TB testing in children on biologics

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Signature of ratifying Group Chair	
Author(s) and title	Dr Sanjay Patel, Consultant Paediatric Infectious Disease
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Relevant national or international Guidance e.g. NICE, SIGN, BTS, BSPED	n/a
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Does this document replace or revise an existing document?
No

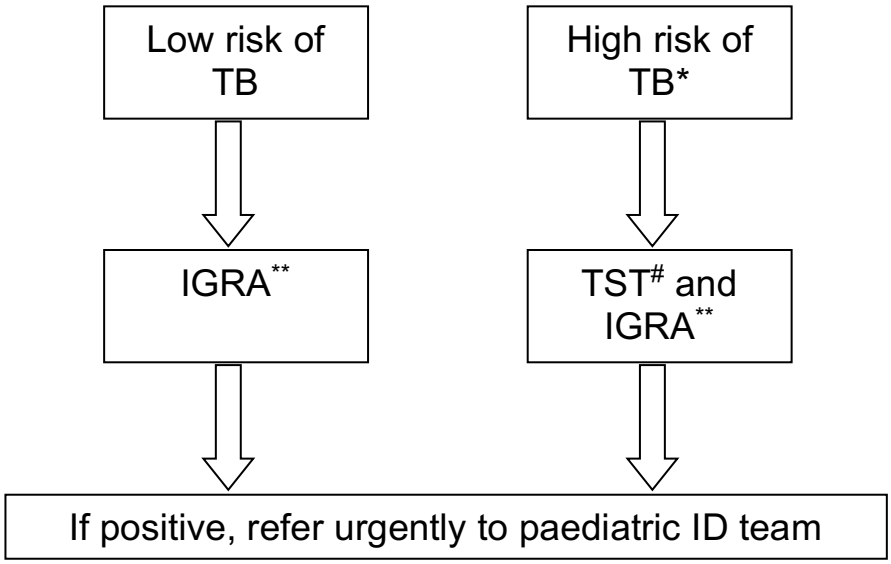
Flowchart

Appendices

FLOWCHART

This flowchart applies to all children with pathologies that may require future treatment with biologics that confer increased susceptibility to tuberculosis, including anti-TNF agents (1), anti interleukin-6 receptor agents (tociluzumab) (2) and Janus kinase (JAK) inhibitors (tofacitinib) (3). The risk of TB reactivation is higher with infliximab and adalimumab compared to etanercept. (4)

Ideally, testing should be performed before any immunosuppressive therapy is commenced. The sensitivity of all tests is reduced if performed when a child is on any immunosuppressive agent.



* Definition of high risk - if they are born in an area of the UK where the rates of TB are high (≥40 per 100,000) – see https://www.gov.uk/government/publications/tuberculosis-in-england-annual-report , if they have a parent or grandparent who was born in a country where there is a high rate of TB (≥40 per 100,000) – see https://www.gov.uk/government/publications/tuberculosis-tb-by-country-rates-per-100000-people , children who have had a known contact with TB or have previously been treated for TB.

** Interferon-gamma release assay (Quantiferon or T-spot TB test)
# Tuberculin Skin Testing / Mantoux (TST) testing should ideally be performed by local TB services##. If necessary, testing may need to be performed in acute hospital setting.

Contact details for TB services:

Southampton (Rachael Brown / Francisca Nwoguh) -023 8071 3180
Winchester (Jane Butcher/Sharron Neville) 01962825763/07780225725
Basingstoke (Lucy Picton-Tubervill) 01256313641
Portsmouth (Nuala Whitehead) 02392286000 ext 1389/6665
Frimley (Pam Hoad) 01252649739 ext 3739
Bournemouth (David Thomas) 01202704560
Dorchester - 01305 254238

1 1.1 Introduction

This algorithm applies to all children with pathologies that may require future treatment with biologics that confer increased susceptibility to tuberculosis, including anti-TNF agents (1), anti interleukin-6 receptor agents (tociluzumab) (2) and Janus kinase (JAK) inhibitors (tofacitinib) (3). The risk of TB reactivation is higher with infliximab and adalimumab compared to etanercept. (4) The risk of Tb reactivation is highest in the first 6 months of treatment.

