



ème

31 CONGRÈS NATIONAL
LA SOCIÉTÉ TUNISIENNE
DE PATHOLOGIE INFECTIEUSE

19 - 20
Mai 2022

à Hôtel Radisson Blu

Hammamet

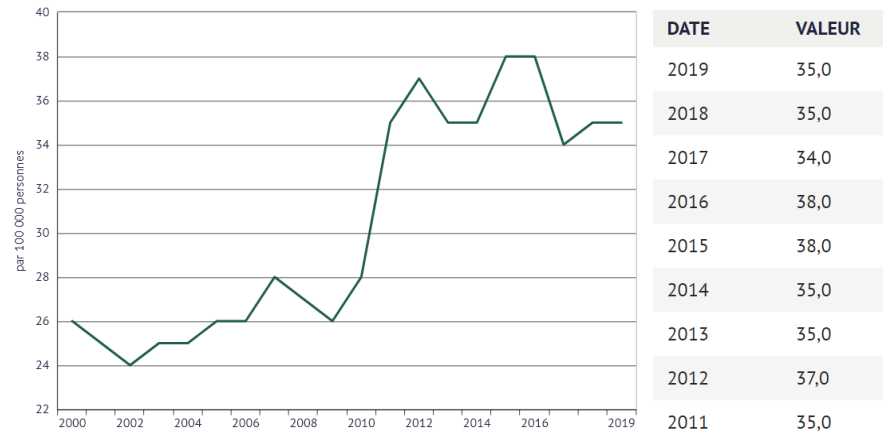
Particularités du diagnostic microbiologique de la tuberculose extra-pulmonaire

Dr Manel Marzouk

Laboratoire de Microbiologie CHU F. Hached Sousse

Introduction

- Tuberculose = Problème de santé publique Mondial
- Incidence en Tunisie \approx 35/100 000 habitants (2019)
- Localisation pulmonaire et/ou extra-pulmonaire

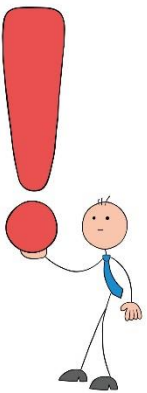


La TBC peut atteindre n'importe quel organe

Définition

Peu ou pas contagieuses

+/- localisation pulmonaire



- Localisation autre que le parenchyme pulmonaire

- ✓ Ganglionnaire

Caractéristiques épidémiolo-cliniques de la tuberculose génitale chez la femme tunisienne: une série de 47 cas

Souheil Zayet^{1,2,*}, Aida Berriche^{1,2}, Lamia Ammari^{1,2}, Mariem Razgallah^{2,3}, Rim Abdelmalek^{1,2}, Mohamed Khrouf^{2,4}, Badreddine Kilani^{1,2}, Hanène Tiouiri Benaissa^{1,2}

- ✓ Pleurale

Peritoneal tuberculosis
La tuberculose péritonéale
A. Guirat^{1,2,*}, M. Koubaa^{1,2}, R. Mzali^{1,2}, B. Abid^{1,2}, S. Ellouz^{1,2}, N. Affes^{1,2}, M. Ben Jemaa^{1,2}, F. Frikha^{1,2}, M. Ben Amar^{1,2}, M.L. Beyrouti^{1,2}

Update on urogenital tuberculosis in Southern Tunisia: a review of a 5-year period

M. Hammami^{1,1}, Makram Koubaa^{2,1}, Houda Ben Ayed³, Khaoula Rekiq⁴, Maissa Ben Jemaa⁵, Mariem Ben Hmida⁶, Maroua Trigui⁷, Chakib Marrakchi⁸, Jamel Dammak⁹, Mounir Ben Jemaa¹⁰

- ✓ OA, rachidienne

Prise en charge diagnostique et thérapeutique de la tuberculose ganglionnaire en

Neuroradiologic manifestations of central nervous system tuberculosis in 122 adults

B Kilani^{1,2,*}, L. Ammari, H Tiouiri, A Goubontini, F Kanoun, F Zouiten, T.-B Chaabène

- ✓ Méningée

Tunisie

Hajer Ben Brahim¹, Ikbel Kooli^{1,4}, Abir Aouam¹, Adnene Toumi¹, Hawki Loussaief¹, Jamel Koubaa², Mohamed Chakroun¹

Tuberculose hépatique : étude d'une série tunisienne de 14 cas

30/11/09

Doi: 10.1016/j.revmed.2009.10.214

E. Benjazia, M. Khalifa, W. Hachfi, N. Kaabia, A. Alaoua, A. Krifa, A. Letaief, F. Bahri
Médecine interne, hôpital Farhat Hached, Sousse, Tunisie

- ✓ Généralisée

La tuberculose cérébro-méningée chez l'immunocompétent : à propos de 20 cas - 30/11/09

Doi: 10.1016/j.revmed.2009.10.206

W. Hachfi, Z. Hattab, N. Ben Lasfar, M. Khalifa, N. Kaabia, F. Bahri, A. Letaief
Médecine interne, hôpital Farhat Hached, Sousse, Tunisie

Tuberculose ostéoarticulaire : à propos de 35 cas

M. Ben Azaïez, I. Kooli, N. Belhaj Salah, W. Marrakchi, A. Aouam, A. Toumi, H. Ben Brahim, M. Chakroun
CHU Fattouma Bourguiba, Monastir, Tunisie

- ✓ Urogénitale, cutanée, Oculaire, ...

La tuberculose oculaire : une série de 14 cas

Ocular tuberculosis : A case series

M. Koubaa^{1,2,*}, F. Smaoui^{3,4}, S. Gargouri⁵, H. Ben Ayed^{4,6}, K. Rekiq^{4,6}, I. Abid⁵, I. Maaloul⁷, Marrakchi^{4,6}, M. Ben Jemaa^{3,6}

Cutaneous tuberculosis in Tunisia

La tuberculose cutanée en Tunisie

R. Abdelmalek^{1,2,*}, A. Mebazaa^{1,2}, A. Berriche^{1,2}, B. Kilani^{1,2}, A. Ben Osman^{1,2}, M. Mokni^{1,2}, H. Tiouiri Benaissa^{1,2}

La tuberculose hypophysaire : à propos d'un cas - 17/09/17

Doi: 10.1016/j.ando.2017.07.330

B. Arfaoui, Dr. R. Abid, Dr. S. Sayhi, Dr. N. Bousetta, Dr. F. Ajili, Dr. R. Battikh, Pr. S. Othmani, Pr. Hôpital militaire de Tunis, service de médecine interne, Tunis, Tunisie

Un peu d'Histoire...



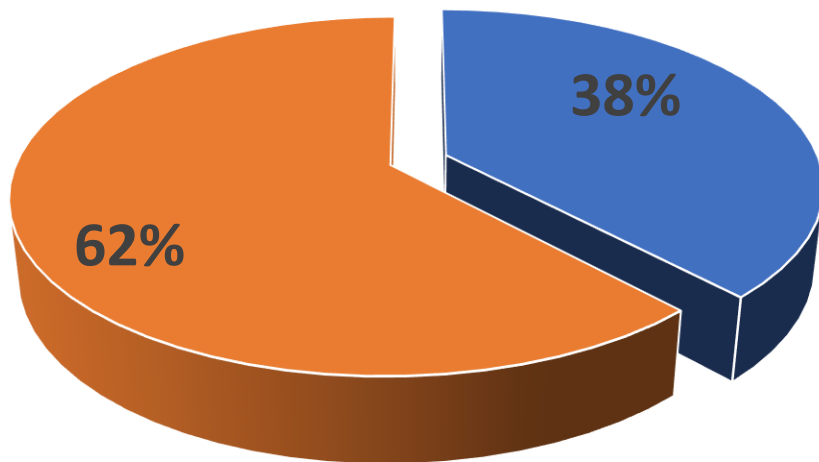
- **Ancienneté de la TBC** : attestée par l'existence de TEP...
- Lésions osseuses (mal de Pott) découvertes sur des squelettes très anciens (Néolithique, momies de l'Egypte ancienne...)

Egypt - pre-Columbian civilizations
Pott's disease?

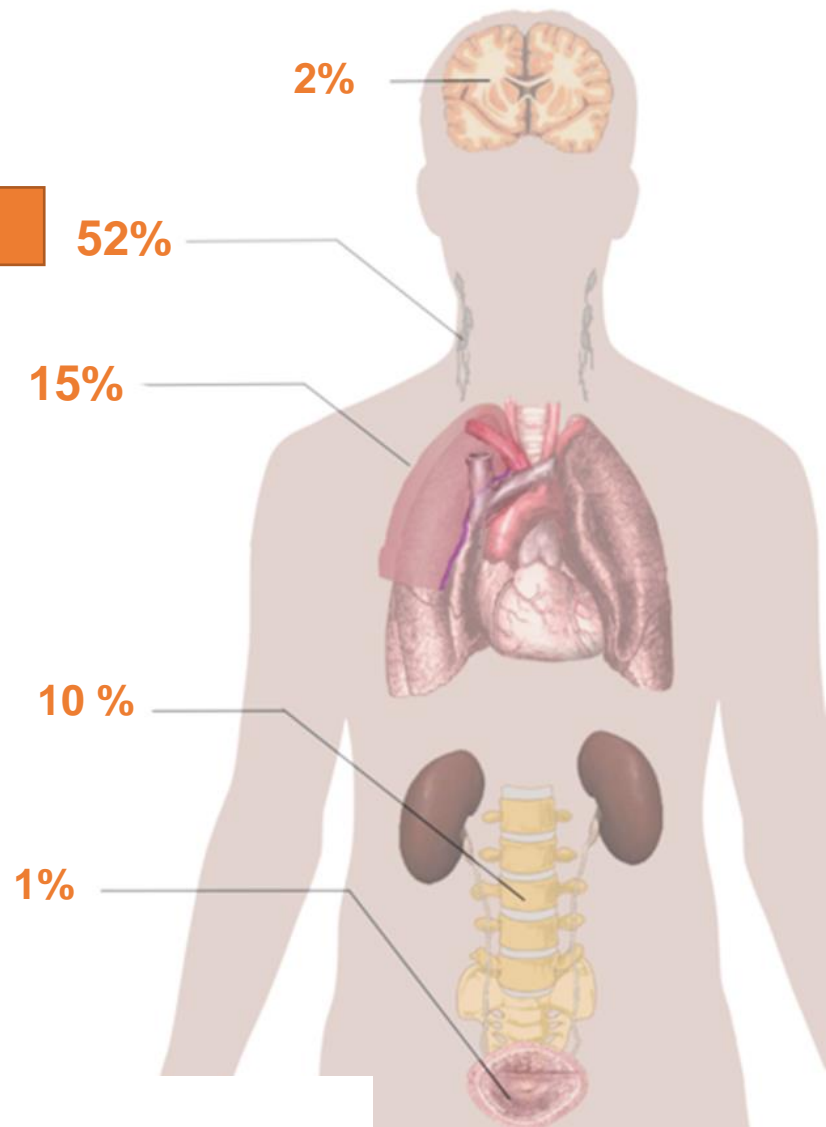


Fréquence et localisations en Tunisie

2,3 (1993) à 18/100000 (2017)



■ TP ■ TEP



Diagnostic

Difficile

Expressions cliniques très diverses

Présomptif

Certitude

- Clinique
- Imagerie
- Anatomopathologique

- Microbiologique +++
- **MAIS** peu réalisé !!!
 - Méconnaissance
 - Difficulté localisation,
 - Caractère paucibacillaire...



