Imported Monkeypox:
In the era of the high consequence infectious disease network

Tropical and Infectious Diseases Unit RLUH

Where we all make a difference
Learning Outcomes

• Define high consequence infectious diseases (HCID)

• Understand the history behind our HCID unit

• Monkeypox in the HCID era

• Explore key operational factors and lessons learnt in managing HCID cases.
PHE definitions of High Consequence Infectious Diseases
High Consequence Infectious Diseases

Definition:
• acute infectious illness
• ability to spread person-to-person
• high case-fatality rate
• difficulty in rapid recognition and detection
• lack of effective treatments
• co-ordination at national level to appropriately respond

https://www.gov.uk/guidance/high-consequence-infectious-diseaseshcid
Examples: Contact HCIDs

Also known as viral haemorrhagic fever (VHF):
- Crimean-Congo haemorrhagic fever (CCHF)
- Ebola virus disease
- Lassa fever
- Marburg virus disease
- Lujo virus disease
- Argentinian and Bolivian haemorrhagic fever
- Severe fever with thrombocytopenic syndrome
Examples: Airborne HCIDS

- “Bird Flu”: Influenza A H5N1, H7N9
- Middle East respiratory syndrome (MERS)
- Monkeypox
- Nipah virus
- Pneumonic plague
- Severe acute respiratory syndrome (SARS)
- Andes virus infection (hantavirus)
NHS England HCID program goals

- Agreed approach to managing an ‘end to end patient pathway’
- Known (confirmed) and unknown (but highly suspect) HCID cases
- Ensure sustainable response in place
- Ensure response efficiently and effectively actionable
History of HCID network
8/Aug/14 WHO declares Ebola public health emergency

Mid. Sep 14 Nationwide call for volunteers

30/Sep/14 EVD diagnosed in Liberian man visiting family in Dallas

6/Oct/14 First EVD transmission outside Africa in Spain.

8/Oct/14 Plans for ‘surge units’ in the event of return of infected UK HCW, 

..... Sheffield and Liverpool were requested to support the Royal Free as ‘surge centres’, in conjunction with Newcastle.

There was no UK experience in developing or using centres to manage such patients outside the Trexler facilities in London and in Newcastle
Initial challenges

There was no advanced preparedness on what to do with the patient. There was no protocol, there was no system. The nurses were asked to call the Infectious Disease Department. The Infectious Disease Department did not have clear policies to provide either.
Developing the “Surge” unit

- In 4 months or so!
  - Developing robust policies
  - Reconfiguration of isolation unit
  - Sustainable staffing rota, fully trained staff
  - Appropriate PPE
Spring 2015  RLH fully operational ‘Surge Centre’ with national Health and Safety approval

November 2015  NHS EPRR framework published
Consolidate the lessons from Ebola
HCID commissioning programme commenced

Jan 2018  Royal Liverpool TIDU ‘formally’ commissioned to provide airborne HCID care

22/Aug/18  First HCID patient arrives!
HCID process

St Elsewhere
- HCID suspected

IFS @ PHE
- Case discussed
- On call rota

EPRR @ PHE

HCID network activated

RLUH
Newcastle
Royal Free
Guys St Thomas’
Sheffield

Patient transferred to unit
Managing HCID patients at RLH

MERS
Managing HCID patients at RLH

Monkeypox
Monkeypox Case 1 RFH

• MERS discharged 6\textsuperscript{th} September
• HCID network stepped down........
32 year old Nigerian Naval Officer

- 01/09/18- Fever/Myalgia in Abuja while in Abuja
  - Abrasions from shaving pubic hair, no spots, prescribed ciprofloxacin and IM injection “for malaria and typhoid”
- 02/09/18 flew to UK to attend a military training course in Cornwall
- 03/09, medical naval officer, flucloxacillin 250mg for folliculitis
  - Commenced training course with other officers
- 06/09 - New lesions arms, scalp, trunk. Discussed with military ID Consultant
  - Advised self-isolation
- Further new lesions over scrotum, penis, palms, feet; ongoing night sweats
- Images obtained and reviewed remotely by RFH HCID Team
Royal Free ID team opinion

• ‘Unlikely to be monkeypox, but should exclude’
• Testing discussed with PHE Rare and Imported Pathogens Laboratory (RIPL)
• Continue self-isolation at naval base
• HCID team will help to arrange on-site sampling
• Six skin swab samples sent to RIPL by specialist courier
7th Sept: RIPL results & further actions

• 15:00 orthopox virus DNA detected by PCR
• 17:00 monkeypox virus DNA detected by PCR
  – PHE National Incident Management Team meets
• 18:30 **Airborne HCID Network re-activated**
  – For specialist ambulance transfer to Royal Free HCID Unit
8th September

- C/O fatigue, groin & scalp discomfort, eye pain
- No myalgia, cough, coryza, sore throat, urinary symptoms, gastrointestinal symptoms
Background history

