MCHENRY COUNTY
TUBERCULOSIS CARE AND TREATMENT BOARD MEETING
2200 N. SEMINARY AVE. BUILDING A
WOODSTOCK, ILLINOIS 60098
January 16, 2018
8:00 AM

AGENDA

1. Call to Order

2. Public Participation

3. Minutes of November 2017 Meeting.

4. Consent Agenda
   A) Disbursements; November-December 2017
   B) Income and Expense Report; November-December 2017

5. Monthly Report
   A) TB Nurse Report
   B) Statistics
   C) TB Profile
   D) IDPH Report

6. Program Highlights

7. Old Business (For Discussion)
   A) Update on XDR case

8. New Business (For Discussion)

9. Board Issues (For Discussion)

10. Information and Communication (For Discussion)

    Xie, X., Li, F., Chen, J.-W., Wang, J. (August 2014). Risk of tuberculosis infection in anti-TNF- α biological therapy: From bench to bedside. *Journal of Microbiology, Immunology and Infection*, 47(4), 268-274. Retrieved from http://www.sciencedirect.com/science/article/pii/S168411821300039X

11. Executive Session

12. Adjournment

MINUTES AND CONSENT AGENDA

MCHENRY COUNTY TUBERCULOSIS AND TREATMENT BOARD

MEETING MINUTES

NOVEMBER 28, 2017

CALL TO ORDER:

Marylou Ludicky RN MPH called the meeting to order at 8:05am; TB Board Members present were: James Mowery M.D, Marylou Ludicky RN MPH, and Rebecca Rockwood M.T; Staff present were: Michael Hill MPH, MPA, FACHE, CHES, Administrator, Susan Karras RN, BSN, MBA, Director of Nursing, Jennifer Schorsch, BS, RN, NE-BC, Assistant Director of Nursing, Sara Boline MPH Communicable Disease Coordinator, Amanda Kurka BSN RN, and Karen Stephenson TB RN.

MINUTES:

James Mowery M.D made motion to approve TB Board Minutes for September/October 2017; second by Rebecca Rockwood M.T.

FINANCIAL STATUS:

Marylou Ludicky RN MPH reviewed the Disbursements as well as the Income and Expense Report for September/October 2017. Rebecca Rockwood M.T made motion to approve; second by James Mowery M.D.

MONTHLY REPORTS:

Sara Boline MPH Communicable Disease Coordinator, reviewed TB Nurse Report for September/October 2017.

Skin testing

- In September 16 clinics were held with 45 clients tested
- In October 17 clinics were held with 63 clients tested

Doctor clinic

- On September 18th, Doctor's clinic was held with 7 chest x-rays and 14 charts reviewed
- On October 16th, Doctor's clinic was held with 11 chest x-rays and 19 charts reviewed

Patient update

- All 9 contacts of our XDR patient had their final evaluations and were discharged
- 38 year old gentleman on 12 week LTBI program was discharged

Activities

- PADS TB testing 10/17/17 at the center and 10/23/2017 at evening church sites

Webinars/Trainings

10/16/2017 Prednisone Attenuates IRIS in TB-HIV

10/17/2017 Point of Care Assay Zeros in on Drug-Resistant TB Mutations

10/24/2017 TB Vaccines Where are We & What Needs to be Done

10/25/2017 What's the Plus in Quantiferon

10/17/2017 Point of Care Assay Zeros in on Drug-Resistant TB Mutations

10/24/2017 TB Vaccines Where are We & What Needs to be Done

10/25/2017 What's the Plus in Quantiferon

OLD BUSINESS:

NEW BUSINESS:

A) New Assistant Nursing Director Jennifer Schorsch
B) New TB Nurse Amanda Kurka
C) Updates for Building B no resolution yet until December's meeting

BOARD ISSUES:

NFORMATION:

Cousins, Sophie. (2017, October 16). 3 innovations that could transform TB diagnosis and care. Retrieved from: https://www.devex.com/news/3-innovations-that-could-transform-tb-diagnosis-and-care-91271

ADJOURNMENT:

Marylou Ludicky RN MPH made motion to adjourn meeting at 8:30am; second by Rebecca Rockwood M.T.

MCHENRY COUNTY HEALTH DEPARTMENT
TB - DISBURSEMENTS
November-December 2017 ~ Preliminary as of 1/8/2017
SUMMARY

PERSONAL SERVICES:	ACCT#		PAYROLL	
Acevedo, Lola	3010	$	7,188.74	
Cazares, Maria	3020	$	4,443.27	
Kurka, Amanda	3010	$	9,888.98	Name Changed from Appner
Schoen, Faith	3010	$	10,288.05	
Stephenson, Karen	3010	$	6,610.96	
	3025	Included in above		
FICA	3105	$	2,918.43	
IMRF	3110	$	3,929.46	
INSURANCE	3146	$	7,164.72	INS for Sept-Nov posted in Nov-17
	Subtotal		52,432.61	12/29/17 Payroll not posted as of 1/8/18

DESCRIPTION:	ACCT #	AMOUNT
Contractual Services	4001	5,199.00
Assoc. Dues/Memberships	4005	
Training	4006	
Subscriptions	4008	
Printing	4055	
Telephone	4096	59.97
Rent	4101	
Maint. Agreements	4130	
Maint Office Equipment	4131	
Medical	4246	748.00
Special Consultants	4435	
Private Lab Services	4442	43.76
Refuse disposal	4449	50.00
Contingent	4570	
Office Supplies	5010	288.75
Office Equipment	5020	
Postage	5030	
Mileage	5040	187.25
Meeting Expenses	5050	64.71
Supplies	5070	500.00
Medical Supplies	5080	
Medication	5085	390.64
Fuel, oil, grease	5160	
TB Test Refund	8090	10.00
TOTAL EXPENSES		
	Expense Total	7,542.08
	Grand Totals	**$ 59,974.69**

MCHENRY COUNTY HEALTH DEPARTMENT
TB - DISBURSEMENTS
November 2017 (FY17)~ Preliminary as of 12/19/2017

Personal Service	ACCT #	PAYROLL	
Acevedo, Lola	3010	$2,850.00	
Cazares, Maria	3020	$1,767.84	
Kurka, Amanda	3010	$3,940.51	Name Changed from Appner to Kurka
Schoen, Faith	3010	$4,086.00	
Stephenson, Karen	3010	$2,624.60	
	3025	Included in above	
FICA	3105	$1,168.08	
IMRF	3110	$1,572.72	
INSURANCE	3146	$5,373.54	INS for Sept-Nov posted in Nov-17
	Payroll Total	**$23,383.29**	

VD	VENDOR	ACCT #	AMOUNT
JE217882	HD Adm'n Charge - Q4	4001	$5,000.00
VD317177	VERIZON WIRELESS	4096	$31.05
VD317572	VERIZON WIRELESS	4096	$28.92
VC285461	METRO INFECTIOUS DISEASE CONSULTANTS	4246	$500.00
VC286035	MERCY HEALTH SYSTEM CORP	4246	$248.00
VC285805	ACL LABORATORIES	4442	$26.86
VC286177	ACL LABORATORIES	4442	$16.90
VC286174	HEALTHCARE WASTE MANAGEMENT	4449	$50.00
VD316860	WAREHOUSE DIRECT INC	5010	$159.95
VD317072	WAREHOUSE DIRECT INC	5010	$128.80
VD316861	PEREZ ANGELICA	5040	$29.96
VD317289	STEPHENSON KAREN	5040	$37.45
VD317289	ACEVEDO LOLA	5040	$29.96
VD317289	ACEVEDO LOLA	5040	$59.92
VD317289	PEREZ ANGELICA	5040	$29.96
VD317179	KURKA AMANDA	5050	$64.71
VD316861	WALMART WOODSTOCK	5070	$500.00
VC285460	BRANDT PHARMACY INC	5085	$6.09
VC285459	BRANDT PHARMACY INC	5085	$87.70
VC285807	BRANDT PHARMACY INC	5085	$105.24
VC285806	BRANDT PHARMACY INC	5085	$35.08
VD317290	SMITH MEDICAL PARTNERS	5085	$1.00
VD317290	SMITH MEDICAL PARTNERS	5085	$0.20
VC286188	BRANDT PHARMACY INC	5085	$50.09
VC286185	BRANDT PHARMACY INC	5085	$70.16
VC286181	BRANDT PHARMACY INC	5085	$35.08
VD316963	CALARA JAYSON	8090	$10.00
		Total Expenses	**$7,343.08**
		Grand Total	**$30,726.37**

