GUIDELINE TITLE: PREVENTION OF MYCOBACTERIUM TUBERCULOSIS INFECTION IN PATIENTS WITH ESTABLISHED KIDNEY FAILURE Version 2	University Hospitals of Leicester NHS NHS Trust **RRCV CMG** **Nephrology Service** **Trust Ref: C63/2015**

1. Introduction and Who Guideline applies to

Chronic kidney disease is associated with immunodeficiency, particularly a reduction in cell mediated immunity, leading to an increased risk of infections. Mycobacterium tuberculosis (MTB) infection has been shown to occur with a much higher incidence in patients with established kidney failure (EKF). It may be difficult to diagnosis because of non-specific findings and a high percentage of cases with extrapulmonary disease.

The relative immune deficiency of patients with kidney failure constitutes a significantly increased risk (up to 25 fold) of progression from latent TB infection (LTBI) to active tuberculous disease. In addition, the close and frequent contact between different patients and between patients and staff within outpatient haemodialysis units represents potentially a further significant risk of transmission of MTB from infected patients to other patients and staff. This risk is contingent on a number of factors, including the presence or absence of environmental controls (physical barriers, air flow patterns, space between beds), workload and the routine use by staff of respiratory protection. The interaction of these quite independent risk factors has been underestimated in the past.

In 2012, a serious untoward incident occurred at a UHL-managed satellite dialysis unit where patients and staff were thought to have been infected by person to person transmission. Following this, an expert group was convened to develop local guidance to try to prevent transmission of MTB in haemodialysis or other areas within the renal service.

This guidance summarises the main recommendations.

This guideline will be used in the UHL Trust haemodialysis units, renal wards at the LGH site and other sites where patients with EKF under the management of UHL receive care. It is to be used by registered nursing and medical staff with appropriate renal experience.

Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt, consult a senior colleague or expert.

This guideline does not replace the UHL guidance on the prevention and management of tuberculosis but is additional specific advice relevant to the renal department [insert link].Who it applies to, does it cover all staff, specific groups of staff or specific patient groups.

2. Guideline Standards and Procedures

2.1 The aim of the guideline is to reduce the risk of MTB infection in patients with EKF, particularly to reduce the risk of transmission in the outpatient haemodialysis setting where there is frequent and close contact between patients and staff.

2.2 This will be achieved by:-

- Screening all new EKF patients for latent TB

- Establishing a standard procedure for deciding on contact tracing amongst haemodialysis patients and staff when a prevalent HD patient is diagnosed with TB

- Raising awareness and acting quickly when there is a suspected diagnosis of active TB in EKF patient

2.3 Screening of all new patients starting renal replacement therapy for latent TB

2.3.1 Patients with latent TB and EKF are at high risk of progression to active TB with an estimated annual incidence of active TB of 600/100000 RRT patients based on a local audit of 48 cases with CKD 4/5 in Leicester between 2000-2010. This screening approach had recently been considered by an expert group convened by the British Thoracic Society (1) and not recommended. However, it was felt by TB, health protection and microbiology experts that in the light of the local problems and other recent data, screening should be undertaken.

2.3.2 All new patients starting dialysis or being listed for kidney transplantation should be screened for latent TB by performing interferon gamma release assay testing (IGRA) – either Quantiferon (instructions for Quantiferon at UHL at end of this guideline) or T-spot test. Note for accurate interpretation of results Quantiferon samples must be delivered to the laboratory within 16 hours of collection. The laboratory will only accept samples until 5pm.

2.3.3 Patients can be screened at following times

- In advanced CKD clinic at time decision is made to start dialysis or refer for transplant work up
- At time of first outpatient dialysis (if not already screened)
- During PD training (if not already screened)
- At transplant work up clinic (if not already screened)

2.3.4 In Leicestershire the Infection Prevention Nurse for Renal will maintain a list of patients starting RRT (this to be supplied weekly from PROTON). He/she will monitor the completion and results of IGRA testing and liaise with the unit sister and patient's consultant. In units outside of Leicestershire the unit TB link Nurse will ensure all new patients are tested and any positive result is communicated to the patient's consultant, named nurse and unit sister.

2.3.5 Patients identified with positive IGRAs must be referred to the local TB service for assessment of the risk/benefit of chemoprevention. To avoid diagnostic delay in patients developing active disease, those that were IGRA positive but not treated prophylactically would be highlighted as a potential risk if they developed any suspicious symptoms (persistent cough, fever of unknown origin, weight loss). A negative IGRA test at screening does not exclude future disease with absolute certainty but makes this far less likely.

2.4 Contact tracing and further management of other haemodialysis patients and staff following diagnosis of an index patient with active TB

When a diagnosis of active TB is made in a prevalent haemodialysis patient an augmented approach to contact screening is necessary.

