What else could it be?

Professor Paul Johnson (Austin Health & University of Melbourne) and colleagues...
Declaration of Financial Interests or Relationships

Speaker Name: Professor Paul Johnson; Austin Health & University of Melbourne

I have no financial interest or relationship(s) to disclose
Austin Hospital and Mercy Hospital for Women
Likely acquisition of 600 human Buruli infections near Melbourne (2011-16)

Loftus, M. et al EID 2018
BURULI ULCER

Rapid, accurate diagnosis from swab (picture: Paul Johnson, Austin Hospital 2005)

No ulcer? - biopsy: histo, culture PCR - specifically request *M. ulcerans* PCR

*M. ulcerans* PCR!

*Mycobacterium ulcerans* (*M. ulcerans*); culture takes 8-12 weeks
13 year old girl from Hampton

- Noticed leg lesion over last 2 months
- Painful + on swabbing, not undermined
- Would you test for BU?
- What else?
Myco Ulcersars PCR

SPECIMEN: SWAB
SITE: Leg ulcer

Mycobacterium ulcerans PCR
M ulcerans PCR Result: - NOT detected

A negative result may not exclude the presence of Mycobacterium ulcerans. In addition to this test routine culture is recommended.

(Testing performed at Victorian Infectious Diseases Reference Laboratory)

Austin Pathology, Austin Health (APA). NATA/RCPA Lab Accred’n No 2741
A/Prof T Leong, A/Prof B Howden, Dr Q Lam, A/Prof C Smith
13 year old girl from Hampton

• Noticed this lesion over last 2 months after trip to beaches in southern Italy (sand flies) and New York (bed bugs)
• Would you test for BU –YES, NEGATIVE
• What else?
Sandflies can get through fly screens and bed nets (due to size) - permethrin soaking helps.

LEISHMANIASIS in the WHO EUROPEAN REGION
*Final Report*

PCR - Not Listed

SPECIMEN: SWAB
SITE: Leg Ulcer

PCR for Leishmania DNA
PCR Result: POSITIVE

GENERAL COMMENT:
This test is still undergoing development and is not fully validated. Results should be interpreted in association with all other clinical information (clinical and laboratory) on the patient. As such this test is not currently NATA/RCPA endorsed. Refer to Medical Testing Field Document 5.5.1.2 Subclause (iii).

Test performed by St Vincent's Pathology, Sydney.

Fresh tissue (biopsy) best
Leishmaniasis

Clinical Setting

- Cutaneous, mucosal (Espundia), or visceral (Kala-Azar) leishmaniasis.
- Treatment of cutaneous leishmaniasis is determined by severity of disease
  - Mild Disease: 4 or fewer lesions (1 cm or more), none ≥ 5 cm in diameter; no lesions in cosmetically sensitive areas, no lesions over joints or genitalia; may observe.
  - Complex Disease: > 4 lesions and/or one over 5 cm in diameter and/or lesion(s) over joints or in cosmetically sensitive area(s), or failure of previous treatment, or substantial local or lymphatic nodules, or large regional lymphadenopathy.
- Leishmaniasis in travelers frequently responds to observation or local therapy (Clin Infect Dis 57:370, 2013).
- Mucosal disease (L. brasilensis or less commonly other Vianna genus species; new world only)
  - palate, oropharynx including vocal cords; essentially never seen in travelers.
21 year old male
Fit and well
Non-healing ulcer Present for 8 months
Lives Melbourne (St. Kilda)
One month in Peruvian rainforest (University field trip)

DIAGNOSIS
Skin punch biopsy, neck - benign skin with chronic perifolliculitis, including a small non-necrotising granuloma, no micro-organisms detected.

Non-healing ulcer

PCR - Not Listed
Laboratory Number: 16P394579

SPECIMEN: Tissue
SITE: Neck
Result Comment
Leishmania PCR

Leishmania DNA by PCR:
Leishmania PCR Positive.

This test is still undergoing development and is not fully validated. Results should be interpreted in association with all other clinical information (clinical and laboratory) on the patient. As such this test is not currently NATA/RCPA endorsed. Refer to Medical Testing Field Document 5.5.1.2 Subclause (iii).