MCHENRY COUNTY HEALTH DEPARTMENT
TB - DISBURSEMENTS Preliminary as of
December 2017 (FY18)

Personal Service	ACCT #	PAYROLL	
Acevedo, Lola	3010	$4,338.74	
Cazares, Maria	3020	$2,675.43	
Kurka, Amanda	3010	$5,948.47	
Schoen, Faith	3010	$6,202.05	
Stephenson, Karen	3010	$3,986.36	
	3025	Included in above	
FICA	3105	$1,750.35	
IMRF	3110	$2,356.74	
INSURANCE	3146	$1,791.18	Not posted as of 1/4/2018
	Payroll Total	$29,049.32	12/29/17 Payroll not posted as of 1/8/18

VD	VENDOR	ACCT #	AMOUNT
VD317552	STANS OFFICE MACHINES INC	4001	$199.00
		Total Expenses	$199.00
		Grand Total	$29,248.32

TUBERCULOSIS CARE AND TREATMENT FY2017

Preliminary 1-11-18

LINE ITEM	DEC	JAN	FEB	MARCH	APRIL	MAY	JUNE	JULY	AUG	SEPT	OCT	NOV	TOTAL		ANNUAL BUDGET	BALANCE REMAINING	% received
7010-PROPERTY TAXES						$16,688.07	$111,286.83	$2,722.26	$5,842.94	$107,103.57	$3,352.40	$2,371.83	**$249,367.90**	7010	$ 250,000.00	$ 632.10	99.7%
8090-FEES FOR SERVICE	$360.00	$220.00	$310.00	$230.00	$460.00	$480.00	$270.00	$425.20	$540.00	$430.00	$250.00	$210.00	**$4,185.20**	8090	$ 19,000.00	$ 14,814.80	22.0%
9405													**$0.00**	9405		$ -	0.0%
9417-MEDICAID				$4.00		$12.00	$32.00		$8.00	$16.00	$48.00	$4.00	**$124.00**	9417		$ (124.00)	#DIV/0!
9510-INTEREST INCOME	$204.50	$236.49	$203.71	$253.49	$266.88	$260.03	$335.88	$405.18	$390.86	$439.90	$460.25	$427.12	**$3,884.29**	9510	$ 600.00	$ (3,284.29)	647.4%
9511-RE TAX DIST INT													**$0.00**	9511	$ 25.00	$ 25.00	0.0%
9990													**$0.00**	9990	$ 106,451.00	$ 106,451.00	0.0%
TOTAL REVENUE	**$564.50**	**$456.49**	**$513.71**	**$487.49**	**$726.88**	**$17,440.10**	**$111,924.71**	**$3,552.64**	**$6,781.80**	**$107,989.47**	**$4,110.65**	**$3,012.95**	**$257,561.39**		**$ 376,076.00**	**$ 118,514.61**	**68.5%**
3010-REGULAR SALARIES	$17,745.79	$9,436.28	$13,726.11	$13,039.81	$12,728.07	$13,716.59	$19,769.84	$11,152.94	$9,560.30	$9,082.26	$3,197.78	$12,826.05	**$145,981.82**	3010	$ 166,215.00	$20,233.18	87.8%
3020-PART TIME SALARY	$2,449.99	$1,473.71	$1,760.22	$1,680.21	$1,680.21	$1,684.02	$2,560.32	$1,680.21	$1,767.84	$1,680.21	$974.16	$1,680.21	**$21,071.31**	3020	$ 20,665.00	($406.31)	102.0%
3025-Holiday	$1,510.22	$1,929.64		$773.94	$905.17	$93.32	$906.94	$1,186.52		$565.66	($747.31)	$762.69	**$7,886.79**	3025	$ 9,836.00	$1,949.21	80.2%
3040-Overtime					$270.76								**$270.76**	3040		($270.76)	#DIV/0!
3050-MERIT POOL													**$0.00**	3050	$ 3,934.00	$3,934.00	0.0%
3105 -SOC.SEC/CTY SHARE	$1,660.50	$982.23	$1,184.70	$1,185.28	$1,192.19	$1,185.28	$1,777.63	$1,072.51	$866.60	$866.60	$274.89	$1,168.08	**$13,416.49**	3105	$ 15,350.00	$1,933.51	87.4%
3110 -ILL MUNIC RET FUND	$2,222.68	$1,322.48	$1,595.10	$1,595.88	$1,605.18	$1,595.88	$2,393.43	$1,444.04	$1,166.81	$1,166.81	$358.82	$1,572.72	**$18,039.83**	3110	$ 20,667.00	$2,627.17	87.3%
3146-EMPLOYEES HEALTH		$2,647.18	$1,791.18			$5,373.54	$1,791.18	$1,791.18		$3,582.36		$5,373.54	**$22,350.16**	3146	$ 33,222.00	$10,871.84	67.3%
PERSONNEL SUBTOTAL:	**$25,589.18**	**$17,791.52**	**$20,057.31**	**$18,275.12**	**$18,381.58**	**$23,648.63**	**$29,199.34**	**$18,327.40**	**$13,361.55**	**$16,943.90**	**$4,058.34**	**$23,383.29**	**$229,017.16**		**$ 269,889.00**	**$40,871.84**	**84.9%**
4001-Contractual Services			$199.00	$5,000.00			$5,000.00			$5,000.00		$5,000.00	**$20,199.00**	4001	$ 25,000.00	$4,801.00	80.8%
4005-ASSOC.DURS/STAFF								$130.00					**$130.00**	4005	$ 350.00	$220.00	37.1%
4006-TRAINING													**$0.00**	4006	$ 1,000.00	$1,000.00	0.0%
4008-SUBSCRIPTIONS													**$0.00**	4008		$0.00	#DIV/0!
4055-PRINTING													**$0.00**	4055	$ 400.00	$400.00	0.0%
4096-TELEPHONE		$28.30	$27.29	$30.45	$28.53	$28.05	$27.83	$35.85	$29.35	$32.74	$27.69	$59.97	**$356.05**	4096	$ 1,800.00	$1,443.95	19.8%
4101-RENT													**$0.00**	4101		$0.00	
4130-MAINTENANCE Agreement			$25.29		$1,347.75	$18.19		$19.52			$16.15		**$1,426.90**	4130	$ 562.00	($864.90)	253.9%
4131-MAINTENANCE OFFICE EQUIP				$38.28									**$38.28**	4131	$ 500.00	$461.72	7.7%
4246-MEDICAL			$372.00	$1,120.00	$496.00	$1,686.00	$620.00	$124.00	$1,000.00	$310.00	$1,930.00	$748.00	**$8,406.00**	4246	$ 35,000.00	$26,594.00	24.0%
4320-Repair and Maintenance													**$0.00**	4320		$0.00	#DIV/0!
4442-LAB			$14.94	$14.94	$9.96	$9.96	$34.86	$9.96	$29.88	$14.94	$29.88	$43.76	**$213.08**	4442	$ 2,500.00	$2,286.92	8.5%
4449-GARBAGE DISPOSAL				$50.00			$50.00			$100.00		$50.00	**$250.00**	4449	$ 850.00	$600.00	29.4%
4570-Contingent-Jane Doe Expense													**$0.00**	4570		$0.00	#DIV/0!
CONTRACTUAL SUBTOTAL:	**$0.00**	**$28.30**	**$638.52**	**$6,253.67**	**$1,882.24**	**$1,742.20**	**$5,732.69**	**$319.33**	**$1,059.23**	**$5,457.68**	**$2,003.72**	**$5,901.73**	**$31,019.31**		**$ 67,962.00**	**$36,942.69**	**45.6%**
5010-OFFICE SUPPLIES						$94.33		$20.74	$175.50	$37.37		$288.75	**$616.69**	5010	$ 1,700.00	$1,083.31	36.3%
5020-OFFICE EQUIPMENT													**$0.00**	5020	$ 1,500.00	$1,500.00	0.0%
5030-Postage			$21.27										**$21.27**	5030	$ 100.00	$78.73	21.3%
5040-MILEAGE		$154.44	$100.58	$59.92	$29.96	$125.19	$81.32	$172.27	$66.34	$134.82	$29.96	$187.25	**$1,142.05**	5040	$ 4,000.00	$2,857.95	28.6%
5050-MEETING EXPENSE										$188.86		$64.71	**$253.57**	5050	$ 1,000.00	$746.43	25.4%
5070-SUPPLIES												$500.00	**$500.00**	5070	$ 2,000.00	$1,500.00	25.0%
5080-MEDICAL SUPPLIES					$0.16	$0.16			$447.04				**$447.36**	5080	$ 5,000.00	$4,552.64	8.9%
5085-MEDICATION		$532.73	$157.86	$561.28	$175.40	$536.67	$564.68	$825.80	$192.94	$445.47	$438.50	$390.64	**$4,821.97**	5085	$ 20,425.00	$15,603.03	23.6%
5115 Computer components under $5k													**$0.00**	5115	$ 500.00	$500.00	0.0%
5125 Computer Software under $5K													**$0.00**	5125	$ 2,000.00	$2,000.00	0.0%
5160-Vehicle										$15.00			**$15.00**	5160		($15.00)	#DIV/0!
5210-PUBLICATIONS													**$0.00**	5210		$0.00	0.0%
5099 -PETTY CASH													**$0.00**	5099		$0.00	0.0%
COMMODITIES SUBTOTAL:	**$0.00**	**$687.17**	**$279.71**	**$621.20**	**$205.52**	**$756.35**	**$646.00**	**$1,018.81**	**$881.82**	**$821.52**	**$468.46**	**$1,431.35**	**$7,817.91**		**$ 38,225.00**	**$30,407.09**	**20.5%**
														fund balance			
TOTAL EXPENSES	**$25,589.18**	**$18,506.99**	**$20,975.54**	**$25,149.99**	**$20,469.34**	**$26,147.18**	**$35,578.03**	**$19,665.54**	**$15,302.60**	**$23,223.10**	**$6,530.52**	**$30,716.37**	**$267,854.38**		**$ 376,076.00**	**$108,221.62**	71.2%
																	% received
NET INCOME	**($25,024.68)**	**($18,050.50)**	**($20,461.83)**	**($24,662.50)**	**($19,742.46)**	**($8,707.08)**	**$76,346.68**	**($16,112.90)**	**($8,520.80)**	**$84,766.37**	**($2,419.87)**	**($27,703.42)**	**($10,292.99)**				
BANK BALANCE:	**$436,058.81**	**$417,910.31**	**$397,448.48**	**$373,990.38**	**$353,882.22**	**$337,945.93**	**$421,624.39**	**$404,450.22**	**$396,224.92**	**$480,740.03**	**$467,374.00**	**$434,172.40**					