World Health Organization

Preuve bactériologique

=

Seule preuve formelle de l'infection TBC

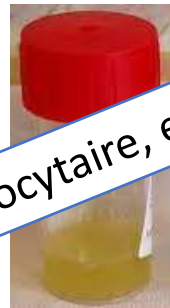


Prélèvements

Prélèvements

Liquides de ponction

- Ganglionnaire
- Abscès du psoas
- Pleurale
- Articulaire
- Ascite
- LCR



lymphocytaire, exsudatif

Hypochlorurachie

Biopsies tissulaires

- Ganglionnaire
- Disco-vertébrale
- Pleurale
- Synoviale
- Digestive



Autres: Urines, prélèvements génitaux, pus...

Prélèvement : ganglionnaire

- **Ponction ganglionnaire: aspiration à l'aiguille**
 - Transvaser dans **un tube stérile**
 - Ou envoyer la seringue **sans** aiguille



Prélèvement : ganglionnaire



**Biopsie
ganglionnaire**

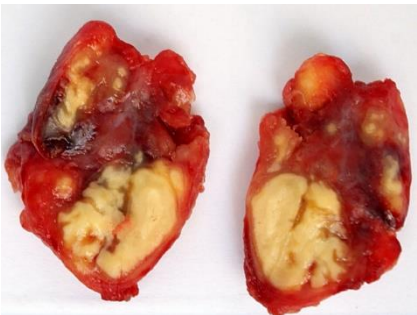
Tube stérile +/- Eau distillée stérile

Examen microbiologique

Examen histologique

+ Formol ou liquide de Bouin

Penser à Fractionner le prélèvement



Prélèvement : ganglionnaire

- Ecouvillonnage du pus

A éviter !!!!

- Adénopathie fistulisée ouverte à la peau

- Issue du pus

Mycobactéries hydrophobes
→ Risque de faux négatifs



Ecouvillon d'alginate ou polypropylène dans un milieu de transport → ssb ↗ ↗

Résultat rendu : "prélèvement sur écouvillon- Examen non contributif"

Prélèvements : résumé

- Liquide de ponction et/ou Biopsie
- Avant tout TTT antimycobactérien
- Récipients stériles à fermeture hermétique
- Acheminement rapide
- Sinon → conservation à +4°C (jusqu'à 7 jours) +++



Penser à envoyer les
prélèvements au labo de
Microbiologie



Pas de conservateur !!

- **Bouin, formol**
 - **Ecouvillons**
- Faux (-)**





Au laboratoire...

Traitement des prélèvements

Biopsie



Broyage



Techniqué



Broyage manuel
(Broyeur de Potter)



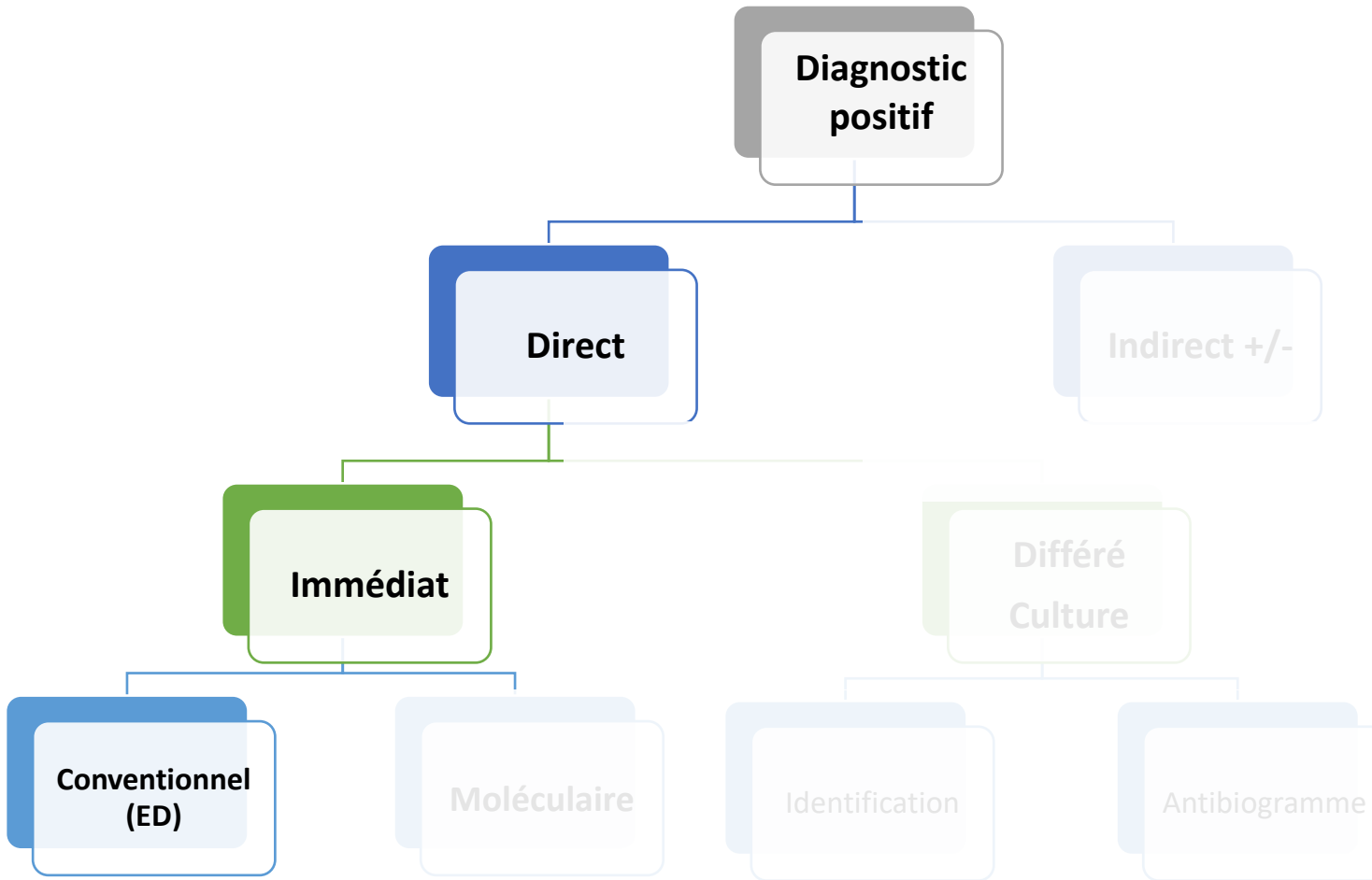
Broyage automatisé
(stomacher)

Traitement des prélèvements

Prélèvements polymicrobiens	Prélèvements monobactériens
<ul style="list-style-type: none">• Décontamination<ul style="list-style-type: none">• Petroff (NaOH)• Kubica (N-acétyl-cystéine)	<ul style="list-style-type: none">• issus d'un site normalement stérile• paucibactériens <p>→ Pas de décontamination</p>

Dans la plupart des cas de TEP pas de décontamination

Diagnostic microbiologique



Diagnostic : Examen Direct

Coloration de Ziehl Neelsen

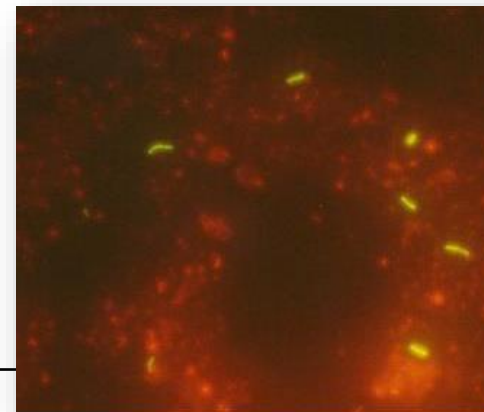
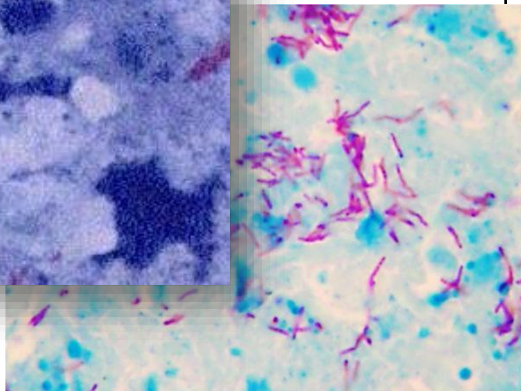
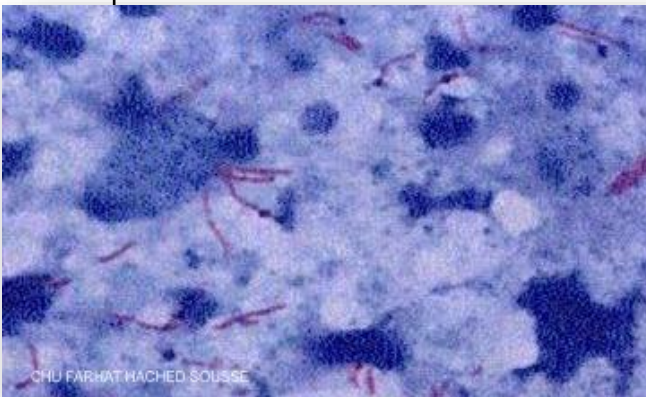
Coloration à l'auramine

Limites:

- Lente
 - Spécificité
 - +/- Sensibilité
- Seuil (+) > 10^3 BAAR/ml; > 10^6 bactéries/g de tissu
Lecteur-dépendent

Avantages:

- Facilité, Rapidité, peu coûteux
- Efficacité du traitement (BAAR fragmentés)





Communication brève

Diagnostic de la tuberculose ganglionnaire périphérique en Tunisie

Diagnosis of peripheral tuberculous lymphadenitis in Tunisia

C. Marrakchi^{a,*}, I. Maâloul^a, D. Lahiani^a, B. Hammami^a,
 T. Boudawara^b, M. Zribi^c, M. Ben Jemaâ^a

Direct

Sensibilité (%) Spécificité (%)

12	100
28	98,6
43	98
	-

120

C. Marrakchi et al. / Médecine et maladies infectieuses 40 (2010) 119–122

Tableau 1
 Résultats de l'étude microbiologique en fonction de la technique de prélèvement ganglionnaire.
Microbiological results according to the technique of lymph node sampling.

