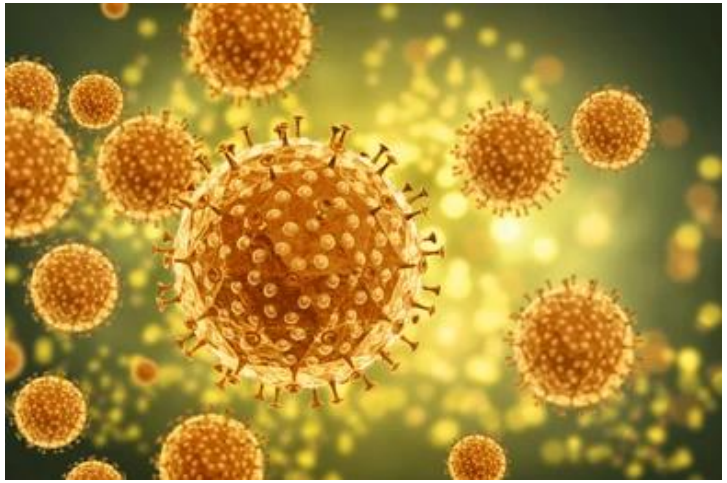


Microbiology Trainee Clinical case discussion club

Session 2: 15th March 2023, 12-1pm GMT

Supported by:

The Association for Clinical Biochemistry
Microbiology Group

Housekeeping

- Cases involve real patients. Please do not divulge any patient identifiable information. The content of the session is strictly confidential.
- Please keep your microphones on mute.
- Post any questions in the chat. There will be opportunity throughout the call to get to these. The session chair will ensure any queries are covered.
- When making a comment (as part of the interactive element) – please provide reasoning! We are all here to learn). There is no judgement if you are unsure.
- Please engage with the session and enjoy.

Call for presenters

- Please contact: Callum Goolden (callum.goolden@lthtr.nhs.uk) if you have a case you would like to present or if you would like to gain some experience chairing meetings.

- Presenting trainees must be accompanied by a suitably qualified (FRCPath) colleague to provide clinical oversight.
- Please ensure that cases are forwarded to the session chair in advance to facilitate any necessary formatting.

Micro Trainee Clinical Case discussion club 15/03

Callum Goolden – Trainee Clinical Scientist (STP)

Lancashire Teaching Hospitals NHS Foundation Trust

Presentation

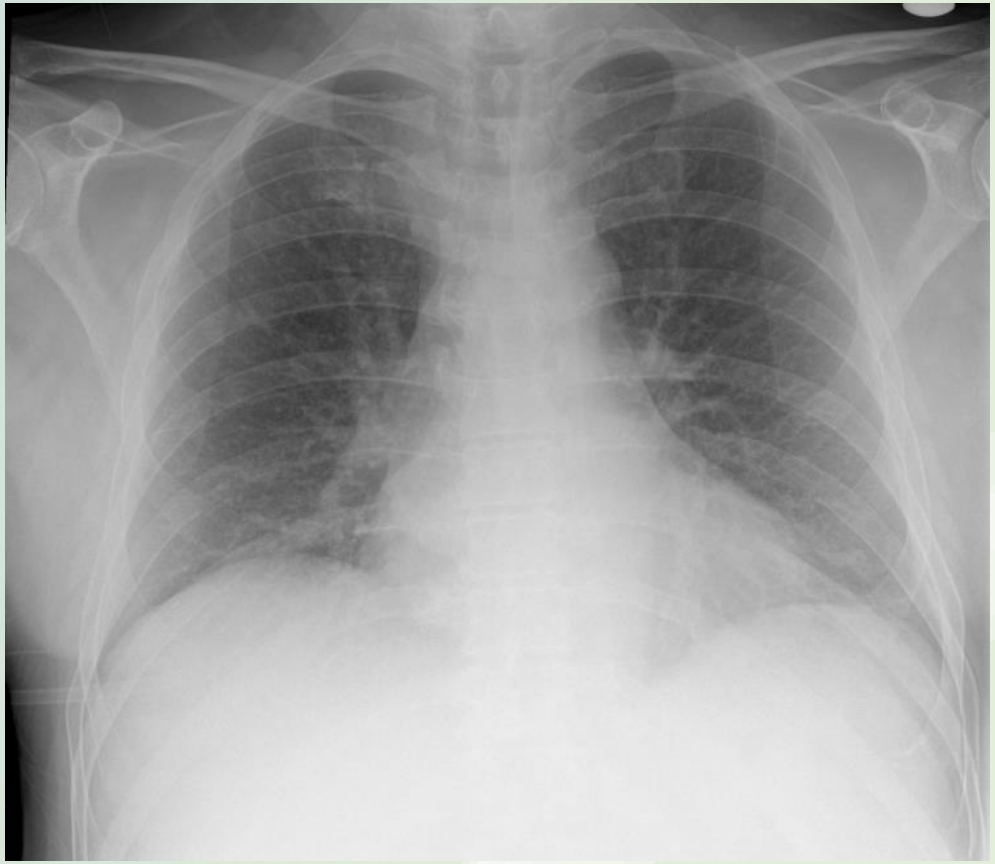
- 59M
- PC: Fevers w/rigors and confusion.
- HPC: 1/52 history of fever and intermittent confusion, hallucinations, SOB, painful swelling in right calf, unsteady on feet, back pain. Diarrhoea 6-7 times/day.
- PMH: HTN, Hypercholesterolaemia.
- SH: Lives independently with Wife, Smoker (20/day) for 40 years, EtOH excess, no pets.
- TH: Recent foreign travel to Lanzarote to all-inclusive hotel (returned 1-week prior). Reports falling unwell mid-trip (Rigors).
- On examination: Pyrexial, nil respiratory concerns (+ CXR clear), nil cardiac concerns, nil CNS concerns, ABD soft, non-tender.
- Ix: CRP 258, WCC 5.7, NEWS 7
- Implications: Sepsis ?source. Started on 1.5g CEFUROXIME & STAT GENTAMICIN. Blood cultures taken. Additional requests for Stool/urine cultures, urine Ag.