TUBERCULOSIS CARE AND TREATMENT FY2018

LINE ITEM	DEC	JAN	FEB	MARCH	APRIL	MAY	JUNE	JULY	AUG	SEPT	OCT	NOV	TOTAL		ANNUAL BUDGET	BALANCE REMAINING	% expended
7010-PROPERTY TAXES													$0.00	7010	$ 250,000.00	$ 250,000.00	0.0%
8090-FEES FOR SERVICE	$150.00												$150.00	8090	$ 6,000.00	$ 5,850.00	2.5%
9405													$0.00	9405		$ -	0.0%
9417-MEDICAID													$0.00	9417		$ -	#DIV/0!
9510-INTEREST INCOME													$0.00	9510	$ 2,600.00	$ 2,600.00	0.0%
9511-RE TAX DIST INT													$0.00	9511	$ 25.00	$ 25.00	0.0%
9990													$0.00	9990	$ 79,275.00	$ 79,275.00	0.0%
TOTAL REVENUE	$150.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$150.00		$ 337,900.00	$ 337,750.00	0.0%
3010-REGULAR SALARIES	$19,071.08												$19,071.08	3010	$ 169,515.00	$150,443.92	11.3%
3020-PART TIME SALARY	$2,500.17												$2,500.17	3020	$ 21,075.00	$18,574.83	11.9%
3025-Holiday	$1,525.37												$1,525.37	3025	$ 10,036.00	$8,510.63	15.2%
3040-Overtime	$36.43												$36.43	3040		($36.43)	#DIV/0!
3050-MERIT POOL													$0.00	3050	$ 4,514.00	$4,514.00	0.0%
3105 -SOC.SEC./CTY SHARE	$583.45												$583.45	3105	$ 15,693.00	$15,109.55	3.7%
3110 -ILL MUNIC RET FUND	$785.58												$785.58	3110	$ 20,549.00	$19,763.42	3.8%
3146-EMPLOYEES HEALTH													$0.00	3146	$ 21,918.00	$21,918.00	0.0%
PERSONNEL SUBTOTAL:	$24,502.08	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$24,502.08		$ 263,300.00	$238,797.92	9.3%
4001-Contractual Services	$199.00												$199.00	4001	$ 20,500.00	$20,301.00	1.0%
4005-ASSOC.DUES/STAFF													$0.00	4005	$ 350.00	$350.00	0.0%
4006-TRAINING													$0.00	4006	$ 500.00	$500.00	0.0%
4008-SUBSCRIPTIONS													$0.00	4008		$0.00	#DIV/0!
4055-PRINTING													$0.00	4055	$ 300.00	$300.00	0.0%
4096-TELEPHONE													$0.00	4096	$ 500.00	$500.00	0.0%
4101-RENT													$0.00	4101		$0.00	
4130-MAINTENANCE Agreement													$0.00	4130	$ 1,500.00	$1,500.00	0.0%
4131-MAINTENANCE OFFICE EQUIP													$0.00	4131	$ 300.00	$300.00	0.0%
4246-MEDICAL													$0.00	4246	$ 30,000.00	$30,000.00	0.0%
4320-Repair and Maintenance													$0.00	4320		$0.00	#DIV/0!
4442-LAB													$0.00	4442	$ 1,000.00	$1,000.00	0.0%
4449-GARBAGE DISPOSAL													$0.00	4449	$ 600.00	$600.00	0.0%
4570-Contingent-Jane Doe Expense													$0.00	4570		$0.00	#DIV/0!
CONTRACTUAL SUBTOTAL:	$199.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$199.00		$ 55,550.00	$55,351.00	0.4%
5010-OFFICE SUPPLIES													$0.00	5010	$ 1,000.00	$1,000.00	0.0%
5020-OFFICE EQUIPMENT													$0.00	5020	$ -	$0.00	#DIV/0!
5030-Postage													$0.00	5030	$ 50.00	$50.00	0.0%
5040-MILEAGE													$0.00	5040	$ 2,500.00	$2,500.00	0.0%
5050-MEETING EXPENSE													$0.00	5050	$ 1,000.00	$1,000.00	0.0%
5070-SUPPLIES													$0.00	5070	$ 1,500.00	$1,500.00	0.0%
5080-MEDICAL SUPPLIES													$0.00	5080	$ 3,000.00	$3,000.00	0.0%
5085-MEDICATION													$0.00	5085	$ 10,000.00	$10,000.00	0.0%
5115 Computer components under $5k													$0.00	5115	$ -	$0.00	#DIV/0!
5125 Computer Software under $5K													$0.00	5125	$ -	$0.00	#DIV/0!
5160-Vehicle													$0.00	5160		$0.00	#DIV/0!
5210-PUBLICATIONS													$0.00	5210		$0.00	0.0%
5099 -PETTY CASH													$0.00	5099		$0.00	0.0%
COMMODITIES SUBTOTAL:	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00		$ 19,050.00	$19,050.00	0.0%
														fund balance			
TOTAL EXPENSES	$24,701.08	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$24,701.08		$ 337,900.00	$313,198.92	7.3%
																	% received
NET INCOME	($24,551.08)	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	($24,551.08)				
BANK BALANCE:	$412,178.62																

MONTHLY REPORT

MCDH TB Nurse Report

November/ December 2017

Skin Testing

- In November 16th clinics were held with 39 clients tested
- In December 15 clinics were held with 47 clients tested

Doctor Clinic

- On November 13th Doctors clinic was held with 9 chest x-rays and 26 charts reviewed.
- On December 22 Doctors clinic was held with 13 chest x-rays and 25 charts reviewed.