Techniques	Aspiration (28 cas) (%)	Biopsie (9 cas) (%)	Sensibilité (%)
Examen direct positif ^a	9 cas (31,2)	2 cas (22)	29,7
Culture positive ^b	3 cas (11)	1 cas (11)	10,8

^a Présence de bacilles acido-alcoolorésistants (BAAR).

^b Isolement du *Mycobacterium tuberculosis*.

Tuberculosis lymphadenitis in a southeastern region in Tunisia: Epidemiology, clinical features, diagnosis and treatment



Salma Smaoui^{a,b,*}, Mohamed Amine Mezghanni^a, Bousaima Hammami^c, Neila Zalila^d,
 Chema Marouane^{a,b}, Sana Kammoun^{a,b}, Abdelmonoom Ghorbel^e, Mounir Ben Jemaa^c,
 Férièle Messadi-Akrout^{a,b}

	FNA n/n' (%)	Excision n/n' (%)
AFB smear	5/21 (23.8%)	5/36 (13.8%)



PLOS ONE | <https://doi.org/10.1371/journal.pone.0255146> July 29, 2021

RESEARCH ARTICLE

Diagnostic efficacy of Light-Emitting Diode (LED) Fluorescence based Microscope for the diagnosis of Tuberculous lymphadenitis

Gebeyehu Assefa^{1,2}*, Kassu Desta²†, Shambel Araya²†, Selfu Girma¹©, Adane Mihret¹, Tsegaye Hailu¹, Abay Atnafu¹, Nigatu Endalfer¹, Adugna Abera³, Shiferaw Bekele¹, Leila Birhanu⁴, Getu Diriba³, Yordanos Mengistu¹, Biniyam Dagne³, Kidist Bobosha¹, Abraham Aseffa¹†

Comparison of LED and conventional acid-fast bacilli in an area with high prevalence of tuberculosis
Manel Marzouk*, Asma Ferjani, Mohamed

Table 1
Accuracy using a culture reference standard.

	TP/C+	Sensitivity [95% CI]
a) All samples		
CFM	143/180	79.4% [72.7–84.9]
LED-FM	148/180	82.2% [75.7–87.4]
b) Respiratory samples		
CFM	120/131	91.6% [85.1–95.5]
LED-FM	122/131	93.1% [87–96.6]
c) Non-respiratory samples		
CFM	23/49	46.9% [33.8–61.6]
LED-FM	26/49	53.1% [37.4–67.2]

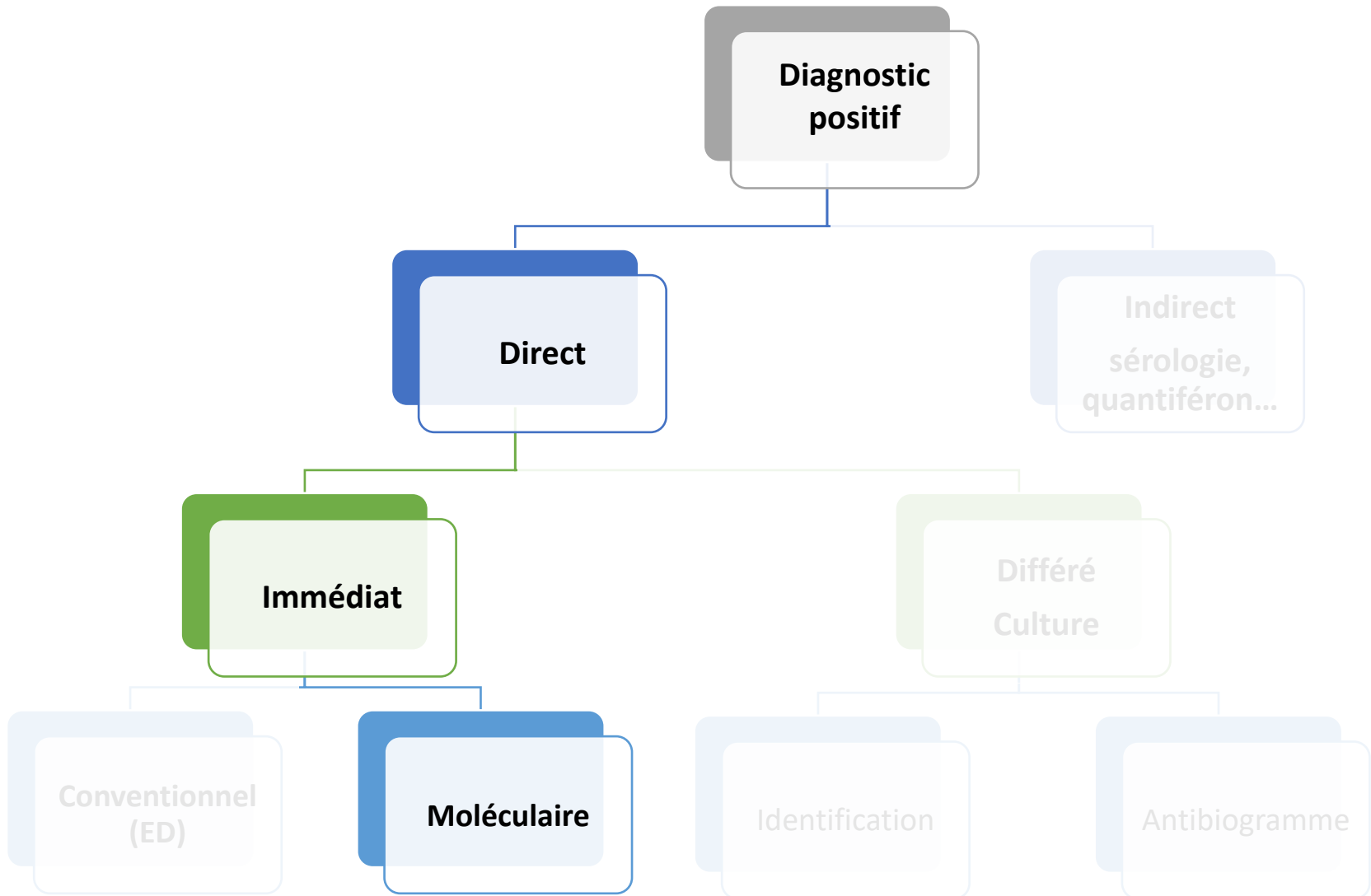
TP = true positive; TN = true negative; C+ = culture positive; C- = culture negative

Table 4. Overall diagnostic accuracy of conventional ZN microscopy, LEDFM, and cytology against culture result data data at a specialized hospital. Addis Ababa, Ethiopia.

	ZN microscopy	LEDFM
Sensitivity [95% CI]	30% [17.9–44.6]	66% [51.2–78.8]
Specificity [95% CI]	91.3% [85.8–95.2]	77.6% [70.4–83.8]
NPV [95% CI]	89.1% [87.2–90.8]	82.5% [76–87.5]
PPV [95% CI]	35.5% [22.2–51.4]	58.9% [50.3–67.1]
Likelihood ratio (+) [95% CI]	3.45 [1.79–6.65]	2.95 [2.08–4.19]
Likelihood ratio (-) [95% CI]	0.767 [0.936–0.925]	0.438 [0.295–0.65]

**Sensibilité Microscopie LED (53-66%) > ZN (30-46%)
MAIS manque de spécificité !!**

**ED (-) n'élimine nullement le diagnostic de TEP
Paucibacillaire !!!!**



PCR conventionnelle






REPORTS
Scientific RepoRtS | (2020) 10:7102
 nature research
 009 XXX-XXX
 Check for updates
 Communication
Diagnostic performance of IS6110 PCR for the rapid diagnosis

SSb: 68%, Spc: 95%
TBC gg:73% > TBC péritonéale: 66% > TBC Pleurale: 56%

Mohita Gaur¹, Anoop Singh¹, Vishal Sharma¹, Gayatri Tandon¹, Ankur Bothra¹,
 Aarushi Vasudeva¹, Shreeya Kedia¹, Ashwani Khanna², Vishal Khanna³, Sheelu Lohiya³,
 Mandira Varma-Basil⁴, Anil Chaudhry², Richa Misra^{1,6} & Yogendra Singh^{1,2}

35	97.22 (85.47–99.93)
20	76.92 (56.35–91.03)

e routine diagnosis of s
V. Chandrasekharan[†]
[†] Department of Chemistry, Faculty of Science, University of

Test
 PCR
 Pulm
 Extra
 Total
 Smea
 Smea

Extra-pulmonary:		Reference standard (Confirmed TB cases)		
Lymph n	Molecular test	PTB (n = 62)	EPTB (n = 67)	
Cervical	Stool IS6110 PCR			
Mediasti	^b Sensitivity (%; 95% CI)	55/62; 88.71 (78.11–95.34)	46/67; 68.66 (56.16–79.44)	87.12)
Others	^c Specificity (%; 95% CI)	2/41; 95.12 (83.47–99.40)	2/41; 95.12 (83.47–99.40)	
Abdomi	^d PPV (%; 95% CI)	96.49 (87.65–99.07)	95.83 (85.50–98.90)	88.18)
Mesenter	^e NPV (%; 95% CI)	84.78 (73.43–91.83)	65.00 (56.41–72.71)	
Intestina	^f Accuracy (%; 95% CI)	91.26 (84.06–95.93)	78.70 (69.78–86.00)	
Ascites		v1	v2	
Pleural Effusion		16	09	
Ocular		01	01	100 (2.50–100.00)
Uterus		01		100 (2.50–100.00)

Délaissée en routine par la plupart des laboratoires

Samples with a final diagnosis				
Confirmed TB cases	Possible TB cases	Non-tuberculous patients	Total	
6	3	14	2	25
0	0	1	17	18
6	3	15	19	43*

Sensitivity = 0.9200 (95% CI 0.7397–0.9902).
 Specificity = 0.9444 (95% CI 0.7271–0.9986).
 PCR = polymerase chain reaction; TB = tuberculosis; EPTB = extra-pulmonary TB; CI = confidence interval.