1.2 Purpose

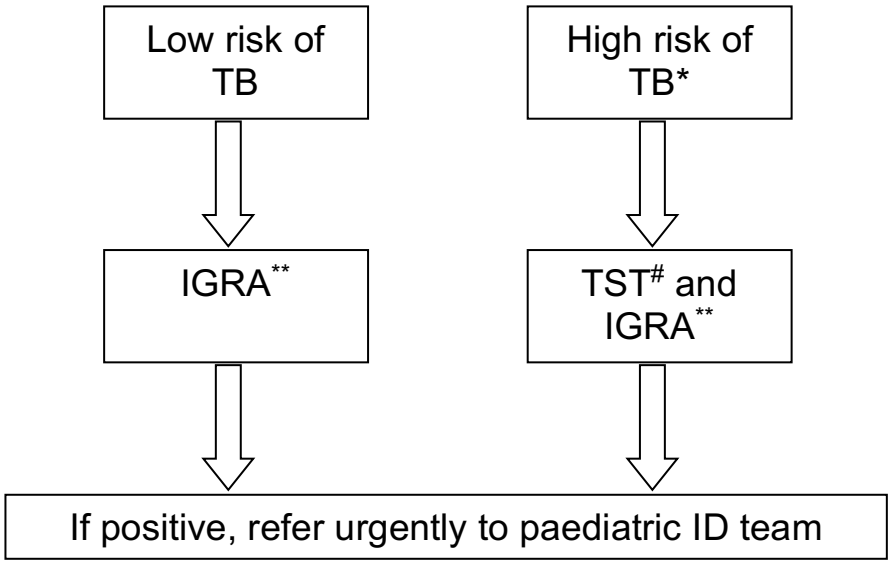
These algorithms should form part of a care pathway for children with inflammatory bowel disease, connective tissue disease (juvenile idiopathic arthritis) etc. This guideline is applicable to any paediatric specialist who manages patients using biologics as outlined above.

2. Guideline

This guideline is applicable to any paediatric specialist that manages patient using biologics as outlined above.

2.1 Testing at the time of original diagnosis with inflammatory bowel disease / juvenile idiopathic arthritis

Ideally, testing should be performed before any immunosuppressive therapy is commenced. The sensitivity of all tests is reduced if performed when a child is on immunosuppression.



* Definition of high risk - if they are born in an area of the UK where the rates of TB are high (≥40 per 100,000) – see https://www.gov.uk/government/publications/tuberculosis-in-england-annual-report , if they have a parent or grandparent who was born in a country where there is a high rate of TB (≥40 per 100,000) – see https://www.gov.uk/government/publications/tuberculosis-tb-by-country-rates-per-100000-people , children who have had a known contact with TB or have previously been treated for TB.

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2.2 Repeat testing at the time of commencing biological therapy

Repeat quantiferon + TST testing is not required unless a significant period of time has elapsed since the original TB screening tests (>1 year) or if there have been risk factors for TB infection since the time of original screening (known contact with TB or contact with individual with symptoms suggestive of TB; travel to high incidence country (≥40 per 100,000))

A chest X-ray should be performed on all high risk* children before biological therapy is commenced (if not performed in the preceding 3 months).

If a child is diagnosed with active or latent TB, anti-TNFa therapy should ideally be delayed until the patient has received 2 months of treatment. If this is not feasible, urgent discussion with the infectious diseases team is recommended. If another biological agent is being considered, please discuss with the infectious diseases team.

2.3 Regular TB testing in children at high risk of TB

Children at high risk for developing TB* should have a quantiferon test performed annually whilst on biological treatment. Although a negative/indeterminate quantiferon result is hard to interpret, a positive one would prompt further investigations and treatment. An annual chest X-ray is not required.

3 References

1. Wallis RS. Tumour necrosis factor antagonists: structure, function, and tuberculosis risks. *Lancet Infect Dis*. 2008;8:601-611.

2. Cantini F, Niccoli L, Goletti D. Tuberculosis risk in patients treated with non-anti-tumor necrosis factor-alpha (TNF-alpha) targeted biologics and recently licensed TNF-alpha inhibitors: data from clinical trials and national registries. *J Rheumatol Suppl*. 2014;91:56-64.

3. Winthrop KL, Park SH, Gul A, et al. Tuberculosis and other opportunistic infections in tofacitinib-treated patients with rheumatoid arthritis. *Ann Rheum Dis*. 2016;75:1133-1138.

4. Tubach F, Salmon D, Ravaud P, et al. Risk of tuberculosis is higher with anti-tumor necrosis factor monoclonal antibody therapy than with soluble tumor necrosis factor receptor therapy: The three-year prospective French Research Axed on Tolerance of Biotherapies registry. *Arthritis Rheum*. 2009;60:1884-1894.

Appendices: Appendix A

Documentation of regional consultation:

Trust	Name of person consulted* (print)	Designation	Signature
Dorchester	Will Verling		
Hampshire Hospitals Foundation Trust	Katie Yallop		
Poole	Steve Wadams		
Portsmouth	Amanda Freeman		
Salisbury	Seb Gray		
Southampton	Sanjay Patel		
IOW	Arun Gulati		

*this person agrees they have read the guidelines, consulted with relevant colleagues and members of MDT, managers and patients, young people & their families as appropriate. Any queries raised during consultation and review process should be documented with responses and any changes made to the guideline.