Patient Update

On 12/18: admitted 35 year old possible Active case on daily DOT

On 12/27/17 culture ID Mycobacterium kansasii and gastri

He was discharged 12/28/17

Activities

Old firehouse 11/6/17 11 people were tested

Inservice on TB testing November 16th at Valley Hi Nursing home

NITCA Conference at DuPage County November 16th

Pads TB testing 12/11/17 at evening church site 7 people were tested

Webinars/Trainings:

12/6/2017	Use of EMR's Benefits and Challenges
12/6/2017	Understanding TB Diagnosis Guidelines
12/7/2017	TB Program Evaluation network

Up-coming events

MCDH annual TB testing January 9th

Pads Day site testing January 8th and 11th

Pads evening testing at evening church sites January 24th and 26th

Outreach Old Firehouse Assistance Center TB testing scheduled Feb 20th & 23rd.

TUBERCULOSIS PROGRAM MONTHLY REPORT FY 2017

EDUCATION

TB STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
PRESENTATIONS														
# of Presentations												1	1	3
# of Attendees												9	9	185
1:1 EDUCATION (PUBLIC & HCPs) ***(HOURS)***														
Phone contacts	6.16	6.84	7.92	8.67	7.5	9.91	6.25	3.92	5.08	5.17	7	5.33	79.75	96.09
Face to Face contacts (@MCDH)	10.09	19.92	13.83	15.25	15.25	13.83	15.92	15.42	25.33	11.75	31	16.59	204.18	191.32
Case Mangement	5.25	7.09	10.75	4.75	8.17	7.75	7.67	5.75	6.5	7	6..58	4.33	75.01	109.07
TB Board Meeting Prep		2		2		2				2		2	10	5.75

TESTING

TB SKIN TEST STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
MCDH (Annex B)														
# of Clinics	18	16	16	18	15	17	17	16	18	16	17	16	200	199
# of IGRAs														
# of skin tests	53	87	46	58	52	34	36	46	93	45	63	39	652	703
Outreach Testing														
PADS / Old Firehouse														
RN time	5.5	4.5	6.5	5.5	7	7		2.5			4	2	44.5	45.5
# of site visits	2	2	3	2	2	2		2			4	2	21	17
# of skin tests	6	5	3	3	2	6		9			20	11	65	35
Contact Investigation Testing														
RN time														
# of site visits														
# of skin tests														
Total Skin Tests	59	92	49	61	54	40	36	55	93	45	83	50	717	761

POSITIVE SKIN TEST STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Positive skin tests/Outside agency	4	2		1	6	1	6	1	1	1	2		25	23
Positive skin tests /MCDH clinics	1	1	1	1		1		1	1	2	1	1	11	6
Positive skin tests/PADS														
Positive skin tests /Outreach Sites														
Positive skin tests/Contacts														
Total	5	3	1	2	6	2	6	2	2	3	3	1	36	29
County Positive Skin Test Rate^	1.63	0.98	0.33	0.65	1.95	0.65	1.95	0.65	0.65	0.98	0.98	0.33	11.71	9.44

DIAGNOSTIC STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
X-Rays Ordered	7	4	9	7	5	5	6	6	4	5	5	5	68	63
Sputum Collected		9	9			6	6		6	3	3		42	12
Laboratory Tests Ordered	4	1	3	10	2	4	1	2	6	5	3	2	43	17

MD CLINIC (HOURS)

MD CLINIC *(HOURS)*	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Pre Clinic RN Prep Time		2.83	2.5	1	1	5.58	1	2.75	2.75	4.33	4	1.5	29.24	36.93
Pre Clinic Clerical Prep Time		14.25	16.75	3.5	2.5	2.75	3.5	1.5	1.25	16.5	13.25	10.75	86.5	184.25
Total Pre Clinic Prep Time		17.08	19.25	4.5	3.5	8.33	4.5	4.25	4	20.83	17.25	12.25	115.7	221.2
Total Clinic Time		2		2	3.25	2.17	1	1	1	2	3	1.58	19	25.08
Post Clinic RN Time		3		2.5	2.33	1.5	2	2.5	1	2.83	2.5	2	22.16	30.58
Post Clinic Clerical Time		18.75		13.25	11.5	9.25	10.25	8.75	4.5	7.5	6.75	4.25	94.75	180.42
Total Post Clinic Contact		21.75		15.75	13.83	10.75	12.25	11.25	5.5	10.33	9.25	6.25	116.9	211
Total		40.83	19.25	22.25	20.58	21.25	17.75	16.5	10.5	33.16	29.5	20.08	251.7	457.3

LTBI

PREVENTIVE STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Positive clients transferred into county														
Positive Interviews	7	4	6	7	5	5	6	2	2	2	5	2	53	70
Clients Starting LTBI	3	1	3	10	1	2	2	1	2	3	2	1	31	25

^Rate is per 100,000 using the 2015 estimated census population of 307,357 from the US Census Bureau

CLIENTS STARTING LTBI	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
GENDER														
Male	1	1	1	4		1	1	1	1	1			12	5
Female	2		2	6	1	1	1		1	2	2	1	19	20
AGE														
Children (0-18 years)	1			3					1				5	2
Adult (19-64 years)	2	1	2	6	1	1	1	1	1	3	2	1	22	22
Senior Adult (65+ years)			1	1		1	1						4	1
FOREIGN BORN														
Yes	3		3	9	1	2	2			2	1	1	24	14
No		1		1				1		1	1		5	11

TREATMENT COMPLETION	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Clients Completing LTBI	1	1	4					2			1	2	11	7
Failure to Complete		2				1	3			3	1	9	19	21
Moved		1								1			2	3
Lost to F/U							3				1	9	13	16
Declined- Personal						1				2			3	
Declined-Medical		1											1	2
Deceased														
Other														

ACTIVE TB

ACTIVE TB STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
# Active TB Cases Identified														1
County Active TB rate^														0.325
Active Cases Transferred OUT of McHenry County														1
Active Cases Transferred INTO McHenry County														2
Total Active TB Caseload*	1	1											1	2
DOT Visits	21	14											35	205
DOT Visit/Travel Time (Hours)	10.5	6.5											17	135.5
# TB Contact Investigations Initiated														
# Suspects Investigated														

*Number does not accumulate, it reflects the number of people for whom the DOT visits and DOT time account for

TREATMENT COMPLETION	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Cases Completing Active TB Medication		1											1	
Failure to Complete														
Moved														
Lost to F/U														
Declined- Personal														
Declined-Medical														
Deceased														
Other														

RESISTANCE CLASSIFICATIONS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
#MDR Cases Identified														
#XDR Cases Identified														

ACTIVE TB STATISTICS														
LOCATION OF ACTIVE TB IDENTIFIED	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 17	YTD 16
Pulmonary														
Extrapulmonary														1
GENDER														
Male														1
Female														
AGE														
Children (0-18 years)														
Adult (19-64 years)														1
Senior Adult (65+ years)														
FOREIGN BORN														
Yes														1
No														

^Rate is per 100,000 using the 2015 estimated census population of 307,357 from the US Census Bureau