PCR en temps réel

- Artus RG *M.tuberculosis* (Qiagen), RealTime MTB Assay (Abbott)...
- **GeneXpert MTB-RIF® (Cepheid)**

Système automatisé de PCR en temps réel

Détection:

✓ Complexe *tuberculosis*

✓ Rif (R) (mutations gène *rpoB*)

Directement à partir du prélèvement

Prélèvements extra pulmonaires ??



Performance du GeneXpert® dans le diagnostic de la TBEP selon la littérature

Étude	Année	Pays	Sensibilité (%)	Spécificité(%)
<u>Hillemann D et al.</u>	2011	Allemagne	77,3	98,2
<u>Tortoli E et al.</u>	2012	Italie	79	97,3
<u>Chang K et al.</u>	2012	Chine	80,4	86,1
<u>Vadwai V et al.</u>	2011	Inde	81	99,6
<u>Maynard-Smith L et al.</u>	2014	Royaume-Uni	83	98
<u>Diallo AB et al.</u>	2015	Dakar	94,74	97,95
<u>Zeka AN et al.</u>	2011	Turquie	100	63
Notre étude	2016-2018	Centre Tunisien	91,1%	100%

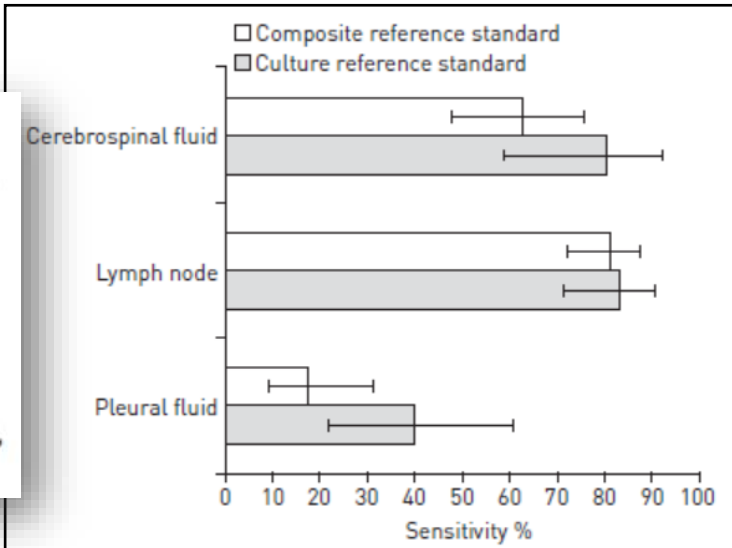
GeneXpert® MTB/RIF

		Sensibilité (%)	Spécificité (%)	VPP (%)	VPN (%)
Prélèvements extra-pulmonaires	Biopsies ganglionnaires	87,5	100	100	90,4
	Autres biopsies tissulaires	85,7	100	100	98,1
	LCR	100	100	100	100
	Liquide pleural	100	100	100	100
	Autres liquides de ponction	100	100	100	100

Eur Respir J 2014; 44: 435–446

Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis

Claudia M. Denkinger^{1,2}, Samuel G. Schumacher², Catharina C. Boehme⁴, Nandini Dendukuri^{2,3}, Madhukar Pai^{2,3} and Karen R. Steingart⁵



Ssb Liq pleural (40%) < LCR=gg (87%)

INT J TUBERC LUNG DIS 2015; 19(3):278–284

Diagnostic accuracy of the Xpert[®] MTB/RIF assay for extrapulmonary tuberculosis: a meta-analysis

E. Penz,* J. Boffa,† D. J. Roberts,‡ D. Fisher,§ R. Cooper,¶ P. E. Ronksley,# M. T. James**

Table 2 Pooled estimates stratified by disease site

	Studies <i>n</i>	Specimens <i>n</i>	Sensitivity % (95%CI)	<i>I</i> ² % (95%CI)	Specificity % (95%CI)
Overall	36	9523	0.77 (0.66–0.85)	99 (87–92)	0.97 (0.94–0.98)
Site					
Lymph	12	822	0.87 (0.75–0.95)	90.98 (85–97)	0.92 (0.81–0.97)
Pleural fluid	13	1014	0.37 (0.26–0.50)	92.41 (88–97)	0.98 (0.95–0.99)
CSF	13	1008	0.69 (0.54–0.81)	40.85 (0–96)	0.97 (0.95–0.98)
Gastro-intestinal	5	358	0.86 (0.67–0.98)	42.13 (0–100)	0.98 (0.98–1.00)
Genito-urinary	8	725	0.70 (0.53–0.95)	6.90 (0–100)	0.94 (0.71–0.99)
Other	12	1765	0.80 (0.66–0.90)	77 (63–93)	0.97 (0.97–0.98)

CI = confidence interval; LR = likelihood ratio; += positive; -= negative

Ssb Liq pleural (37%) < LCR (69%) < gg (87%)

Low diagnostic accuracy of Xpert MTB/RIF assay for extrapulmonary tuberculosis: A multicenter surveillance

Mohammadreza Allahyartorkaman^{1*}, Mehdi Mirsaeidi^{2*}, Gholamreza Hamzehloo³, Sirus Amini², Mona Zakiloo² & Mohammad Javad Nasiri^{3*}

Category	Specimen type	Number (%)	Xpert MTB/RIF Error & Invalid	True negative	False negative	True positive	False positive	Xpert Sensitivity (%) with 95% CI	Xpert Specificity (%) with 95% CI
Pulmonary	BAL	340 (16.5)	4	327	0	3	6	100 (29.2–100)	98.2 (29.2–100)
	Tracheal	30 (1.4)	0	29	0	1	0	100 (25–100)	100 (88–100)
	Sputum	848 (41.2)	20	626	8	175	19	95.6 (91.5–98)	97 (95.4–98.2)
Extrapulmonary	Urine	44 (2.1)	2	40	0	2	1	100 (15.8–100)	97.5 (86.8–99)
	Abscess	49 (2.4)	1	36	0	10	2	100 (69.1–100)	94.7 (82.2–99)
	Osteoarticular	80 (3.4)	2	66	2	3	7	60 (14.6–94.7)	90.4 (81.2–96)
	Biopsy	162 (7.8)	9	119	5	13	16	72.2 (46.5–90.3)	88.1 (81.4–93)
	Pericardium	120 (5.8)	2	112	3	2	1	40 (5.2–85.3)	99.1 (95.1–99)
	Cerebrospinal fluid (CSF)	44 (2.1)	1	39	0	2	1	100 (15.8–100)	97.5 (86.8–99)
	Gastric Lavage	111 (5.4)	2	103	1	4	1	80 (28.3–99.4)	99 (94.7–99.9)
	Blood	15 (0.7)	2	13	0	0	0	—	100 (75.2–100)
	Plural fluid	175 (8.4)	7	153	4	7	4	63.6 (30.7–89)	97.4 (93.6–99)
	Ascites	38 (1.8)	2	33	0	3	0	100 (29.2–100)	100 (89.4–100)
Pulmonary		1218 (59.2)	24	982	8	179	25	95.7 (91.7–98.1)	97.5 (96.3–98)
Extrapulmonary		838 (40.7)	31	713	15	49	30	76.5 (64.3–86.2)	95.9 (94.2–97)

Ssb: 76,5%; Spc: 96,9%

Ssb Pus d'abcès/urines/LCR/Ascite: 100%
> Biopsie tissulaire/OA/pleural: 60-72%

RESEARCH

Open Access

Diagnostic utility of GeneXpert MTB/RIF assay versus conventional methods for diagnosis of pulmonary and extra-pulmonary tuberculosis

Asmaa Mohammed Elbrolosy^{1*}, Rana H. El Helbawy², Osama M. Mansour³ and Reda Abdel Latif⁴

2021

Table 4 GeneXpert MTB/RIF diagnostic system performance for PTB and EPTB in relation to LJ culture as the reference standard

Specimen type	PTB (n = 449)		EPTB (n = 133)					PTB	EPTB
	Sputum	BAL	Pleural fluid	CSF	Ascetic fluid	Pus	Urine		
No.	430 (95.8%)	19 (4.2%)	26 (19.5%)	62 (46.6%)	19 (14.3%)	12 (9.0%)	14 (10.5%)	449	133
True-positive	106	4	7	12	5	3	3	110	31
False-positive	0	1	2	4	1	0	1	1	9
True-negative	272	12	13	40	11	5	7	284	75
False-negative	12	0	2	1	1	2	2	12	7
Invalid or error	40 (9.3%)	2 (10.5%)	2 (7.7%)	5 (8.1%)	1 (5.3%)	2 (16.7%)	1 (7.1%)	42 (9.4%)	11 (8.3%)
Sensitivity	89.8%	100%	77.8%	92.3%	83.3%	60.0%	60.0%	90.2%	81.6%
Specificity	87.2%	80.0%	76.5%	81.6%	84.6%	71.4%	77.8%	86.9%	78.9%
PPV	100%	80.0%	77.8%	75.0%	83.3%	100%	75%	99.1%	77.5%
NPV	95.8	100%	86.7%	97.6%	91.7%	71.4%	77.8%	95.9%	91.5%
False-positive rate	0.0%	20%	11.8%	10.2%	7.7%	0.0%	11.1%	0.3%	9.5%
False-negative rate	4.2%	0%	22.2%	0%	16.7%	40.0%	40.0%	9.8%	18.5%

Ssb: 81,6%; Spc: 78,9%

Ssb LCR (92%) > Ascite (83%) > Pleural (77%)
> Pus et urines (60%)

Xpert MTB-Rif[®] Ultra

IS6110 and IS1081

SCIENTIFIC REPORTS

nature research

2020

A Comparative Evaluation of the New Genexpert MTB/RIF Ultra and other Rapid Diagnostic Assays for Detecting Tuberculosis in Pulmonary and Extra Pulmonary Specimens

John Osei Sekyere^{1,3}, Nontobeko Maphalala², Lesibana A. Malinga^{3,4}, Nontombi M. Mbelle¹ & Nontuthuko E. Maningi^{1*}

Sample material	Sensitivity % (95% CI) TP/(TP+FN)	Specificity % (95% CI) TN/(TN+FP)	PPV % TP/(TP+FP)	NPV % TN/(TN+FN)	Accuracy % (95% CI) (TP+TN)/(TP+FP+TN+FN)
All samples	90 (56–100) 9/10	99 (93–100) 71/72	90 9/10	99 71/72	98 (91–100) 80/82
Lymph node biopsy	100 (3–100) 1/1	75 (19–99) 3/4	50 1/2	100 3/3	87 (77–97) 14/16
Lymph node aspirate	100 (40–100) 4/4	100 (72–100) 11/11	100 4/4	100 11/11	100 (95–100) 15/15
Pus samples	100 (16–100) 2/2	100 (77–100) 14/14	100 2/2	100 14/14	100 (79–100) 16/16
Other biopsies	100 (3–100) 1/1	100 (75–100) 13/13	100 1/1	100 13/13	100 (77–100) 14/14
Fluid samples	0 (0–98) 0/1	100 (88–100) 28/28	0 N/A	97 28/29	97 (82–100) 28/29
Gastrointestinal lavage	100 (3–100) 1/1	100 (16–100) 2/2	100 1/1	100 2/2	100 (30–100) 3/3