Weak positive for Leishmania species. Speciation unavailable due to low DNA yield.

Test performed by Sydpath, St Vincent's Pathology

Myco Ulcers PCR

SPECIMEN: SWAB
SITE: Leg ulcer

Mycobacterium ulcerans PCR
M ulcerans PCR Result: NOT detected

A negative result may not exclude the ulcerans. In addition to this test result

(Testing performed at Victorian Infectious Disease Reference Laboratory)
Status of endemicity of cutaneous leishmaniasis worldwide, 2015

Countries reporting imported CL cases
- Iran - 908
- Turkey - 815
- Jordan - 187
- Iraq - 186
- France - 105
- Lebanon - 95
- Egypt - 30
- Colombia - 20
- United Kingdom - 15
- Suriname - 12
- Portugal - 9
- Qatar - 9
- Vietnam - 6
- Kuwait - 4
- Paraguay - 4
- Venezuela - 4
- Argentina - 3
- Belarus - 2
- Bulgaria - 2
- Greece - 2
- Russian Federation - 2
- Czech Republic - 1
- Mexico - 1
- Thailand - 1

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved.

Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization
Leishmaniasis

- **Cutaneous:** *L. braziliensis* of any severity
  - [Sodium Stibogluconate] (Pentostam) or Meglumine antimoniate (Glucantime)] 20 mg/kg/day IV/IM x 20 days
  - Liposomal Amphotericin B 3 mg/kg IV once daily days 1-5 and days 14, 21 or days 1-5 and 10 ([J Am Acad Dermatol 68:284, 2013](https://doi.org/10.1016/j.jaad.2013.04.061)).

- **Mucosal**
  - Liposomal Amphotericin B (regimens vary) with total cumulative dose of 20-60 mg/kg ([Trans R Soc Trop Med Hyg 108:176, 2014](https://doi.org/10.1093/trstmh/trv196)) or Pentavalent antimony (Sb) [Sodium Stibogluconate (Pentostam) or Meglumine antimoniate (Glucantime)] 20 mg/kg/day IV or IM x 28 days or Amphotericin B 0.5-1 mg/kg IV daily or qod to total dose of 20-45 mg/kg.
3mg/kg liposomal amphotericin Days 1-5 and day 10 Healed within 1 week

(picture after 6 months)
M60, fish pond in garden; cleans and maintains *Mycobacterium marinum*
Mycobacterium marinum?

F 82 on steroids for COPD; tropical fish fancier

IDENTIFICATION OF REFERRED ISOLATE

Report status: Final
Specimen type: Nodule
Specimen site: LEFT ARM

Senders smear result: Negative
Culture result (1): Mycobacterium chelonae
Culture result (2):
  Gene probe result:
    TB DNA type 1:
    TB DNA type 2:
    TB DNA type 3:

Sensitivities
isoniazid..... rifampicin..... ethambutol..... pyrazinamide.
cycloserine... ethionamide... amikacin..... I rifabutin....
ciprofloxacin. R clarithromycin. S azithromycin.. capreomycin..
sulphonamide.. trimethoprim... doxycycline.. R cefoxitin.... R
polymyxin..... erythromycin... imipenem..... R kanamycin....
unknown....... unknown.......
Female 57

- active fit, visits Blairgowrie, teaches dinghy sailing
- Rapidly progressive very painful ulcer last 5 days
- Referred by retired BU pathologist who lives next door Kew
  - ?acute oedematous BU
- Notices whole leg is swollen
Sanford Guide

Rifampicin  
Ciproxin (? Sea water gram negative)
**Final Report**

**Myco Ulcersans PCR**

**SPECIMEN:** SWAB  
**SITE:** Leg ulcer

Mycobacterium ulcerans PCR  
M ulcerans PCR Result: - NOT detected

A negative result may not exclude the presence of Mycobacterium ulcerans. In addition to this test routine culture is recommended.