TUBERCULOSIS PROGRAM MONTHLY REPORT FY 2018

EDUCATION

TB STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
PRESENTATIONS														
# of Presentations														
# of Attendees														
1:1 EDUCATION (PUBLIC & HCPs) *(HOURS)*														
Phone contacts	3.24												3.24	6.16
Face to Face contacts (@MCDH)	19.75												19.75	10.09
Case Mangement	3.33												3.33	5.25
TB Board Meeting Prep														

TESTING

TB SKIN TEST STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
MCDH (Annex B)														
# of Clinics	15												15	18
# of IGRAs														
# of skin tests	47												47	53
Outreach Testing														
PADS / Old Firehouse														
RN time	3.5												3.5	5.5
# of site visits	2												2	2
# of skin tests	7												7	6
Contact Investigation Testing														
RN time														
# of site visits														
# of skin tests														
Total Skin Tests	54												54	59

POSITIVE SKIN TEST STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Positive skin tests/Outside agency														4
Positive skin tests /MCDH clinics	3												3	1
Positive skin tests/PADS														
Positive skin tests /Outreach Sites														
Positive skin tests/Contacts														
Total	3												3	5
County Positive Skin Test Rate^	0.98												0.98	1.63

DIAGNOSTIC STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
X-Rays Ordered	16												16	7
Sputum Collected	3												3	
Laboratory Tests Ordered	2												2	4

MD CLINIC (HOURS)

MD CLINIC *(HOURS)*	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Pre Clinic RN Prep Time	3.17												3.17	
Pre Clinic Clerical Prep Time	2.5												2.5	
Total Pre Clinic Prep Time	5.67												5.67	
Total Clinic Time	1												1	
Post Clinic RN Time														
Post Clinic Clerical Time														
Total Post Clinic Contact														
Total	6.67												6.67	

LTBI

PREVENTIVE STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Positive clients transferred into county														
Positive Interviews	16												16	7
Clients Starting LTBI	3												3	3

^Rate is per 100,000 using the 2015 estimated census population of 307,357 from the US Census Bureau

CLIENTS STARTING LTBI	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
GENDER														
Male	1												1	1
Female	2												2	2
AGE														
Children (0-18 years)														1
Adult (19-64 years)	3												3	2
Senior Adult (65+ years)														
FOREIGN BORN														
Yes	1												1	3
No	2												2	

TREATMENT COMPLETION	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Clients Completing LTBI	1												1	1
Failure to Complete														
Moved														
Lost to F/U														
Declined- Personal														
Declined-Medical														
Deceased														
Other														

ACTIVE TB

ACTIVE TB STATISTICS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
# Active TB Cases Identified														
County Active TB rate^														
Active Cases Transferred OUT of McHenry County														
Active Cases Transferred INTO McHenry County														
Total Active TB Caseload*														1
DOT Visits	7												7	21
DOT Visit/Travel Time (Hours)	4.25												4.25	10.5
# TB Contact Investigations Initiated														
# Suspects Investigated	1												1	

*Number does not accumulate, it reflects the number of people for whom the DOT visits and DOT time account for

TREATMENT COMPLETION	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Cases Completing Active TB Medication														
Failure to Complete														
Moved														
Lost to F/U														
Declined- Personal														
Declined-Medical														
Deceased														
Other														

RESISTANCE CLASSIFICATIONS	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
#MDR Cases Identified														
#XDR Cases Identified														

ACTIVE TB STATISTICS														
LOCATION OF ACTIVE TB IDENTIFIED	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	YTD 18	YTD 17
Pulmonary														
Extrapulmonary														
GENDER														
Male														
Female														
AGE														
Children (0-18 years)														
Adult (19-64 years)														
Senior Adult (65+ years)														
FOREIGN BORN														
Yes														
No														

^Rate is per 100,000 using the 2015 estimated census population of 307,357 from the US Census Bureau

McHENRY COUNTY DEPARTMENT OF HEALTH

McHenry County TB Board

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Tuberculosis Care and Treatment Program
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Tuberculosis Profile

McHenry County TB Cases and Rates as of 1/11/2018

Year	Confirmed Active Cases	Male	Female	Pulmonary and Pleural	Extrapulmonary	Rate/100,000
2007	5	2	3	3	2	1.61
2008	5	4	1	2	3	1.59
2009	3	3	0	2	1	0.95
2010	0	0	0	0	0	0
2011	4	3	1	4	0	1.29
2012	2	2	0	1	1	0.65
2013	1	1	0	1	0	0.32
2014	5	3	2	4	1	1.62
2015	1	0	1	1	0	0.32
2016	1	1	0	0	1	0.32
2017	0	0	0	0	0	0

TB Cases and Rates-US, Illinois, McHenry County, 2007-2016^

Year	Case Count			Rate/100,000		
	US	Illinois	McHenry Co	US	Illinois	McHenry Co
2007	13,293	521	5	4.4	4.1	1.61
2008	12,906	466	5	4.2	3.6	1.59
2009	11,545	418	3	3.8	3.2	0.95
2010	11,181	372	0	3.6	2.8	0
2011	10,528	359	4	3.4	2.9	1.29
2012	9,945	347	2	3.2	2.7	0.65
2013	9,588	327	1	3.03	2.54	0.32
2014	9,412	320	5	3.0	2.49	1.62
2015	9,563	344	1	2.98	2.67	0.32
2016	9,287	342	1	2.9	2.66	0.32

^Data Obtained from: Illinois Department of Public Health, Map of Illinois Case Rates found at
http://dph.illinois.gov/topics-services/diseases-and-conditions/diseases-a-z-list/tuberculosis

IDPH TB report

Presented at last NIPHC meeting 12/20/2017 from Elaine Darnall

I. Number of Cases

There have been 284 cases of active TB reported and confirmed as of Monday, Dec 18. Compared to the same week last year, there were 296 cases. We have 12 less cases than the number reported this week last year.

	2017 to date
DuPage County	35
Kane County	15
Kendall	3
Lake County	9
McHenry	0
Will County	9
Winnebago	2
Suburban Cook	61
Chicago	115

II. Drug Resistance

Of the 284 cases reported thus far, 221 were culture positive.
184 (83.3%) had drug susceptibilities completed with
23 showing single drug resistance.

INH resistance: 15
PZA resistance: 7
Streptomycin resistance: 1

III. Dead at Diagnosis or Died on Therapy

Of the 284 cases reported thus far, 29 cases were either dead at dx, or died during therapy.

PROGRAM HIGHLIGHTS

OLD BUSINESS

NEW BUSINESS

BOARD ISSUES

INFORMATION

Journal of Microbiology, Immunology and Infection (2014) 47, 268–274

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

REVIEW ARTICLE

Risk of tuberculosis infection in anti-TNF-α biological therapy: From bench to bedside

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KEYWORDS
Anti-TNF-α;
Biological therapy;
Tuberculosis

Anti-tumor necrosis factor-α (TNF-α) biological agents, including soluble TNF-α receptors and anti-TNF-α monoclonal antibodies, bring new hope for treating rheumatic diseases such as rheumatoid arthritis, but also increase the risk of infection, especially tuberculosis (TB) infection. Recent findings have shown that the physiological TNF-mediated signaling was somehow impaired by TNF antagonists, leading to the exacerbation of chronic infection associated with aberrant granuloma formation and maintenance. Although both receptor and antibody agents appear to pose an equally high risk in causing development of new TB infections, monoclonal anti-TNF-α antibody seems more inclined to reactivate latent TB infection. This review is focused on the underlying mechanisms that cause the TB risk in the anti-TNF-α therapy and also the strategies to deal with it, with the aim of reducing the TB incidence during anti-TNF-α biological therapies.
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Introduction

The development of anti-tumor necrosis factor-α (TNF-α) therapy brings new hope for treating rheumatic diseases in which TNF-α plays a crucial role, including rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and other inflammatory arthritis. Anti-TNF-α therapy not only relieves symptoms, but also reduces bone erosions to a minimal degree, which may lead to a better prognosis. However, TNF-α is also a key cytokine in host defense against intracellular infection, such as mycobacterium tuberculosis (MTb) infection.[1,2] In daily practice it is confirmed that anti-TNF-α therapy is also associated with increased susceptibility to infections, especially tuberculosis (TB).[3] It is also found that anti-TNF-α monoclonal antibodies appear to pose a higher risk in TB infection than

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TNF-α receptors.[4] In this review we focus on the underlying mechanisms that cause the differences in MTb risks among different kinds of anti-TNF-α agents, with the aim of reducing the MTb incidence to a minimal degree during anti-TNF-α biological therapies.