Ssb=90%, Spc=99%



Narrative review

The rapid molecular test Xpert MTB/RIF ultra: towards improved tuberculosis diagnosis and rifampicin resistance detection

O. Opota^{1,*}, J. Mazza-Stalder², G. Greub^{1,3}, K. Jaton¹

2019

Diagnostic performance	Study 1	Study 2	Study 3
Respiratory specimen all specimen	87.5/81 (+6.5) 88/83 (+5.4) 89.3/82.1 (+7.2) 95.7/82.9 (+12.8)	98.7/98.7 (0) 96/98 (-2) 95.6/100 (-4.4) 96.7/97.3 (-0.7)	Chakravorty, Simmons et al., 2017 retrospect. (n = 277) Dorman, Schumacher et al., 2018 prosp. (n = 1753) Berhanu et al., 2018* (n = 237) Opota et al., 2019** (n = 196)
Respiratory smear positive specimen	98.9/97.8 (+1.1) 100/100 (0)	— —	Chakravorty, Simmons et al., 2017 retrospect. (n = 277) Opota et al., 2019** (n = 196)
Respiratory smear negative specimen	78.9/66.1 (+12.8) 63/46 (+17) 91.7/66.7 (+25) 90.77 (+13)	— — — —	Dorman, Schumacher et al., 2017 retrospect. (n = 277) Schumacher et al., 2018 prosp. (n = 1753) Opota et al., 2019* (n = 196) Dorman, Schumacher et al., 2018 prosp. (n = 1753)
Adult HIV-positive only (all respiratory specimen)	88.2/76.5 (+11.7)	—	Berhanu et al., 2018 prosp. (n = 237)
Adult HIV-negative only (all respiratory specimen)	89.5/89.5 (0)	—	Berhanu et al., 2018 prosp. (n = 237)
Extrapulmonary specimens	83.7/67.4 (+16.3)	92.0/96.0 (-4)	Wu et al., 2019 prosp. (n = 200)
Paediatric patient	64.3/53.6 (+10.7) 65.8/64.4 (+1.4) 73.7/63.2 (+10.5)	100/100 (0) 96.6-99.6 (-3)	Sabi, Rachow et al., 2018 prosp. (n = 215) Nicol, Workman et al., 2018 (n = 306) ^a Nicol, Workman et al., 2018 (n = 76) ^b
Paediatric patient (HIV-negative only)	52.6/47.4 (+5.2)	—	Sabi, Rachow et al., 2018 prosp. (n = 215)
Paediatric patient (HIV-positive only)	88.9/67.7 (+21.2)	—	Sabi, Rachow et al., 2018 prosp. (n = 215)
Rifampicin resistance detection	92.7/92.7 (0) 95/95 (0)	98/99 (-1) 98/98 (0)	Chakravorty, Simmons et al., 2017 retrospect. (n = 277) Dorman, Schumacher et al., 2018 prosp. (n = 1753)

Ssb Ultra (83%) >> Xpert (67%)

Xpert MTB/RIF Ultra for detection of *Mycobacterium tuberculosis* and rifampicin resistance: a prospective multicentre diagnostic accuracy study

Lancet Infect Dis 2018;

Tuberculosis detection*

	Sensitivity: all culture-positive (95% CI; n/N)	Sensitivity: smear-negative (95% CI; n/N)	Sensitivity: HIV-negative (95% CI; n/N)†	Sensitivity: HIV-positive (95% CI; n/N)	Specificity (95% CI; n/N)
Xpert	83% (79 to 86; 383/462)	46% (35 to 57; 137/300)	90% (84 to 96; 145/161)	90% (68 to 94; 88/155)	98% (97 to 99; 960/977)
Xpert Ultra	88% (85 to 91; 408/462)	63% (54 to 71; 86/137)	90% (86 to 95; 145/159)	90% (83 to 95; 103/115)	96% (94 to 97; 934/977)
Difference (Xpert Ultra minus Xpert)	5.4% (3.3 to 8.0; 25/162)	17% (10 to 24; 23/137)	1.3% (-1.8 to 4.9; 2/159)	13% (6.4 to 21; 15/115)	-2.7% (-3.9 to -1.7; 36/977)

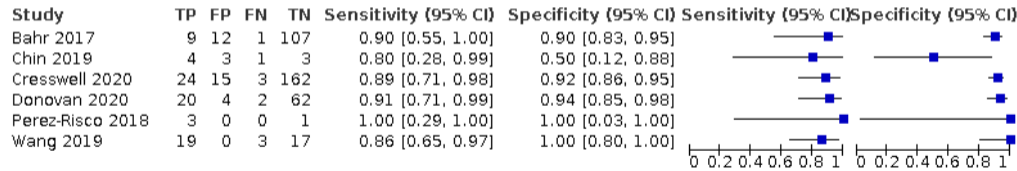
Ssb Ultra (88%) > Xpert (83%)

ED (-): Ssb Ultra (63%) > Xpert (46%)

Xpert MTB-Rif[®] Ultra

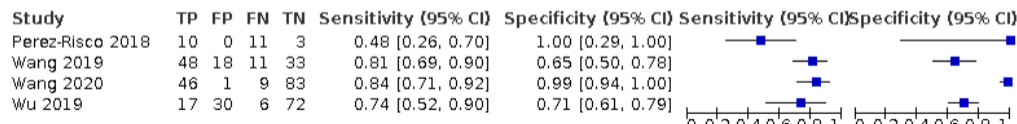
Test 1. Cerebrospinal fluid, Xpert Ultra, culture

Cerebrospinal fluid, Xpert Ultra, culture



Test 7. Pleural fluid, Xpert Ultra, culture

Pleural fluid, Xpert Ultra, culture



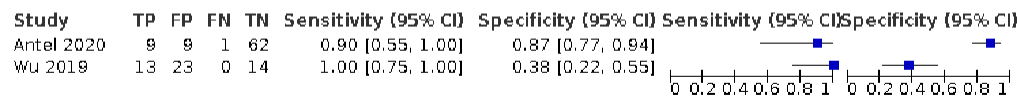
Test 13. Lymph node aspirate, Xpert Ultra, culture

Lymph node aspirate, Xpert Ultra, culture



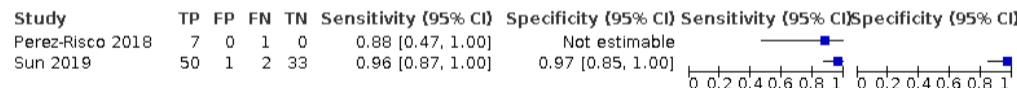
Test 17. Lymph node biopsy, Xpert Ultra, culture

Lymph node biopsy, Xpert Ultra, culture



Test 24. Bone or joint aspirate, Xpert Ultra, culture

Bone or joint aspirate, Xpert Ultra, culture



	Ssb %	Spc %
LCR	80-100	50-100
Liquide pleural	48-84	65-100
Ponction ganglionnaire	78	79
Biopsie ganglionnaire	90-100	38-87
Biopsie OA	88-96	97

PCR : résumé...



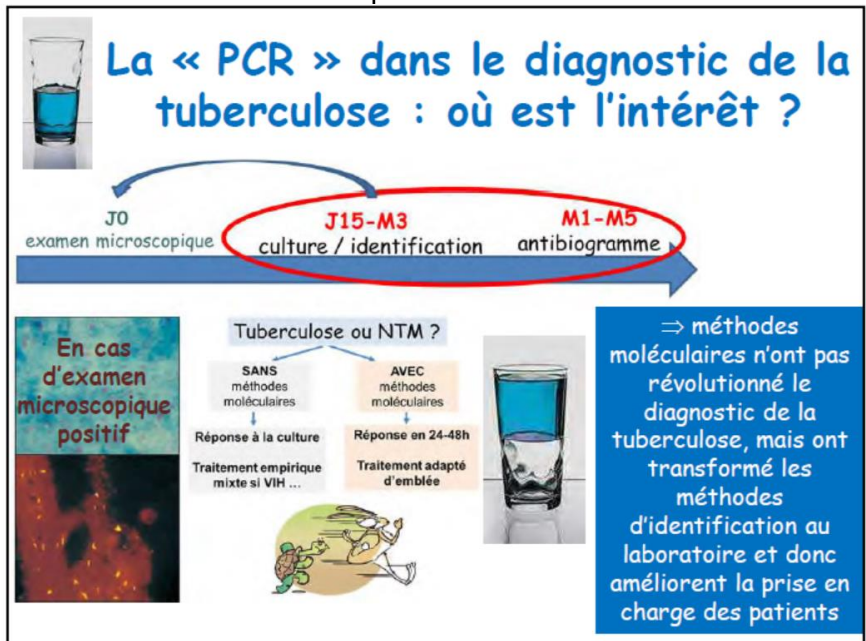
Principaux problèmes:

