INTEFERON GAMMA RELEASE ASSAY (IGRA)

NB/PEI CHICA Chapter

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IMMUNITY TO TB AND THE IGRA STORY

• Immunity may be **humoral** or **cellular**

• Humoral Immunity
  ‣ Depends upon circulating antibodies mainly IgM and IgG immunoglobulins
  ‣ Vaccines provide immunity mainly with IgG
Cellular Immunity

- Lymphocytes identify antigens and send chemical messages to cells to fight the antigens
- TB stimulates lymphocytes
- Once exposed to TB the lymphocytes develop immunological memory
- Lymphocytes release Cytokinins which are chemical messengers which initiate immune response
INTERFERON GAMMA
(IFN GAMMA)

• When exposed to TB the lymphocytes release Interferon Gamma (IFN Gamma)

BUT

• The lymphocytes do not release IFN Gamma when exposed to any other common Mycobacteria

• Once exposed to TB once a person’s lymphocytes are sensitized and produce high levels of IFN Gamma if exposed again (like a booster response to vaccines)

• Can now take blood and expose to TB antigen in lab
  ‣ If IFN Gamma released then know that person was exposed to TB previously
INTERFERON GAMMA RELEASE ASSAY (IGRA)

• Two IGRA tests licenced in Canada
• The Quantiferon-TB Gold test done in Saint John, NB
• **When TST positive the IGRA is positive only when the person was previously exposed to TB**
• TST Positive when
  ‣ Exposed to TB previously
  ‣ Exposed to BCG previously
  ‣ Allergic reaction to TST
  ‣ False + reading
• Never consider a TST easy to read
IGRA – TECHNICALLY DIFFICULT

• The blood for an IGRA should be processed immediately after being drawn
• Difficult if patient cannot get to lab easily
• Very difficult for Long Term Care Facility (LTCF)
• Have to book everyone to come into lab and virtually at same time (once month or for TB contact investigation)
• Should do IGRA within 72 hours of TST being administered for contact investigation (IGRA may booster "may" positive giving false +)
• The IGRA is not 100% reliable but reliability increases as further studies done
• Cannot use IGRA to diagnose TB
• Cannot rely on IGRA yet for highest risk or close contacts (household, seniors, immunocompromised, etc.)
• Can test low risk (casual contacts) including immunocompromised, seniors, children, all ages.
• For casual contacts with initial TST+, can test with IGRA and if negative IGRA, test by IGRA again at 8 weeks.
• Some doing routine TST and IGRA for **casual** contacts and screening by taking blood when TST administered
• This involves increased expense and time
• We do TST first for **casual** TB contacts and if TST+ in 48 hours, take blood for IGRA before 72 hours
• Presently not routinely screening immigrants for IGRA
• However for immigrant HCW with + TST are doing IGRA and for many others who screen positive particularly if they will take INH
• High rate of TST+ in immigrants due to BCG and exposure to TB
• Refugees usually TST+ due to exposure to TB so most will be IGRA+
• May be some limitations of testing due to increased costs and time needed
• Does save two visits for TST and identifies those positive for TB with one test if only IGRA done
• For those TST + on screening (not contact investigation) will IGRA test at monthly clinic without major concern about induced booster + IGRA (we are awaiting further guidelines)
CONCLUSION

- A major breakthrough in testing for TB particularly in lower risk (casual) contacts
- As more studies are done the reliability of the IGRA will very likely increase
- IGRA negative when TST+ due to BCG very helpful particularly for HCW
- Reduces significantly those with +TST who are offered INH (particularly HCW and immigrants)
- Likely that future guidelines will result in increased tests for IGRA