TB infection

TB is caused by a bacterium called *Mycobacterium tuberculosis* (*M. tuberculosis*). The bacterium usually attacks the lungs, but it can also attack other parts of the body such as the kidney, spine, brain, intestines and so forth. If not treated properly, TB infection can be fatal. Not all patients infected with *M. tuberculosis* become symptomatic. Two TB-related conditions exist: active TB (ATB) disease and latent TB infection (LTBI).

It is noteworthy that LTBI refers to a TB infection status in which the patient is infected with *M. tuberculosis* but remains asymptomatic. The main adverse consequence of LTBI is that approximately 5–10% of these patients will eventually go on to develop ATB at a later stage of their life. The greatest risk of progression to ATB occurs in the first 2 years after infection.[5] However, the risk may be higher if the patient is receiving concurrent immunosuppressive therapy and it is even worse if a patient suffers a disease that disturbs the immune system or is complicated with malnutrition. Moreover, old age is also associated with TB infection, since the immune system weakens with age.[6,7]

Factors increasing the risk of TB infection

There are many factors that increase the risk of TB infection. Among these factors, the immunosuppressive conditions top the list. The risk of developing TB is about 100-fold increased in the HIV-infected population.[8–10] Solid organ transplant recipients have an elevated risk of TB infection because of immunosuppressive therapy.[11,12] In an investigation in Spain, the incidence of TB in recipients was 26.6 times higher than that in the general population and the highest TB incidence was observed among lung transplant recipients, with a relative risk of 73.3.[12] In patients receiving anti-TNF-α treatment, the relative risk of TB infection varies from 1.5 to 17.[13,14] The risk of TB infection is higher with anti-TNF-α monoclonal antibody therapy than with soluble TNF-α receptor therapy.[4,15] In a study in the US, the risk of developing TB attributed to infliximab was more than twofold that of etanercept.[16] Tissue malignancy also has an influence on the risk for TB infection. In patients with hematological malignancies including leukemia and lymphoma, the relative risk of developing TB reaches 16.[17] Additionally, other conditions, such as diabetes mellitus, smokers, alcoholics, also have two- to threefold increased risks of developing TB.[18–20]

Risks of TB infection by different TNF-α antagonists

With increasing biologic agents becoming available for clinical use, there are more and more concerns about the increased rates of infections secondary to the disturbance of physiological cytokine-mediated signalings by these agents.[21] It had been reported that an increased risk of TB infection was associated with biological therapies, including TNF-α antagonists (monoclonal anti-TNF-α antibody: adalimumab, infliximab, certolizumab pegol and soluble TNF-α receptor: etanercept),[3,22] anakinra (IL-1 receptor antagonist),[23] abatacept (CTLA-4 Ig),[24] rituximab (monoclonal anti-CD20 antibody),[25] efalizumab (monoclonal anti-CD11a antibody),[26] daclizumab (monoclonal antibody to the interleukin 2 receptor-CD25)[27]and so on, among which TNF-α antagonists seem extremely prominent for increasing the risks of TB infection.

In a retrospective cohort of 112,300 Canadian RA patients from 1998 to 2003, the rate of TB was investigated to determine whether different disease-modifying antirheumatic drugs (DMARDs) were associated with the risk of TB. The researcher found that the median time from the first prescription with infliximab or etanercept to the presentation of TB was 17 and 79 weeks, respectively.[14] Another research reviewed 90 RA patients treated with infliximab and 103 patients treated with etanercept, by analyzing the data of the Korean National Tuberculosis Association (KNTA) from 2001 to 2005; in the infliximab-treated RA group, two cases of TB developed, while there was no case of TB reported in the etanercept-treated RA group.[15]

In 2008, Wallis[28] reported 248 cases of infliximab-associated and 39 cases of etanercept-associated TB infections, which were recorded from January 1998 to March 2003 in the Adverse Events Reporting System (AERS) database of the Food and Drug Administration (FDA). According to the report, among 197,000 infliximab-treated and 113,000 etanercept-treated patients, the TB incidence rate was 54 per 100,000 and 28 per 100,000, respectively. Monte Carlo simulation revealed that the median time of TB onset after starting etanercept therapy is three to five times longer than infliximab (12–21weeks). A median rate of reactivation of LTBI by infliximab treatment was 12.1 times higher than the etanercept treatment ($p < 0.001$). In contrast, both TNF-α antagonists appeared to pose a high risk of progression of new TB infection.

A French prospective research[4] reported that the annual adjusted incidence rate of TB was 9.3 (range 0.0–9.4) per 100,000 for patients receiving etanercept, 187.5 (range 0.1–374.8) per 100,000 for infliximab, and 215.0 (range 0.0–521.7) per 100,000 for adalimumab, compared with 8.7 per 100,000 for the general French population. The standardized incidence ratio (SIR) was 1.8 (95% CI = 0.7–4.3; $p = 0.20$) for etanercept, 18.6 (95% CI = 13.4–25.8; $p < 0.0001$) for infliximab, and 29.3 (95% CI = 20.3–42.4; $p < 0.0001$) for adalimumab. British research[29] published in 2010 showed that the incidence rate of TB was highest for adalimumab (144 events/100,000 person-years), followed by infliximab (136/100,000 person-years) and then etanercept (39/100,000 person-years). Compared with etanercept, the adjusted incidence rate ratios (IRRs) and 95% CI for adalimumab and infliximab were 4.2 (1.4–12.4) and 3.1 (1.0–9.5), respectively. The median time from the initial TNF-α antagonist use to TB diagnosis was 13.4 months for cases exposed to etanercept, 5.5 months for infliximab and 18.5 months for adalimumab.

From the data above, it can be concluded that the incidence of TB induced by various TNF-α antagonists are different; monoclonal anti-TNF-α antibodies such as

infliximab or adalimumab poses a higher risk of TB incidence than soluble TNF-α receptor, etanercept. The median time of TB onset after receiving monoclonal antibody therapy was shorter than that of soluble receptor. Anti-TNF-α antibody seems more inclined to reactivate a latent TB infection, although both TNF-α antagonists appear to pose an equally high risk in causing the development of new TB infection.[30]

Mechanisms of TB infection in different TNF-α antagonists

The mechanism that underlies increased TB infection in TNF-α antagonist therapies has aroused researchers' interests. TNF-α is a cytokine that plays a central role in establishing and maintaining the inflammatory response against infections.[1,2,31,32] TNF-α has soluble and transmembrane forms, both of which are biologically active and are produced by a wide variety of cells, including macrophages, natural killer cells, granulocytes, fibroblasts, and T cells. Both forms of TNF-α interact with two distinct types of receptors, TNF receptor 1 (TNFR1) and TNFR2. Either or both forms of TNF-α are found in practically all cells of the human body, except red blood cells. TNF-α blockade will result in the interruption of TNFR-mediated functions, which comprises cell activation and proliferation, production of cytokines and chemokines, and the formation and maintenance of granulomas.[33] In the host immune response, the mycobacteria arrives in the alveoli and is engulfed by alveolar macrophages. TNF-α is then released with an autocrine style, an action which further enhances the release of other cytokines and chemokines to attract and activate $CD4^+$, $CD8^+$ and γ/δ lymphocytes. These lymphocytes strengthen T-cell adhesion and antigen presentation, which results in the proliferation and recruitment of more T and B cells. These activated cells also release interferon-γ (IFN-γ), which accelerates antigen presentation and induces intracellular killing of bacilli and macrophage apoptosis. Finally, granuloma formation and infection occurs; however, if the patients have no symptoms, but have mycobacteria within the body, it is termed LTBI. Under such circumstances, MTb-specific central memory T cells ($CCR7^+CD27^+$) and effector memory cells ($CCR7^-CD27^-$) will permanently exist in the body. Thus, anti-TNF-α therapy disturbs the physiological TNF-α mediated immunoinflammatory responses and may cause TB reactivation or dissemination.[33–35]