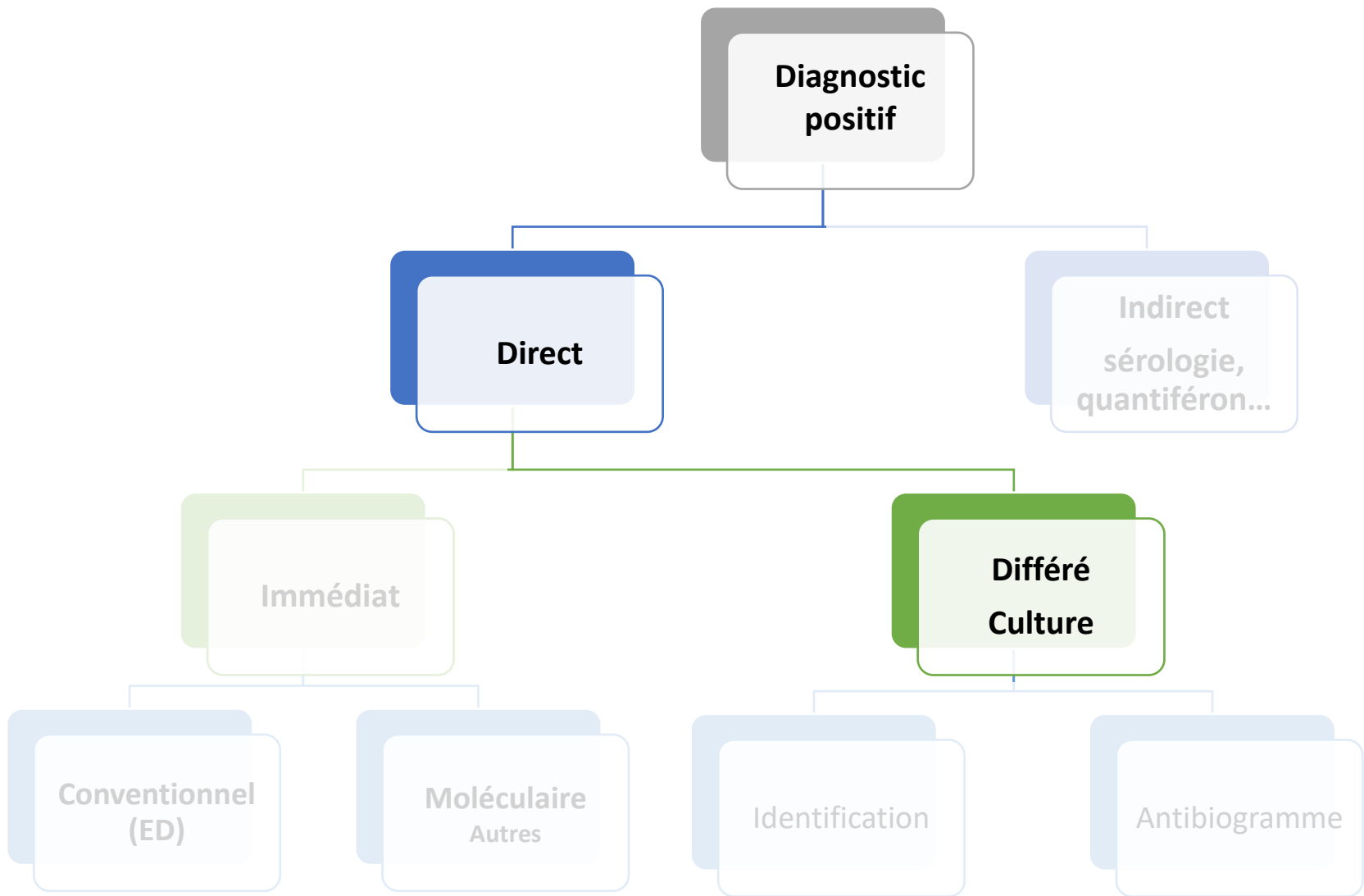
- Sensibilité imparfaite si ED (-) (pallié par Xpert® Ultra)
- Pas de renseignements sur la viabilité de la mycobactérie
- Présence d'inhibiteurs (Hb et hémine)

Dialogue clinico-biologique

+++

Aucun « bon » résultat sans
« bon » prélèvement





Culture



Milieux solides

Löwenstein Jensen (LJ):

- Technique de référence (OMS)
- Sensible

Milieu de Coletsos:

- Enrichi en pyruvate de Na⁺
- Appauvri en glycérol

M. bovis +++

!!! Lenteur (3 semaines à 3 mois)

Milieux liquides

7H9: Bactec[®], MGIT[®], MB/BacT Alert[®]

- Détection automatisée
- !! Coûteux
- Taux de contamination élevé

Détection précoce ≈10j



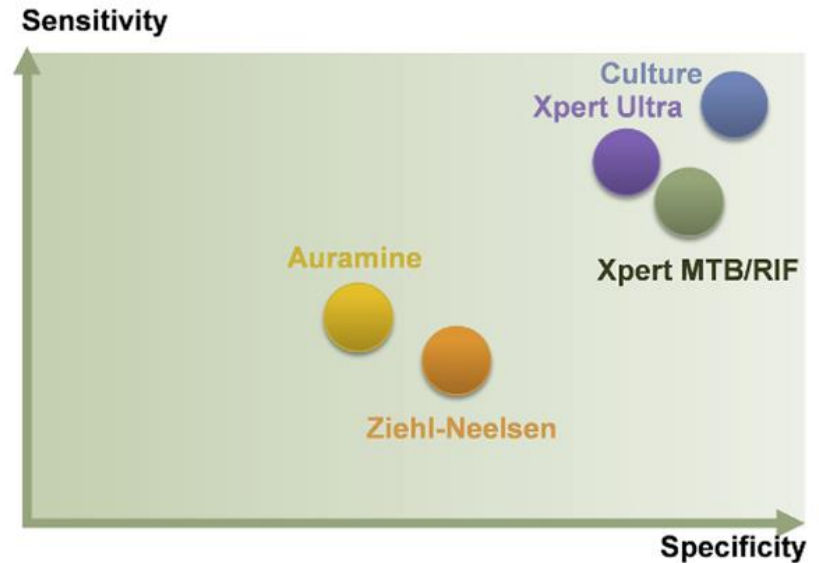
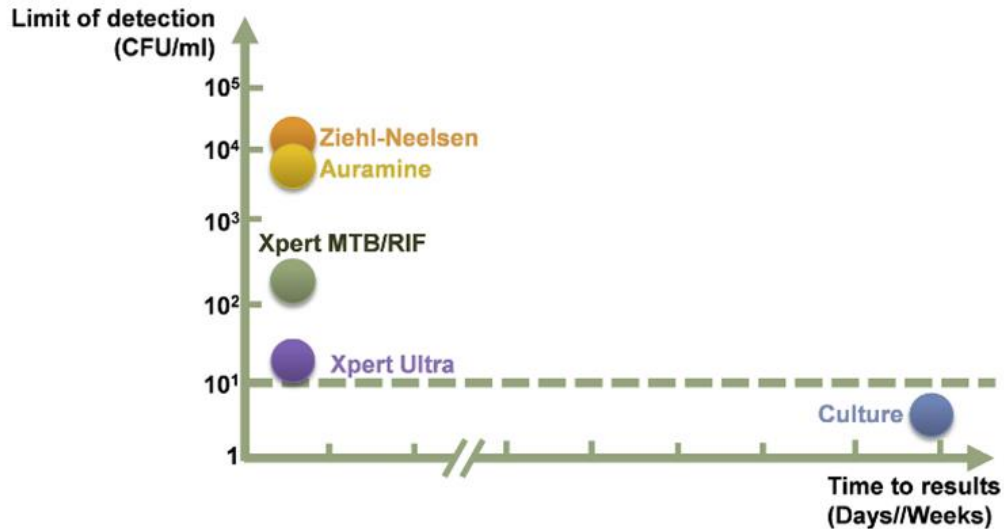
Culture

Performance of solid and liquid culture media for the detection of *Mycobacterium tuberculosis* in clinical materials: meta-analysis of recent studies

Eur J Clin Microbiol Infect Dis (2014) 33:867–870

Milieu de culture	Ssb	Spc	Délai (+)	Particularités
LJ	98%	100%	3-4 sem	Gold standard
Coletsos	-	-	3-4 sem	Détection de <i>M. bovis</i>
Bactec 460	90%	75%	8-18 j	Produits radioactifs
MGIT	96%	82%	8-18 j	Indicateur de fluorescence
BacT Alert	95%	99%	13-16 j	Risque de contamination
Microplaques	97,8%	99%	> 5 ^{ème} j	Risque de contamination

Comparaison des performances

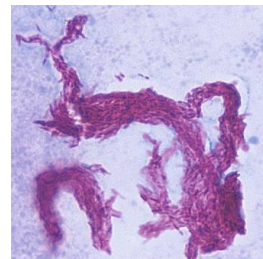
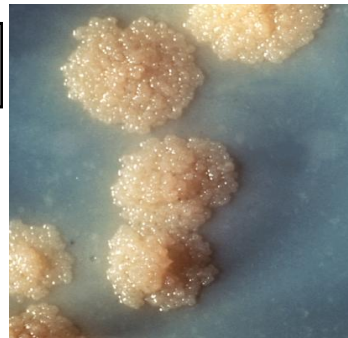


Identification



Phénotypique

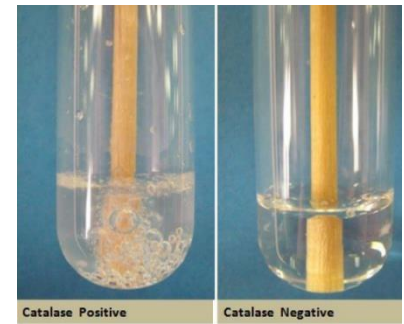
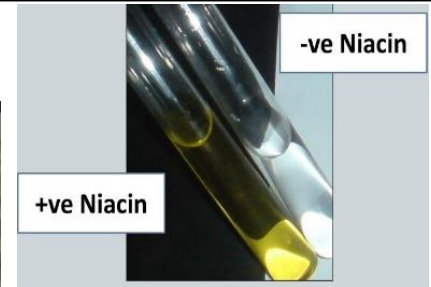
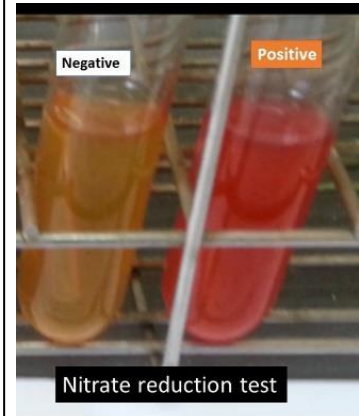
M. tuberculosis



M. bovis



Biochimique



Fastidieuses et dangereuses

Identification

Détection immunochromatographique de l'Ag MPT64



BD MGIT® TBc

1) Utilisation



Prélever:
liquide,
colonies
diluant.

2) Lecture après 15 mn



NEGATIF

Visualisati
ontrôle

POSITIF

Visualisati
ontrôle et
du comple

BIOLINE TB Ag. MPT64

ELSEVIER

Diagnostic Microbiology and Infectious Disease xx (2010) xxx–xxx

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE

www.elsevier.com/locate/diagnicrobio

Spc 100% Ssb: 99%

Evaluation of an immunochromatographic assay for rapid identification of *Mycobacterium tuberculosis* complex in clinical isolates[☆]

Manel Marzouk, Imen Ben Kahla, Naila Hannachi, Asma Ferjeni, Walid Ben Salma, Samira Ghezal, Jalel Boukadida*

Laboratory of Microbiology and Immunology, UR02-SP13, University Hospital Farhat Hached, Sousse 4000, Tunisia

Fait en 10-15 mn, facile et peu couteux
Progrès majeur dans les laboratoires faisant de la culture



M.tuberculosis??