- PMH - nil
- DH - Nil
- Travel - at home in Delta State 19-24/08/18; deployed for sea patrol around Port Harcourt; no rural travel
- Lives in rented modern house, with family - all well.
- No pets/rodents/livestock
- No contact with unwell persons
- No bush meat > 6 months
- No traditional remedies or animal products
- Sexual history – nil of note; HIV neg in August
Examination findings

- HR 80, reg
- BP 123/81 mmHg
- RR 16
- Sats 97% OA
- Temp 37.4°C
- GCS 15/15
- Normal respiratory, cardiovascular, abdominal examinations

- No conjunctival injection; vision normal
- Oropharynx: NAD
- Joints normal
- LN - small left anterior cervical node, nil axilla, bilateral bulky inguinal lymphadenopathy
Skin lesions

- Mixture of:
  - vesicles
  - pustules
  - umbilicated lesions
  - scabs
  - ulcers (predominantly pubic region and genitalia)
Initial management

- Continue Airborne HCID isolation
- Viral throat swab, urine & blood for monkeypox PCR (alternate days)
- Haematology and biochemistry tests

- 09 Sept: Brincidofovir 200mg po, following discussion, approvals and consent
Progress and outcome

• Variable mood
• 14/09 Last new lesion emerged on right lateral foot
• 16/09: agreed no need for further brincidofovir as no new lesions and LFTs deranged
  - Pubic and scrotum lesions slower to heal – serial PCRs
• 2/10 Lesions all dry/healed, no remaining scabs, and all samples PCR negative
• 04/10 (d26), patient discharged.
Monkeypox 2 RLH

- MERS discharged 6th September (16 days)
Presentation

- 10/09: 36M transferred to RLH from Blackpool due to clinical concern re Monkeypox.
  - 7d L groin swelling, fever
  - Rash: face -> scalp -> limbs incl palms / soles
  - Spared torso
  - Severe pain in L foot and lower limb and limited mobility
Travel History

- MCR – CDG – LOS Lagos
- Sapele
  - family wedding
  - shook hands with man with pox-like rash
- UPSI
- Oghara
  - Ate bush meat.
Other History

• PMH
  – Chickenpox as child

• DH
  – Nil significant

• SH
  – Life-long non-smoker.
  – Drinks 5 nights a week, 2L of vodka per week.

• Investigations
  – CRP 75
  – WCC 8.6 PLT 157 Hb 135
  – Malaria film negative
  – UE normal - eGFR N
  – Bili 23 ALT NAD
  – Glucose normal
  – CXR – clear
  – HIV negative
### Examination

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<th>Resp Rate</th>
<th>SpO2</th>
<th>Inspired O2</th>
<th>Temp</th>
<th>BP</th>
<th>Heart</th>
<th>Conscious</th>
<th>Pain Score</th>
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<td>95</td>
<td>21</td>
<td>39.1</td>
<td>117/79</td>
<td>89</td>
<td>A</td>
<td>1</td>
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Where we all make a difference
Examination

- Marked lymphadenopathy
Clinical Challenges

- Severe neuralgia including chest pain
- Difficult parenteral access
- Severe agitation – ? Alcohol withdrawal
- POSSIBLE Collections L lower limb
  - ? Bacterial
  - ? Poxvirus
- Persistent viraemia
Solution:

• ECG
Solution:

- PICC line insertion
- ‘just in time approach’
Solution: USS-guided drainage
Fluid from collections

Microbiology
- Thick yellow/creamy pus
- Leucocytes: ++
- Organisms: None seen
- Bacterial DNA NOT DETECTED by PCR
- 3/10/2018 Discharged (24 days)

Virology

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<tr>
<th>Date</th>
<th>EDTA blood</th>
<th>Drain fluid</th>
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<tbody>
<tr>
<td>7/9/18</td>
<td>33.011</td>
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<td>21/9/18</td>
<td>32.114</td>
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</tr>
<tr>
<td>26/9/18</td>
<td>32.298</td>
<td>Deposit:13.568</td>
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<tr>
<td></td>
<td></td>
<td>Supernatant:16.551</td>
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<tr>
<td>27/9/18</td>
<td>negative</td>
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Values = cycle thresholds
Monkeypox case 3
25th September to 9th November

• 40 y old HCA caring for case 2 before dx of MPX, at Blackpool Hospital.
• Received post-exposure vaccination on day 5 of exposure and became ill 2 weeks after initial contact
• Develops lesions on face, trunk and hands and intense headache, no fever
• Treatment with Brincidofor x2, develops LFT rise
• Aviraemic after 2 weeks but continues to remain throat swab PCR positive
• After 5 weeks of isolation discharged into home isolation
• Throat swab PCR negative after nearly 7 weeks (46 days)

• Issues:
  – Prolonged isolation
  – How long is one infectious?
Monkeypox Cases 4 and 5

- 2 contacts of case 3 admitted to RLH for monitoring
- Both discharged after a number of days
- Full PPE for 3 patients for 48 hrs !!
Monkeypox: Background