- All cases of newly diagnosed TB in haemodialysis patients treated in facilities managed by UHL must be referred to the UHL TB service where an incident group (UHL TB lead, UHL TB manager, deputy director of infection prevention, representative of Health Protection Agency) would make a rapid assessment of infectivity by reviewing clinical, microbiological and radiological data

- If deemed potentially infective, an incident would be declared and a recommendation made about the extent of contact tracing amongst patients and staff in the dialysis unit (this would augment contact tracing done by local Tb service). Potentially infective patients are generally those where identifiable disease was found in the thoracic cavity with or without dissemination.
- Patients and staff from haemodialysis unit would be screened within 2 weeks by CXR and interferon gamma release assay (IGRA) testing (the extent of this would be decided on case by case basis by the incident group)
- Patients declared at risk will be supplied with written information on the rationale for screening and to make them aware of any symptoms to report
- CXRs will be done locally and transmitted to UHL PACS system for local review
- IGRAs will be organized in batches and sent to UHL
- All patients with abnormal CXRs or positive IGRAs will be referred to local TB service
- All negative patients will have repeat CXR and IGRA at 12weeks
- Patients who were negative twice will be deemed at low risk and simply given advice to seek help if any symptoms suggestive of TB
- All staff (nurses, health care assistants, domestic staff, transport drivers and medical staff in close contact) will be screened in the same way according to recommendation of the incident group
- The UHL TB service will be responsible for ensuring all eligible patients and staff were screened
- Other aspects of screening (e.g. screening of family contacts) will be carried out by present arrangements but results of these to be shared with UHL TB service to ensure all decisions are made using full information

2.5 Suspected tuberculosis

Tuberculosis is often raised as part of the differential diagnosis of patients with EKF with persistent fever or respiratory symptoms. Anecdotally, this often takes time to clarify and creates uncertainty regarding necessary infection prevention measures. Any such patients should be referred promptly to a consultant with expertise in tuberculosis (Respiratory Medicine or Infectious Disease consultant) AND to infection control. A rapid decision regarding appropriate isolation precautions needs to be made.

3 **Education and Training**

This guideline will be circulated to HD Matrons, transplant coordinators and medical staff to update them on new guideline.

4. Monitoring Compliance

Key Performance Indicator	Method of Assessment	Frequency	Lead
Outcome of IGRA testing of incident ESRF patients	audit	annual	S Glover

Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidancedocuments

Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt, consult a senior colleague or expert.

5. Supporting References (maximum of 3)

Milburn, et al. Guidelines for the prevention and management of Mycobacterium tuberculosis infection and disease in adult patients with chronic kidney disease. Thorax 2010;65:559-570

6. Key Words

Chronic kidney disease, tuberculosis, IGRA, Quantiferon

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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Author / Lead Officer:	Graham Warwick	**Job Title:** Consultant Nephrologist	
Reviewed by:	Emma Burgin, HD Matron Sarah Taylor, IP Nurse Nelun Perera, Consultant Microbiologist		
Approved by:	above	**Date Approved:** Dec 2015	

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DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**

Request for QuantiFERON®-TB Gold/Plus Test for LGH patients

HIGH RISK Specimen	Yes
	No

Authorizing Clinician		Unit / NHS No.	Hospital	Ward	GP
TB Service					
Public Health England		Surname	Consultant/Doctor		
Infectious Diseases					
Respiratory Medicine		Forename	Address		
Paediatrics					
GU Medicine		Date of Birth			
Rheumatology					
Gastroenterology		Sex			
Dermatology					
Microbiology		DateofCollection	Time ofcollection		
Immunology					
Renal Unit					
Other please state:					

Please complete ALL information above this line; failure to do so will result in delay in processing the sample

	Yes	No	Lab order code
Is this sample part of a trial/ research?	☐	☐	QFTRD
Is this sample part of the NHS latent TB infection testing East Midlands Tender?	☐	☐	QFTIM

If this sample is part of the NHS latent TB infection testing East Midlands tender - Please tick the box below if the patient DOESNOT give consent for a HIV test to be performed if the QuantiFERON result is positive.

I confirm the patient DOESNOT give consent for a HIV test to be performed ☐

IMPORTANT INFORMATION:

QFT tests must be received within the lab between 09:00 to 17:00 Mon-Fri. Deviation from these times can only be made after discussion with lab staff before taking the sample. The lab cannot take responsibility for samples received outside of these hours.

LABUSEONLY

Sample volume 0.8 to 1.2ml Yes / No

Time venepuncture to incubation: _____
(MUST NOT be >16 hours)

LAB NUMBER

Laboratory enquiries Phone (0116) 2586510

QuantiFERON (QFT) –TB Gold test (3 tube test)

Caution: The QFT test is unique in its methodology. Deviation from this method often results in us having to reject specimens and you having to re-bleed the patient.
Should you require further information, please ring **0116 2586510** during normal working hours or your local laboratory

Instructions for use:

1. Collect 1ml of blood by venipuncture into each of the 3 QFT tubes (Mitogen- Purple top, TB Antigen – Red top and Nil – Grey top).
   TUBES SHOULD BE AT 17-25°c AT THE TIME OF BLOOD FILLING.