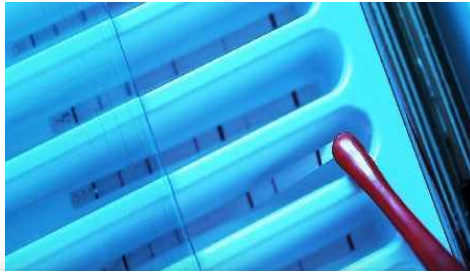
M.bovis??

Complexe *tuberculosis*

- A partir des cultures solides ou liquides
- Basée sur la présence de l'Antigène **MPT64**
- Appartenance des souches au CMT
- Sans discrimination d'espèces
- Recommandé par l'OMS

Mycobactérie: identification

PCR avec Hybridation inverse Genotype™ MTBC (Hain Lifescience)



Published online 2016 October 3.

Case Report

Disseminated Bacille Calmette-Guérin Infection in Immunodeficient Infants; Report of Two Cases

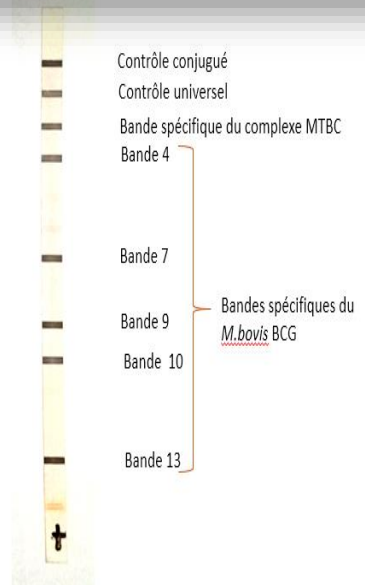
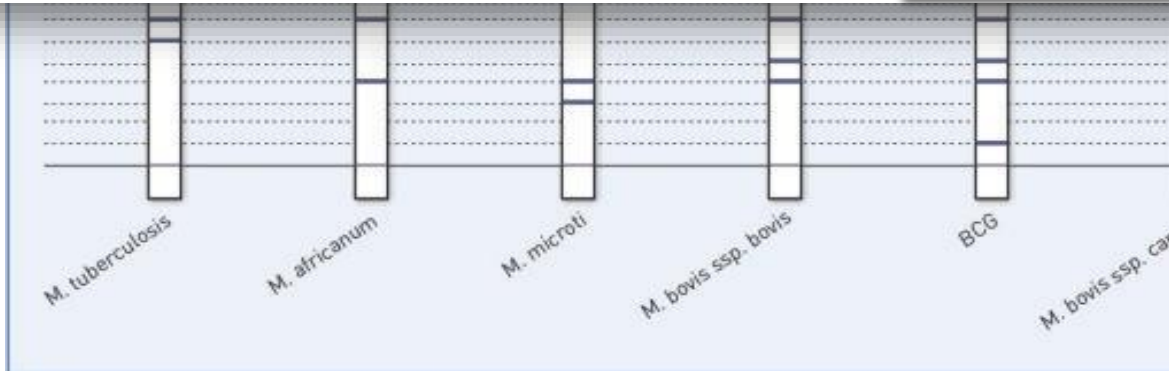
Ahmed Ben Hadj Hassine,^{1,2,*} Manel Marzouk,¹ Hichem Bargui,^{1,2} Miniar Tifha,³ Mohamed Dhaou,¹ and Jalel Boukadida¹

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2002, p. 3076–3078
0095-1137/02/\$04.00+0 DOI: 10.1128/JCM.40.8.3076–3078.2002
Copyright © 2002, American Society for Microbiology. All Rights Reserved.

GenoType Mycobacterium Assay for Identification of Mycobacterial Species Isolated from Human Clinical Samples by Using Liquid Medium

P. Ruiz, J. Gutierrez, F. J. Zerolo, and M. Casal*

Ssb & Spc 99%



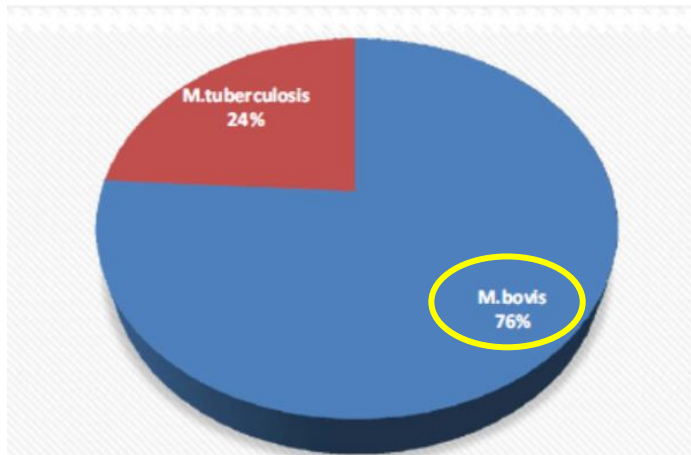
Identification d'une souche de *M. bovis* BCG par le kit GenoType® MTBC

Mycobactéries incriminées

Diagnosis of lymph node tuberculosis using the GeneXpert MTB/RIF in Tunisia

Asma Ghariani ^{a,c,*}, Taha Jaouadi ^{a,c}, Selma Smaoui ^{b,c}, Emna Mehiri ^{a,c}, Chama Marouane ^{b,c}, Sana Kammoun ^{b,c}, Leila Essalah ^a, Maha Driss ^d, Feriele Messadi ^{b,c}, Leila Slim-Saidi ^{a,c}

INTERNATIONAL JOURNAL OF MYCOBACTERIOLOGY 4 (2015) 270–275



Isolation and molecular characterisation of *Mycobacterium bovis* from raw milk in Tunisia

* Ben Kahla I^{1,2}, Boschiroli ML³, Souissi F¹, Cherif N¹, Benzarti M⁴, Boukadida J², Hammami S¹

¹ Veterinary Research Institute of Tunisia, 20, Avenue Djebel Lakhdhar, Tunis, Tunisia; ² Microbiology and Immunology Laboratory, CHU Farhat Hached, Tunis, Tunisia; ³ National and OIE/FAO Bovine Tuberculosis Reference Laboratory, Tunis, Tunisia; ⁴ Laboratory- French Agency for Food, Environment and Occupational Health Safety, 23 Avenue du Général-de-Gaulle, 94706 Maisons-Alfort Cedex, France; ⁵ National Veterinary Medicine School, Sidi Thabet, Tunisia.

Tunisie: TBC bovine endémique

Mesures de lutte contre la TBC bovine depuis 1985 MAIS encore Problèmes d'assainissement des élevages et consommation de lait et dérivés non pasteurisés

Current Diagnosis and Management of Peripheral Tuberculous Lymphadenitis

Jose-Mario Fontanilla,¹ Arti Barnes,² and C. Fordham von Reyn³

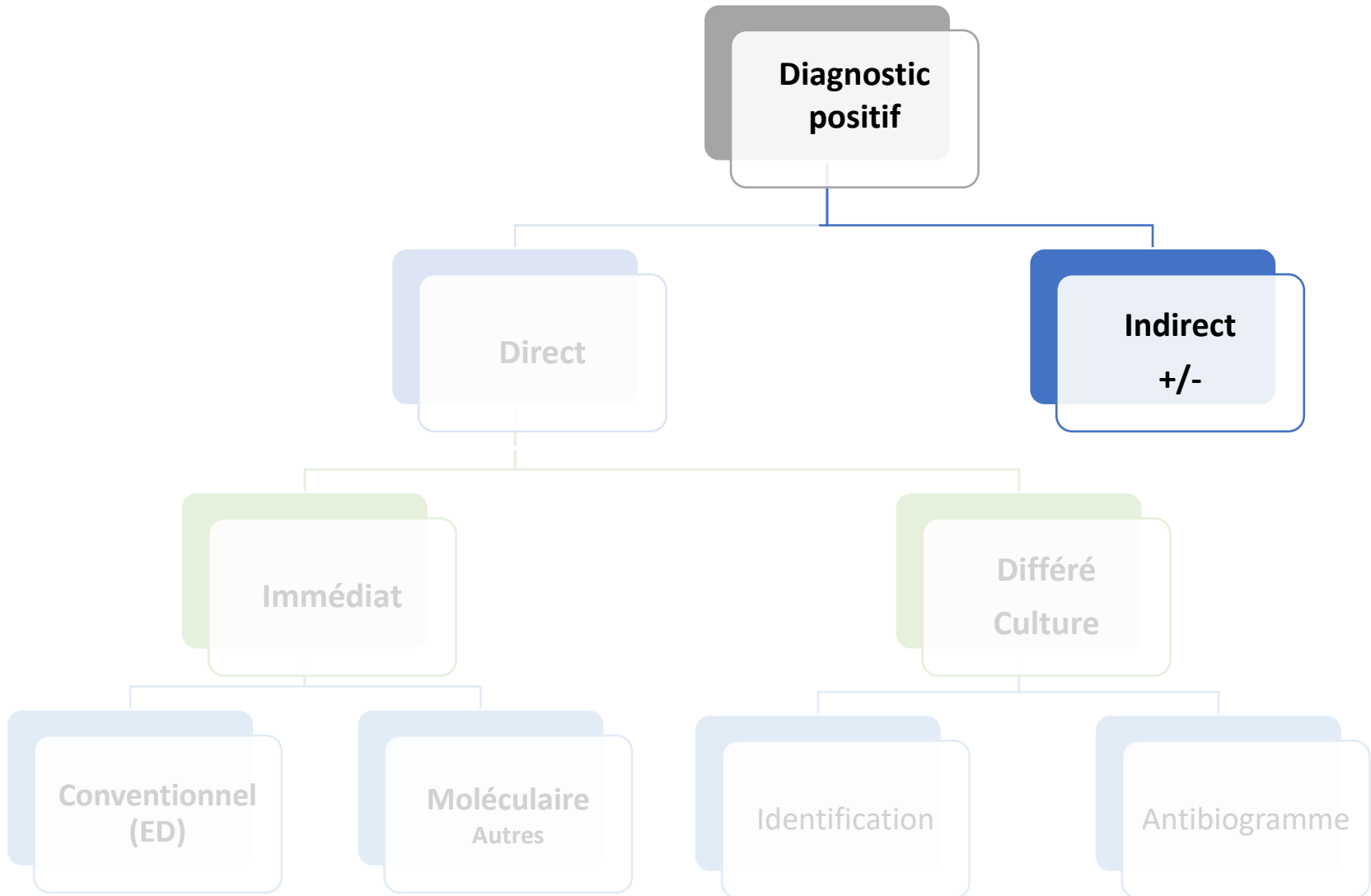
¹Joan C. Edwards School of Medicine, Marshall University, Huntington, West Virginia; ²Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, Mississippi; and ³Infectious Disease and International Health, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

Peripheral tuberculous lymphadenitis accounts for ~10% of tuberculous lymphadenitis in the United States. Epidemiologic characteristics include a 1.4:1 female-to-male ratio, age range of 20–40 years, and dominant foreign birth, especially East Asian. Patients present with a history of painless swelling of a single group of cervical lymph nodes. Definitive diagnosis is by histopathology or nucleic acid amplification of *Mycobacterium tuberculosis*; demonstration of granulomatous inflammation may be helpful. Excisional biopsy has the highest sensitivity, but fine-needle aspiration is less invasive and may be useful, especially in immunocompetent patients. Antimycobacterial therapy remains the cornerstone of treatment. Response is slower than with pulmonary tuberculosis; persistent pain and swelling are common, and paradoxical upgrading reactions may occur in 20% of patients. The role of steroids is controversial. Initial excisional biopsy deserves consideration for both optimal diagnosis and management of the otherwise slow response to therapy.