Plessner et al[36] investigated the effects of anti-TNF-α antibody (MP6-XT22) and soluble TNFR fusion molecule (mTNFR2-Fc) in the murine TB model. Both MP6-XT22 and mTNFR2-Fc resulted in rapid morbidity in acute infection. During chronic infection, mTNFR2-Fc related infection could be controlled, whereas TB infection secondary to MP6-XT22 caused death within 1 month. Histological proof showed that the lung sections of mTNFR2-Fc-treated mice had lower bacterial burden than those of MP6-XT22-treated mice. Also, granuloma formation and maintenance were better in the mTNFR2-Fc group than the MP6-XT22 group, and this effect was more significant with the progression of time and increase in drug dose. During acute infection, flow cytometry revealed increased C3 deposition on $CD4^+$ T cells in the lungs of mice treated with MP6-XT22 compared with those of mTNFR2-Fc-treated mice; there were significantly fewer $CD4^+$ T cells, and not macrophages, in the lungs of MP6-XT22-treated mice compared with those of mTNFR2-Fc-treated mice, during primary infection but not in chronic infection. Drug fluorescent staining analysis showed a higher concentration of MP6-XT22 in the lungs. These findings were a good start to clarify the differences in the mechanism of inducing and exacerbating TB infection by different anti-TNF-α agents. In other research,[37] C57BL/6 mice with chronic TB infection were treated with the TNF-neutralizing antibody MP6-XT22 or normal rat IgG. The results showed that the lymphoid aggregates were well maintained in the infected lungs of rats in the IgG-treated group 9 days after treatment; in contrast, the dissolution of lymphoid nodules in the MP6-XT22-treated group became obvious and continued to be apparent at 21 days. Further immunohistochemical studies showed that the dissociation of B-cell-macrophage units in the infected lungs of the MP6-XT22 treated group was particularly conspicuous, with a marked decrease in the expression of cells with CD19, which is the early differentiation antigen of the B cell. Lin et al[38] undertook an investigation on a cynomolgus macaque model. Macaques were classified as having active or latent disease 6–8 months after TB infection. Then, macaques with acute infection were randomized to receive either adalimumab or no treatment, while macaques with latent infection were randomized to receive treatment with a TNF-neutralizing agent, either p55-TNFRI or adalimumab, or with saline. The results showed that neutralization of TNF in latently infected macaques caused reactivation in a majority of animals, as determined by gross pathologic examination and bacterial burden. A spectrum of dissemination was noted, including extrapulmonary disease. However, macaques that developed primary and reactivated TB after TNF neutralization had a similar granuloma structure and composition to that of control macaques with active disease. TNF neutralization was associated with increased levels of interleukin-12 and chemokine receptor expression, decreased levels of CCL4, and reduced mycobacteria-induced IFN-γ production in blood, but not in the affected mediastinal lymph nodes. Interestingly, the first sign of reactivation often occurred in thoracic lymph nodes. In an *in vitro* study,[39] Saliu et al found that infliximab and adalimumab significantly inhibited T cell activation and reduced the proportion of TB-responsive $CD4^+$ cells by 70% and 50%, respectively, while etanercept produced no significant effect. Infliximab and adalimumab obviously suppressed IFN-γ produced by TB-responsive $CD4^+$ cells. However, IL-10 production was equally suppressed by all three anti-TNF drugs.

Wallis[35] concluded that the differences in risks of TB infection among TNF antagonists are caused by their different structures and functions, including pharmacokinetics and dosing, soluble TNF binding kinetics and stoichiometry, the affinities of TNF antagonists for transmembrane TNF, cytotoxicity, apoptosis and T-cell activation, and cytokine expression.

Diagnosis of latent TB infection before anti-TNF-α therapy

Tuberculin skin test

LTBI is diagnosed in patients who are free from symptoms of ATB disease, but have a positive tuberculin skin test (TST).

TST is widely used to screen high-risk subjects all over the world. A number of countries have generated national guidelines that deal with LTBI before anti-TNF drugs therapy.[7,40,41]

In China, where TB prevalence is very high, the criterion of LTBI diagnosis may be less valuable and the guiding principle for LTBI treatment may not be as strict as in the US or European countries. Considering this, the risk of TB infection induced by biological drugs becomes more unoptimistic. Therefore, the Chinese Rheumatology Association suggested a TST induration diameter $\leq$ 10 mm as the threshold of applying biological agents in RA and AS.[42,43] The specific standards are as follows: (1) the induration diameter $\leq$ 10 mm, and no evidence of TB infection, biologics are available; (2) the induration diameter > 10 mm and $\leq$ 15 mm, without evidence of TB infection, the use of biologics depends on the patient disease condition. If necessary, it is suggested to be applied simultaneously with anti-TB treatment; (3) the induration diameter $\geq$ 15 mm or <15 mm with blister or necrosis, biologics are not recommended unless the TB is controlled after anti-TB treatment. However, TST is easily influenced by many factors, such as Bacille Calmette Guérin (BCG), which is widely used in young Chinese populations.[42,43] Diagnosis of LTBI is necessary, but still challenging in daily practice (Fig. 1).

Interferon-gamma release assay (IGRA)

IGRA is established as an alternative to the TST in TB infection diagnosis, especially when it comes to the diagnosis of LTBI, in which IGRA plays an important and unique role. The development of IGRA should be attributed to the progress of molecular biology and immunology.[44] In 1999, Behr et al[45] performed comparative hybridization experiments on a DNA microarray, to better understand the differences among *M. tuberculosis, Mycobacterium bovis,* and the various BCG daughter strains. Eleven regions (encompassing 91 open reading frames) of H37Rv deleted from BCG vaccines and *M. bovis* were confirmed by sequencing. Five additional regions representing 38 open reading frames were present in *M. bovis,* but absent from BCG strains. The differences between MTB and BCG were determined by these 16 regions denoted RD1—RD16. Of particular importance was that the region of deletion-1 (RD-1) was completely deleted from all BCG strains and most environmental mycobacteria. Therefore, detection of RD-1-encoded antigen-specific T-cells response revealed whether the suspected person was infected with MTB or not. Early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10), which were two of the RD-1-encoded proteins, can theoretically evoke robust $CD4^+$ and $CD8^+$ T-cell responses. When the body was restimulated by a mycobacteria-specific antigen, memory cells which had been immunized primarily would be reactivated rapidly and release IFN-γ. By detecting IFN-γ secretion, it was possible to find out if the body had been infected by TB without interference by previous BCG vaccination or atypical mycobacterial infection. It can be inferred from the abovementioned mechanisms that IGRA is particularly important in the diagnosis of LTBI, since it is asymptomatic. Unfortunately, the current diagnostic kits utilizing production of IFN-γ in response to TB antigens, are unable to distinguish between LTBI and ATB disease. Efforts had been made to distinguish between LTBI and ATB disease, by assessing multiple cytokines such as TNF-α, IL-12 and IL-17, which is helpful to confirm the diagnosis of ATB disease in a TB-endemic population.[46]

There are two different sets of IGRA test, including T-SPOT.TB and Quanti FERON-TB Gold (or Quanti FERON-TB Gold in Tube). The T-SPOT.TB test is based on the high sensitive enzyme-linked immunospot assay that enumerates the number of T-cells releasing IFN-γ in the peripheral blood, which responds to the stimulation by MTb-specific antigens. The method of Quanti FERON-TB is based on the whole-blood ELISA test of IFN-γ released from T-cells, in response to the stimulation by MTb-specific antigens. Because of different local commercial permissions, head-to-head comparisons between these two assays for LTBI are rare and most of them were performed in Japan. A study speculated that T-SPOT.TB might reduce the frequency of indeterminate results of Quanti FERON-TB Gold.[47] However, another study noted that LTBI in younger patients may be better diagnosed by Quanti FERON-TB Gold or Quanti FERON-TB Gold in Tube, while in middle-aged and elderly patients, T-SPOT.TB may be more suitable to exclude LTBI, although the validity of two methods in the exclusion of LTBI are similar and not fully enough to diagnose LTBI separately.[48]