(Testing performed at Victorian Infectious Diseases Reference Laboratory)

Austin Pathology, Austin Health (APA). NATA/RCPA Lab Accred'n No 2741  
A/Prof T Leong, A/Prof B Howden, Dr Q Lam, A/Prof C Smith
Swab Superficial MCS

SPECIMEN:  Lab No: M437562

Specimen Type: SWAB
Description: Left Ankle

MICROSCOPE:

Gram Stain:
Polymorphs: Not seen
Squamous Cells: Not seen
GFC resembling Staphylococci: +++

CULTURE:

Org: Methicillin-resistant Staph aureus (MRSA): +++

SENSITIVITIES:

Org 1
Cefazolin  R
Clindamycin  S
Cefuroxime  S
Flucloxacillin  R
Ticarcillin  S
Penicillin  R
Nitrofurantoin  S
Tetracycline  S
Vancomycin  S

Methicillin Resistant Staphylococcus aureus (MRSA) isolated.
This MRSA has a multi-resistant susceptibility pattern and is resistant to all beta-lactams, including penicillins, cephalosporins and carbapenems.

Bone, skin and soft tissue infections may be treated with
Mycobacteria Culture

SPECIMEN: SWAB

AFB MICROSCOPY
Smear Quality:
Satisfactory

Auramine-Rhodamine Stain (x250 magnification):
No AFB detected

MYCOBACTERIUM CULTURE
Acid Fast Bacilli NOT isolated after 8 weeks.

Austin Pathology, Austin Health (APA). NATA/RCPA Lab Accred'n No 2741
A/Prof T Leong, Dr Marcel Leroi, Dr Q Lam, A/Prof C Smith
Leg, M 26: *Mycobacterium chelonae*?
Not responding to multiple anti-mycobacterial ABs

Final diagnosis: Pyoderma gangrenosum
M56 persistent very painful punched out ulcer on the lateral aspect of his left leg. *S. aureus* has been found at times and there has been a variable response to AB ….was complaining of very significant pain and had not slept well recently. I commenced regular panadol osteo, regular aspro clear, night time Lyrica 75 mg and Targin 1- mg bd with oxynorm 5 mg PRN for breakthrough pain. On phone review today he was much better and had slept well for the first time for several weeks. BU PCR negative x 2; no other diagnosis

Final diagnosis: Pyoderma gangrenosum
CONCLUSION
Right calf, biopsy: Sections reveal an ulcerated skin lesion. There is no evidence of malignancy. The findings are otherwise non-specific. However, given the clinical information provided, they are suggestive of pyoderma gangrenosum.
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Pyoderma gangrenosum: 3-10 per million per year
BU Rye 2018: 350/100,000 per year = 600 x more likely BU!
PCR INVESTIGATION FOR MYCOBACTERIUM ULCERANS

Test performed at: Mycobacterium Reference Laboratory

Mycobacterium ulcerans: DETECTED
F 52 autoimmune hepatitis, immunosuppressed
Skin lesion biopsy suggested vasculitis
Medical immunosuppression increased ++

Wound nurse sent swabs for culture...

<table>
<thead>
<tr>
<th>ORGANISM IDENTIFICATION</th>
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<tr>
<td>CULTURE: Cryptococcus neoformans</td>
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<table>
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<tr>
<th>SUSCEPTIBILITY RESULTS:</th>
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<tbody>
<tr>
<td>Antibiotic</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Amphotericin B</td>
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<tr>
<td>Fluconazole</td>
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<td>Flucytosine</td>
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<td>Itraconazole</td>
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<td>Voriconazole</td>
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COMMENT:
Susceptibility results of submitted isolated, Cryptococcus neoformans
DESCRIPTION: CSF
CRYPTOCOCCAL ANTIGEN
METHOD: IMMY LFA
Cryptococcal Ag CSF: POSITIVE
30 year old, female, thigh
(no other illnesses)
Holiday house MP
Lesion present 1 month

BU confirmed
PCR and culture

65 year old, female, thigh
(SLE, MCTD, Rx prednisolone and Azathioprine). Brief exposure to MP.
Lesion present 2 months

MAC confirmed smear and culture 
(*Mycobacterium avian complex*)
Thank you!

• I would like to acknowledge patients who have graciously allowed me to take clinical photos for educational talks

• For information about Buruli ulcer in Australia
  – see my website:  
  – Or type “Paul Johnson Buruli ulcer” into google
  – (Ozemail page “Buruli ulcer in Australia”)