Pays développés: M.tuberculosis ++

Autres localisations Extra-pulmonaires ??





Dgc indirect: IGRA

Spc +++ >> IDR

Non influencé par BCG

- Interferon Gamma Release Assays
- MEE in vitro de l'immunité cellulaire spécifique \neq TBC
- Détection INF γ produit/ λ T après stimulation/Ag spécifiques du complexe *tuberculosis* (ESAT-6, CFP-10, TB7-7)
 - Quantiféron[®]-TB Gold (Cellestis Ltd., Australia): sur sang total
 - T-SPOT[™].TB (Oxford Immunotec, UK): sur cellules mononuclées

Dgc de TBC latente
Non indiqué pour confirmer une TBC active

MAIS en pratique très utilisé pour le dgc de TEP !?

Interferon-gamma release assays for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis

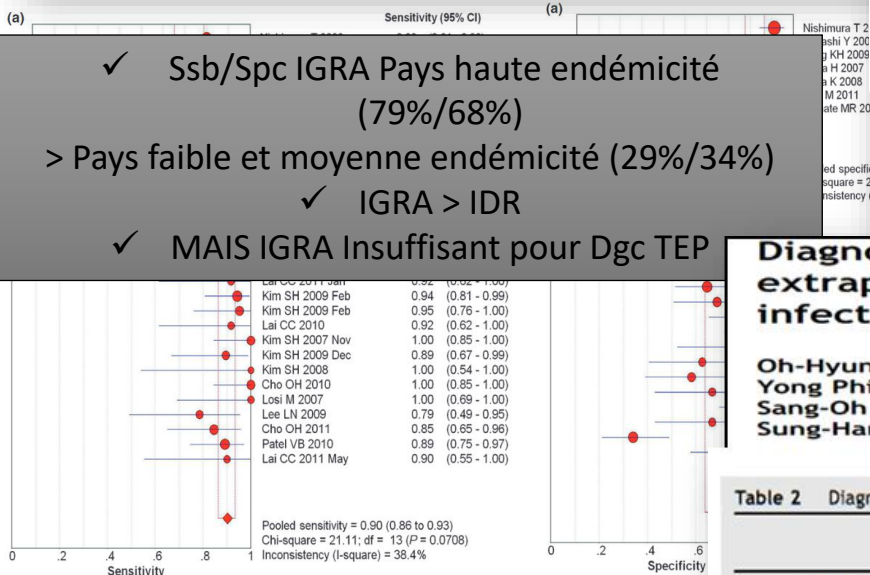
Lin Fan¹, Zhou Chen², Xiao-Hui Hao¹, Zhong-Yi Hu¹ & He-P

The Benefit of Interferon-Gamma Release Assay for Diagnosis of Extrapulmonary Tuberculosis

Cleopas M. Rumende, Edward J. Hadi, Gloria Tanjung, Imelda N. Saputri, Raditya Sasongko

Indones J Intern Med-2018

Indonésie: Pays haute endémicité (2018)
Ssb: 87,7%, Spc: 63%, VPP: 83,3%, VPN: 70,8%



- ✓ Ssb/Spc IGRA Pays haute endémicité (79%/68%)
- > Pays faible et moyenne endémicité (29%/34%)
- ✓ IGRA > IDR
- ✓ MAIS IGRA Insuffisant pour Dgc TEP

Diagnostic performance of T-SPOT.TB for extrapulmonary tuberculosis according to the site of infection[☆]

Oh-Hyun Cho^{a,c}, Ki-Ho Park^a, Sun-Mi Kim^a, Su-Jin Park^a, Song Mi Moon^a, Yong Phil Chong^a, Heungsup Sung^b, Mi-Na Kim^b, Jin-Yong Jeong^a, Sang-Oh Lee^a, Sang-Ho Choi^a, Jun Hee Woo^a, Yang Soo Kim^a, Sung-Han Kim^{a,*}

Journal of Infection (2011)

Table 2 Diagnostic performance of the blood T-SPOT.TB in 325 patients with suspected extrapulmonary tuberculosis.

	Sensitivity % (n/N, ^a 95% CI)	Specificity % (n/N, ^b 95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)
Confirmed or probable tuberculosis (n = 153) versus not tuberculosis (n = 172)				
Site of infection				
Lymph node	84 (129/153, 78–89)	51 (87/172, 43–58)	60 (54–67)	78 (70–85)
Abdominal	89 (48/54, 78–95)	60 (6/10, 31–83)	92 (82–97)	50 (25–75)
Central nervous system	79 (30/38, 64–89)	54 (15/28, 36–70)	70 (55–81)	65 (45–81)
Osteoarticular	74 (26/35, 58–86)	46 (40/87, 36–56)	36 (27–47)	82 (69–90)
Miliary	100 (28/28, 88–100)	55 (21/38, 40–70)	62 (48–75)	100 (85–100)
Disseminated	89 (25/28, 73–96)	not applicable	not applicable	not applicable
Presentation				
Chronic forms	88 (42/48, 75–94)	67 (2/3, 21–94)	98 (88–99)	25 (7–59)
Indeterminate forms	88 (42/48, 75–94)	67 (2/3, 21–94)	98 (88–99)	25 (7–59)
Acute forms	88 (42/48, 75–94)	67 (2/3, 21–94)	98 (88–99)	25 (7–59)
Immune status				
Immunocompetent	88 (105/120, 80–92)	45 (54/120, 36–54)	61 (54–68)	78 (67–86)
Immunocompromised	73 (24/33, 56–85)	63 (33/52, 50–75)	56 (41–70)	79 (64–88)

^a Number of patients with a positive test result/number of patients tested.
^b Number of patients with a negative test result/number of patients tested.

CHINE Pays de Haute endémicité

Ssb IGRA si TB gg, OA (89-100%)
> TB méningée, péritonéale (74-79%)
Spc < 60%
VPP: 36-98%
VPN: 25-100%

Test urinaire de lipoarabinomannane

☐ LAM= Ag

☐ Test imm

✓ Peu co

✓ utilisé

✓ Si co-i

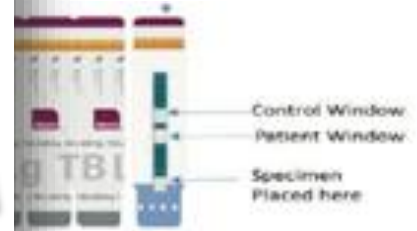
WHO policy recommendations

- Except for persons with HIV infection with low CD4 counts or who are seriously ill, LF-LAM should not be used for the diagnosis of TB (strong recommendation, low quality of evidence)

- LF-LAM is not recommended for the diagnosis of TB (pulmonary and/or extrapulmonary) in HIV positive patients who have a CD4 cell count less than or equal to 350 cells/mm³, or HIV positive patients who are seriously ill regardless of CD4 count or with unknown CD4 count (conditional recommendation; low quality of evidence).

LF-LAM indiqué pour le dgc de TEP si HIV (+)
Ssb ↗ si CD4 ↘

TBC



Comment > J Infect. 2017 Dec

The diagnostic accuracy of urine lipoarabinomannan antigen in detection of culture pulmonary tuberculosis (EPTB)

Fatimah O Juma¹, Gerald Yonga², Peter Waweru¹, Gunturu Revathi³, Mark Nelson⁴, Reena Shah⁵

HIV (-): Ssb: 57,1%; Spc: 93,3%
HIV (+): Ssb: 68,2%; Spc: 93,3%

Asnake Simieneh^{1,2,3*}, Mulalem Tadesse^{1,2*}, Wakjira Kebede^{1,2}, Mulatu Gashaw², Gemeda Abebe^{1,2}

Table 2. Diagnostic performance of TB-LAM and Xpert MTB/RIF test.

Diagnostic Accuracy	Culture as a reference	
	TB-LAM test	Xpert MTB/RIF test
Sensitivity (95%CI)	34.8% (16.4-57.3);8/23	69.6% (47.1-86.8);16/23
Specificity (95%CI)	91.3% (81.1-95.9);94/103	100% (97.1-100);124/124
PPV (95%CI)	47.1% (27.8-67.3);8/17	100%(79.4-100); 16/16
NPV (95%CI)	86.2% (82.2-89.5);94/109	94.7% (90.5-97.1);124/131

Dosage de l'Adénosine Désaminase

VPN (>97%) si < 40UI/L
Excellente VPP si > 70UI/L

- ADA: enzyme de maturation et de κ λ
- Marqueur indirect pour le dgc de la TB dans les liquides d'épanchement (mais \nearrow si sarcoïdose, Néoplasie, LES, PR..)

Type d'atteintetuberculeuse	Prélèvement	Sensibilité [%]	Spécificité [%]	Valeur seuil (UI/l)
Pleurale	Epanchement pleural	88–100	81–97	40
Péricardique	Epanchement péri-cardique	87–93	89–97	40
Abdominale	Ascite	100	97	39
Système nerveux central	Liquide céphalo-rachidien	84–92	87–93	10
Articulaire	Liquide synovial	85	66	40

Conclusion

Penser à envoyer les prélèvements
au laboratoire de Microbiologie

- TEP: fréquente en Tunisie +++
- Dgc Bactériologique +++
- Techniques conventionnelles = Référence malgré leur caractère lourd et fastidieux
- Nouvelles techniques génomiques:
 - Fiabilité non absolue pour le dgc (+)
 - Rapidité +++

Penser à une localisation
pulmonaire concomitante

Pas de techniques parfaites mais
complémentaires

Merci

