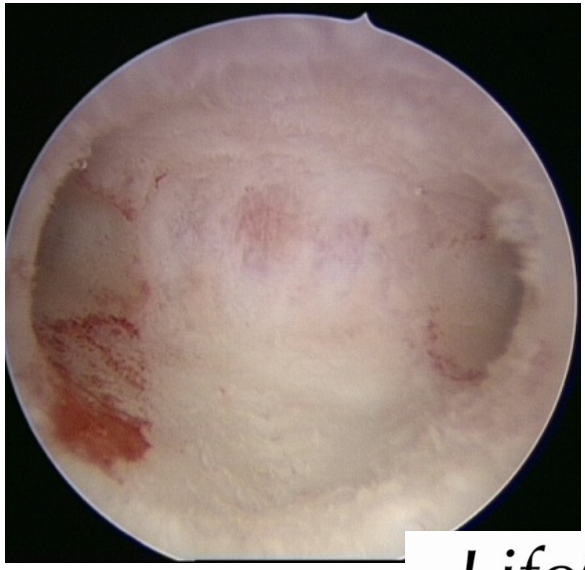
Quiescent disease-pale Endometrium









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Experience

Diagnostic and operative Hysteroscopy (N – 200)

- Normal 56%
- Intra uterine adhesion
- Grade -I – 32%
- Grade – II & III – 4%
- Polyp or hyperplasic Endometrium – 8%

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Treatment

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Genital Tuberculosis Treatment

1st two months – 4 drugs

Drugs	Dose	Side effects
INH	5mg/kg. 300mg max	Hepatoxic Peripheral neuritis
Rifampicin	10mg/kg. 600mg max	Hepatoxic, fever, rash
Ethambutol	15mg/kg. 800-1000 mg max	Ptic neuritis
Pyrizinamide	15-30 mg/kg 1.5-2 gm max	Hepatitis hyperuricemia

For next 4 monts – two drugs INH + nfampicine

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Tubercular Endometritis in Infertility

Are we justified in starting ATT on the basis of a positive molecular (PCR) test, Histochemistry positive test (MTBC) with no other obvious clinical features

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Tubercular Endometritis

Yes

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Genital Tuberculosis – Treatment

Indications for surgery

Persistence of large masses despite medical management 9 months

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Genital Tuberculosis – Treatment

Fertility restored - 65%

Spontaneous pregnancy 32%

- Pregnancy achieved on treatment with in 6 month chemotherapy

IUI – 14%

IVF 18%

Surrogacy - 0.5%

Over 65% have babies

Compiled in 30st June 2013

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Conclusion

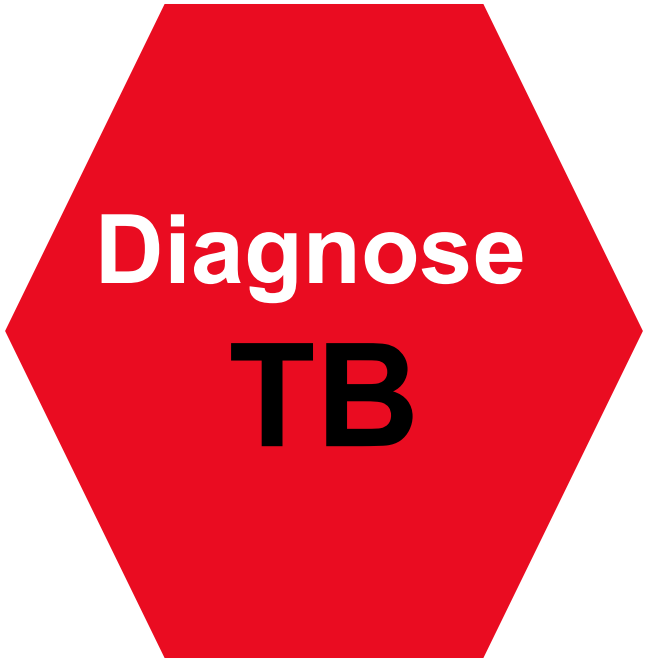
- **Latent Genital TB contributes significantly to Infertility**
- **Suspicion raising Tests are Moutoux test, TVS, Hysteroscopy Laparoscopy**
- **Latent Genital TB is diagnosed by TB PCR, MTBC test, Interferon gamma test.**
- **TB if treated , gives very satisfying success rates in infertility**
- **But Cure starts with Detection**

Thanks to diagnosis of Latent Tuberculosis !
In infertility & Recurrent Miscarriages

We

Simply

must



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Cure Starts with Detection

Genital TB can be treated easily, it's time for you to be screened For TB in infertility & RM !

Thank You

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