Comparison and interaction between TST and IGRA

It is newly accepted that the specificity of IGRA is greatly improved compared with TST (97% for Quanti FERON-TB Gold and 92% for T-SPOT.TB vs. only 66% for TST).[49,50] It had been widely accepted that T-SPOT.TB is superior on the predictability of TB infection in immunosuppressed patients, and it was not influenced by immunosuppression status, such as HIV infection.[51] The new data showed that T-SPOT.TB may be more sensitive than the TST in patients receiving anti-TNF-α therapy.[52]

Considering that the TST has a low specificity in TB diagnosis and its result is always affected by many other factors, IGRA is regarded as an alternative to TST in the diagnosis of ATB disease and LTBI in the US.[53] However, in Britain, the guideline recommends the combination of both methods.[54] Currently, there is a tendency that IGRA may be used as a substitute for TST in the diagnosis of LTBI before starting TNF-α antagonists, especially in countries where TB prevalence is intermediate and the BCG vaccination is mandatory at birth, such as in Korea.[55] In China, T-SPOT.TB was approved by the State Food and Drug Administration in September 2010. A consensus report of a Chinese infliximab and etanercept study group also suggested that T-SPOT.TB should be advised in TST-positive patients before the administration of TNF-α antagonists.[42,43] However, the phenomenon of poor agreement between TST and IGRA was found in many studies of different populations and multicentered, large-scaled and randomized comparative studies between the TST test and IGRA are still lacking. A strategy of simultaneous testing to optimize diagnostic sensitivity is suggested in the clinical use of biological drugs.

A recently published study[56] aimed to figure out the impact of TST on subsequent IGRA results. TST-mediated

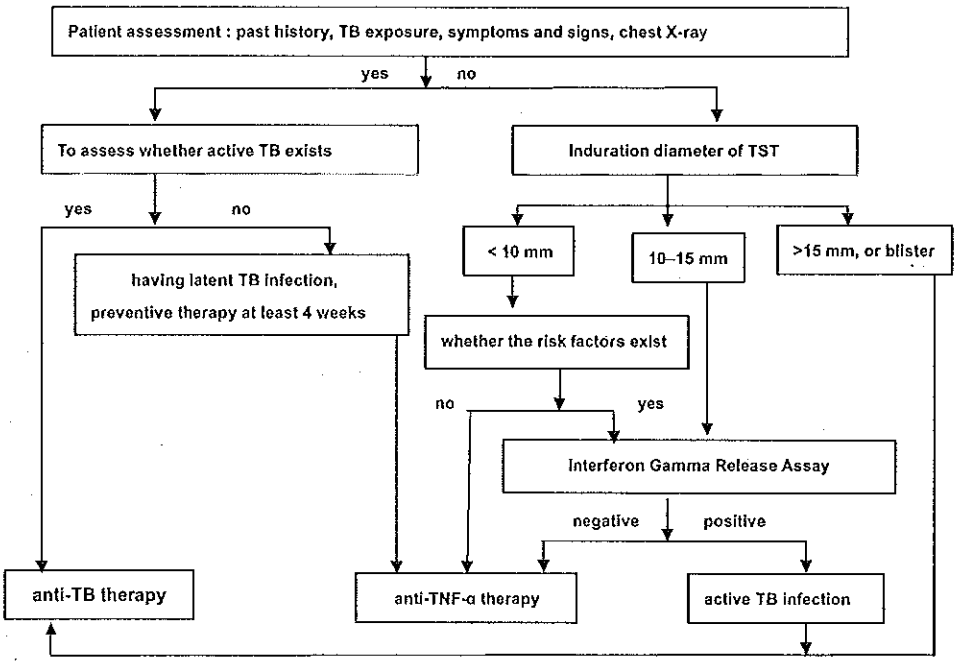

Figure 1. Tuberculosis screening diagram in rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients for anti-TNF-α therapy in our clinic.

boosting of IGRA responses were evaluated in 26 South African volunteers. IGRAs were performed pre-TST, and were repeated four times on Days 3, 7, 28, and 84 post-TST administration. The results showed that IGRAs performed post-TST were obviously elevated since Day 3. The reporter advised that when using a two-step screening strategy, it is better to perform an IGRA within 3 days after performing the TST.

Screening new antigens for diagnosis of TB

Finding new TB antigens specific for MTb is ongoing. Heparin-binding hemagglutinin (HBHA) became a candidate. A study showed that LTBI individuals mount a strong T-cell response to HBHA, whereas patients with ATB disease do not, suggesting that HBHA is a good marker for the immunodiagnosis of LTBI, and that HBHA-specific Th1 responses may contribute to protective immunity against ATB.[57] An updated report published in Nature also demonstrates an underappreciated role of type I IFN-$\alpha\beta$ signaling in the pathogenesis of TB, which has implications for the development of a vaccine and therapy.[58]

Decline in the incidence of LTBI after strengthening TB control

With increasing concerns in the safety of anti-TNF-α agents, especially in patients with possible LTBI, there appeared a decline in the incidence of reactivation of LTBI in the general population. Several retrospective and observational studies suggested that treatment of LTBI before or during anti-TNF-α therapy prevented reactivation effectively.[40,41] In a single-center retrospective study,[59] before starting etanercept use, 78/84 patients were fully or partially treated for LTBI with a mean of 2.5 months (0–12 months); no cases of ATB or newly occurred TB were found, although they were thought to be at high risk for ATB because 80% were born in TB-endemic countries. Similar findings were reported by Carmona et al, who analyzed the Spanish-based BIOBADASER and EMECAR databases. After adoption of formal guidelines to treat LTBI before initiating TNF-a antagonists, 324/384 patients (84%) with a positive purified protein derivative (PPD) received anti-LTBI therapy, and there was a 78% ($p = 0.008$) reduction in TB risk for RA patients treated with infliximab; the TB risk fell to the background rate of RA patients not receiving anti-TNF-a therapy.[41] In Japan, of 5000 cases of RA patients treated with infliximab, 11 TB cases developed in the first 2000 patients, however, after intensified TB screening and prophylactic treatment, only three TB cases developed in the last 3000 patients who received stricter preventive anti-TB treatment (22.3% in the last 3000 patients vs. 14.0% in the first 2000 patients taking prophylactic treatment).[60]

However, treatment of LTBI before anti-TNF-α therapy is not universally effective. A retrospective study[61] in Greece reported that in 613 patients who received anti-TNF-α therapy from July 2000 to June 2004, 11 cases of ATB developed. Of the 11 cases, eight cases received infliximab and three received adalimumab; none received etanercept. Ten cases of ATB developed in the PPD-positive cohort and one case of ATB in the PPD-negative cohort, however, seven of the 11 cases of ATB occurred in patients who had completed or were undergoing LTBI therapy. The failure to prevent developing ATB in this Greek cohort may be attributable to inadequate compliance with recommendations, inadequate length of therapy, higher threshold for initiation of LTBI therapy (10-mm induration on PPD), or the use of infliximab instead of etanercept in a population with a significant background incidence of TB infection.

ATB or reactivation of LTBI associated with anti-TNF-α agents should be paid more attention to, for the safety of biological treatment in rheumatic diseases. Although there lie many puzzles in the mechanism of TB infection under these circumstances, it is convincing that with stricter screening for TB infection, especially LTBI, also combined with aggressive preventive anti-TB treatment, TB infection associated with anti-TNF-α agents will be under control. Based on the available data, we recommended IGRA to be a routine complementary test with TST before anti-TNF-α treatment.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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