2. Tubes fill slowly, hold tube on needle for 2-3 seconds after flow ceases. As a guide to the fill volume, each tube has a **bold black line** approximately 25mm from the base of the tube – this is the desired fill level. If blood level is not close to the black mark, obtain another sample.

3. If using a "Butterfly needle" – prime tubing with a 'purge' tube (not supplied) before filling QFT tubes.

4. Once filled, shake the tubes 10 times, just firmly enough to ensure the inner surface of the tube is coated in blood.
   NOTE – Over energetic shaking may cause gel disruption and could lead to aberrant results.

5. Label each tube completely. Include full name, unit number, date of birth and very importantly – the date and time of blood collection and complete all sections of the form.

6. Do not fridge or freeze tubes once full, as this may create erroneous results, maintain at 22°C ± 5°C. Filled tubes need to be transported to the laboratory rapidly as they need to be incubated at 37ºC within 16 hours of collection. QFT tubes must be received within the lab between 09:00 to 17:00hrs Mon-Fri. Deviation from these times can only be made after discussion with lab staff. The lab cannot take responsibility for samples received outside of these hours.

Laboratories using QuantiFERON outside UHL Trust:

Follow on from point 6 above…

- If the blood is not incubated immediately after collection, but within the 16 hours of collection, re-mix the tubes by inverting 10 times immediately prior to UPRIGHT incubation at 37°C for between 16 to 24 hours.
- After the 16 to 24hr incubation, (the tubes can be maintained at 4°C to 27°C up to 3 days.) centrifuge all tubes for 15 minutes at 2000g to 3000g (RCF)
- Hamilton and Loughborough units send to Leicester Clinical Microbiology. (0116- 258 6542 Ext.6510). Units outside of Leicestershire send to locally approved laboratory for testing.

QuantiFERON (QFT) –TB Gold PLUS test (4 tube test)

Caution: The QFT test is unique in its methodology. Deviation from this method often results in us having to reject specimens and you having to re-bleed the patient.
Should you require further information, please ring **0116 2586510** during normal working hours or your local laboratory

Instructions for use:

1. Collect 1ml of blood by venipuncture into each of the 4 QFT tubes;
   Nil tube -grey cap, TB1 tube -green cap, TB2 tube –yellow cap and a mitogen tube – purple cap.
   TUBES SHOULD BE AT 17-25°c AT THE TIME OF BLOOD FILLING.
2. Tubes fill slowly, hold tube on needle for 2-3 seconds after flow ceases. As a guide to the fill volume, each tube has a **bold black line** approximately 25mm from the base of the tube – this is the desired fill level. If blood level is not close to the black mark, obtain another sample.
3. If using a "Butterfly needle" – prime tubing with a 'purge' tube (not supplied) before filling QFT tubes.
4. Once filled, shake the tubes 10 times, just firmly enough to ensure the inner surface of the tube is coated in blood.
   NOTE – Over energetic shaking may cause gel disruption and could lead to aberrant results.
5. Label each tube completely. Include full name, unit number, date of birth and very importantly – the date and time of blood collection and complete all sections of the form
6. Do not fridge or freeze tubes once full, as this may create erroneous results, maintain at 22°C ± 5°C. Filled tubes need to be transported to the laboratory rapidly, as they need to be incubated at 37ºC within 16 hours of collection. QFT tubes must be received within the lab between 09:00 to 17:15 Mon-Fri. Deviation from these times can only be made after discussion with lab staff. The lab cannot take responsibility for samples received outside of these hours.

Lithium Heparin (LiHe), Blood Collection

a. Alternatively, blood may be collected in a single generic blood collection tube that contains lithium heparin as the anticoagulant. **The minimum volume required is 6 ml**. Gently mix by inverting the tube several times to dissolve the heparin. Please note, use only lithium heparin as a blood anticoagulant, as other anticoagulants interfere with the QFT Plus assay.

b. Do not fridge or freeze tubes once full, as this may create erroneous results, maintain at 22°C ± 5°C. Filled tubes need to be transported to the laboratory rapidly as they need to be processed within 16 hours of collection. LiHe tubes must be received within the lab between 09:00 to 17:00 Mon-Fri. Deviation from these times can only be made after discussion with lab staff. The lab cannot take responsibility for samples received outside of these hours.

Laboratories using QuantiFERON outside UHL Trust

Follow on from point 6 or b above…

- If the blood is not incubated immediately after collection, but within the 16 hours of collection, re-mix the tubes by inverting 10 times immediately prior to UPRIGHT incubation at 37°C for between 16 to 24 hours.
- Lithium heparin tubes should be mixed by gentle inversion prior to aliquoting aseptically; 1ml of blood should be added to 4 labelled QFT Plus tubes on arrival (the black mark on the side of each tube). Ensure the correct caps are replaced on the correct tube. The QFT plus tubes should then be mixed and incubated as above
- Centrifuge all tubes for 15 minutes at 2000 to 3000g (RCF).
- Hamilton and Loughborough units send to Leicester Clinical Microbiology. (0116- 258 6542 Ext.6510). Units outside of Leicestershire send to locally approved laboratory for testing