An emerging threat or sporadic events? Monkeypox

Dr Paul Hine
Tropical and Infectious Diseases Unit RLUH

Where we all make a difference
The UK HCID network
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
Contact HCIDs

- Cimean-Congo haemorrhagic fever (CCHF)
- Lassa fever
- Marburg virus disease

Airborne HCIDs

- Ebola virus disease
- Influenza A H5N1, H7N9
- MERS
- Monkeypox

6 June 2019

VVE: Monkeypox
The HCID-Airborne network

- 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
3 UK Monkeypox cases 2018
Case 1

**PC:** 32M with fever, myalgia, rash.

**HPC:**
- 1/Sep/18, Abuja: empirical treatment for ‘malaria and typhoid’; abrasions from shaving pubic hair
- 2/Sep/18: Abuja → Cornwall
- 3/Sep/18: treated as folliculitis, flucloxacillin.
- 6/Sep/18: widespread new lesions, night sweats.

**Travel**
- Home in Delta state, Sea Patrol 24/Aug/18 -> 1/Sep/18.
- No rural travel / unwell contact / animal contacts / bush meat / animal products / UPSI
Diagnosis

- Royal Free remote review: ‘Unlikely to be monkeypox, but should exclude’
- Self-isolation in naval base.
- Skin swabs → PHE Rare and Imported Pathogens Laboratory (RIPL)
- 7/Sep/19:
  - 17:00 monkeypox virus DNA detected by PCR
  - 18:30 Airborne HCID Network activation
  - Specialist ambulance transfer to Royal Free HCID Unit
Assessment

- Fatigue, groin & scalp discomfort, eye pain
- Afebrile at presentation
- Bilateral bulky lymphadenopathy
- Widespread skin lesions

- vesicles
- pustules
- umbilicated lesions
- scabs
- ulcers (groin)

6 June 2019

VVE: Monkeypox
Progress

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

- 14/Sep/18: Last new lesion R lateral foot
- 16/Sep/18: no further brincidofovir (no new lesions, LFTs)
- Groin lesions slower to heal – serial PCRs
- 2/Oct/18: Lesions dry/healed, all samples PCR negative
- 04/Oct/18: discharged on day 26
- Variable mood noted
Case 2

- 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

- MCR – CDG – LOS
- 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

<table>
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<tr>
<th>Resp Rate</th>
<th>SpO2</th>
<th>Inspired O2</th>
<th>Temp</th>
<th>BP</th>
<th>Heart</th>
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<th>Pain Score</th>
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<td>117/79</td>
<td>89</td>
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</table>
Examination

- Marked lymphadenopathy
Clinical Challenges

• Severe agitation
  • Alcohol withdrawal
• Severe neuralgia including chest pain: ECG
• Difficult parenteral access: ‘just-in-time’ training
• Possible collections L lower limb
• Persistent viraemia
Solution: USS-guided drainage
Progress

Treatment with Brincidofovir x2
Case 3

**PC:** 40F HCA with rash and severe headache, no fever.

**HPC:**
- cared for case 2 before diagnosis of MPX at Blackpool
- PEP vaccination on **day 5** after exposure
- 25/Sep/2018, 2 weeks after initial contact, develops lesions on face, trunk and hands and intense headache, no fever
Progress

• Admitted to Newcastle
• Treatment with Brincidofovir 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)
Clinical care

- 17 F/T staff per week:
  - 2 Consultants
  - 6 Registrars
  - 9 Nurses
- Enhanced PPE
Public Health Management

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

Media Management

VVE: Monkeypox

6 June 2019
Commentary

- Varying presentations
- Varying severity of illness
- Possible neuropsychiatric features in 2 / 3 patients
- Possible viral collection in 1 / 3 patients
- Prolonged viraemia / positive samples
- Uncertain infectivity
- Single human-to-human transmission, despite PEP at day 5 post-exposure.

6 June 2019
Monkeypox: background
History and Virology

• Poxvirus family (genus *Orthopoxvirus*)
• First isolated 1958 in monkeys
  • Natural reservoir unknown, not non-human primates, isolated 2x in wild animals:
    • Rope Squirrel in DRC
    • Sooty Mangabey, Cote D’Ivoire
• First confirmed human case 1970, Zaire (now DRC)
  • Thought to have infected humans for 1000s of years
• 2 clades
  • West African (less virulent)
  • Central African
<table>
<thead>
<tr>
<th>Country</th>
<th>Years</th>
<th>(n) MPX cases</th>
<th>Number of deaths</th>
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<tr>
<td></td>
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</tr>
<tr>
<td>United Kingdom</td>
<td>2018</td>
<td>3</td>
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Case fatality: up to 10% in Africa, <1% for West African clade, 0% in US outbreak
Epidemiology

Transmission:
• Animal-human: scratches, infected meat, fluids
• Human-human: respiratory, contact with fluids

Incubation:
• 7-14 days, shorter incubation if animal bite/scratch

• US outbreak 2003: Pet prairie dogs exposed to African rodents
• Nigeria Outbreak 2017
  • Phylogenetics: 3 outbreak isolates, closely related to 1971 Nigerian strain
  • Not imported, likely spillover event

• Nigeria Outbreak curve 2017 – 2019
• Source: Chikwe Ihekweazu, Nigeria Centre for Disease Control, ECCMID 2019
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
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

- **Brincidofivir**
  - 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
Vaccination

- **Imvanex® / Imvamune®**
- 3rd generation smallpox vaccine
  - 1st/2nd gen: replication competent vaccinia virus
  - 3rd gen: attenuated Modified Vaccinia Ankara
- Trials in HIV
- DRC study: distant smallpox vaccination conferred 81% efficacy
- Based on smallpox data, optimal PEP timing 4 days, considered up to 14 days.
An emerging threat?

• Reservoir remains unknown, source of current Nigerian outbreak remains unknown
• Vigilance required to protect against human-human transmission from imported cases
• Risks:
  – Cessation of smallpox vaccination
  – Rainforest logging, animal displacement
  – Civil unrest
  – Mutation increased human-to-human transmission
Thank you.

paul.hine@rlbuht.nhs.uk

@doc_phine

- HCID network
- Blackpool Victoria Hospital
- NHS EPRR
- Ambulance services
- PHE
- RIPL
- Clinical staff
- Laboratory staff
- Transport staff
- Waste disposal staff
- Patients and families
- Everyone we have forgotten to mention