- Poxvirus family (genus *Orthopoxvirus*)
- First isolated 1958 in monkeys
  - Natural reservoir unknown, not non-human primates
- First human case 1970, Zaire (now DRC)
- 2 clades: West African and Central African
- Animal-human transmission: scratches, infected meat, fluids
- Human-human transmission: respiratory route or by direct contact with infected bodily fluids.
- Incubation 7-14 days
- Case fatality: 10% in Africa, 0% in US outbreak 2003
Monkeypox: Clinical

• Nearly identical to smallpox, although usually less serious
  • Lymphadenopathy rare in smallpox, common in MPX
• Vesicular rash
  • Extremities > trunk
  • Oral MMs, genitals, eyelid, corneal
• Other: headache, D+V, delirium
• Management primarily supportive
Clinical manifestations

- Incubation period of 5 to 21 days (typically 6 to 16 days)
- Prodrome (1-5 days): fever, flu-like illness, lymphadenopathy
- Rash then follows

Few lesions to thousands
Variable size
Different morphologies at the same time
Classically centrifugal spread
Experimental treatments

- Tecovirimat (TPoxx)
  Pan-orthopox p37 inhibitor - prevents virus from leaving an infected cell
  Prevents death in lethal challenge monkeypox and rabbitpox animal models
  Phase I trial – well tolerated, no SAEs - FDA approved for smallpox

- Brincidofovir
  Lipid conjugate prodrug of cidofivir – oral; less renal toxicity
  Active in vitro against orthopox viruses, CMV, adenovirus, BK virus, HSV
  Survival advantage in lethal rabbitpox model, even with delayed treatment
  Phase I trials >1000 subjects; Phase III trials for CMV in STC patients (failed)
  Ongoing trials for adenovirus
  Increased ALT/AST common; diarrhoea with cumulative exposure
11 Weeks of HCID in the UK in 2018

- MERS 22nd Aug-6th September
- MPX 1 7th September to 4th October
- MPX 2 10th September to 3rd October
- MPX 3 25th September to 9th November

(Chart showing timeline of events with MERS, Monkeypox (1) RF, Monkeypox (2) RLH, and Monkeypox (3) RVI)
Managing HCID patients at RLH

HCID PPE
The buddy and the observer

- **Buddy**: supervises the safe doffing (taking off) PPE
- **Buddy and/or observer**: supervise donning PPE, watch patient carer when in room to spot deviations / breaches
- **Observer**: acts as ‘runner’

- Fourth member of staff (senior nurse) overview,
- Consultant: teleconferences, comms, buying the takeaway food
Patient contact

1. Patient care
   Patient’s room

2. Buddy
   Doffing room

3. Observer
   Ante room

4. Support
   Corridor/office
Operational challenges and lessons learnt
Staffing

- Per week - 17:
  - 2 Consultants
  - 6 Registrars
  - 9 Nurses
Public Health

- Teleconferences
- Contact tracing
- Passive follow up
- Active follow up
- Vaccination:
  - 23 of 37 staff vaccinated versus smallpox
  - >120 UK wide
Waste disposal and cleaning

• Carefully planned and managed
• Counter-terrorism unit involved
Patient and staff experiences
PPE

Patient
- Can’t see face
- Voice muffled
- Can’t read body language

Staff
- Hot + bothered
- Hard to hear
- Limited movement
Patient care challenges

• Language barriers
  – MERS patient spoke only Arabic
• No visitors
• Unable to leave room
• Communication
  – Smart phones; MERS patient unable to use!
  – WhatsApp video calling
• Dietary requirements
• Safe management of agitation
  – Health Protection (Part 2A Orders) Regulations 2010
Summary

- HCID network tested for the first time in the UK
- Survival MERS patient
- First cases MPX in UK
- First returned traveller, First imported, First HCW
- MPX case presentations very different
- First use in UK of experimental drugs for MPX
- 79 days of HCID has marked resource issues
P0188 The 5th case of Middle East respiratory syndrome - Coronavirus infection in the UK: our experience and testing of the new high consequence infectious diseases network
A. Al Balushi* (Liverpool, United Kingdom), P. Hine, E. Nsutebu, H. Winslow, L. Ratcliffe, J. Dunning, M. Zambon, T. Blanchard, M. Beadsworth

P0189 Managing monkeypox in the high consequence infectious diseases era: novel management solutions
Thanks to...

- Leeds ID
- Blackpool
- NHS EPRR
- Ambulance services
- PHE and PHE Collindale/Porton Down
- Nick Price and the HCID network (Newcastle, Sheffield, GSTT, RFH)
- Staff at RLUH
- Lab staff at RLUH
- Interventional radiology
- Patients and families
- Everyone we have forgotten to mention
Thank you.

For more details please contact:
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Feedback

“Thank you for the care you gave my dad, all the efforts you have done are highly appreciated”

Felt reassured

“Cannot believe you helped me get better”

Kept informed, even with the language barrier and family not near

“Being able to speak to the same person every day”

All Questions Answered Openly & honestly

Grateful

Engaged

Respected

SAFE