Initial thoughts? Additional investigations? Additional history?

Case timeline

15/1:

- On supplementary O2 and IV fluids. No response in inflammatory markers on Abx. Repeat CXR showed ?Right upper zone patchy opacification. **Still spiking temperatures**.
- Ix: SARS-CoV-2/Influenza negative, GI multiplex PCR negative, Urine Ag for Legionella/Pneumococcus negative, no positive cultures.
- Empirically escalated to TAZOCIN and CLARITHROMYCIN on advice of microbiology. Request also made to perform blood films for malaria, 2 x stool samples and a standard BBV screen.



Case timeline

17/1:

- Patient referred to gastroenterology on b/g of elevated liver blood tests (GGT 191, ALP 160, ALT 151)
- Liver USS showed fatty liver and on review, **acalculous cholecystitis**
- Ix: BBV screen negative, MSU negative, malaria screen negative (x2).
- Patient has no focal signs other than continuing diarrhoea.
- Unclear what we are treating here: Microbiology suggested a CT-Abdo to assess for cause of ongoing diarrhoea and to repeat blood cultures and give STAT Gentamicin if NEWS>7.

- **Additional Microbiology investigations requested by astute Gastro registrar…**

Case timeline

18/1:

- Microbiology consulted again. Patient spiking more fevers, rising inflammatory markers despite treatment. Advised to escalate to MEROPENEM if no improvement.

24/1:

- CRP seemed to fall in response to MEROPENEM, but not as quickly as expected for a simple infection. Is meropenem really helping here?
- Now SARS-CoV-2 positive (HCAI)
- Interestingly, ANCA screen came back STRONGLY positive. Multiple vasculitis markers identified but could not be interpreted. Rheumatology input sought.
- Slow CRP response may be explained by vasculitis if diagnosed, but otherwise surgical review is recommended.

5pm…

Differential diagnoses?

Reference lab result

- Call from RIPL – ***Coxiella burnetii*** **PCR positive**, also **IgG Phase II & IgM positive** (No titration – lab hazard).
- Given onset of illness – deemed probable (acute) Q-fever.
- Advised treatment with DOXYCYCLINE 100mg BD for 2 weeks, prolonged course if still unwell.
- Follow up sample requested in 2 weeks after completion of DOXYCYCLINE.
- Investigate for focus of infection, vasculature, grafts, valves. Please do ECHO and consider PET.
- Isolation not required as person-person transmission is rare.

- ACTION: Patient Switched to DOXYCYCLINE to complete minimum course of 2-weeks (depending on response).

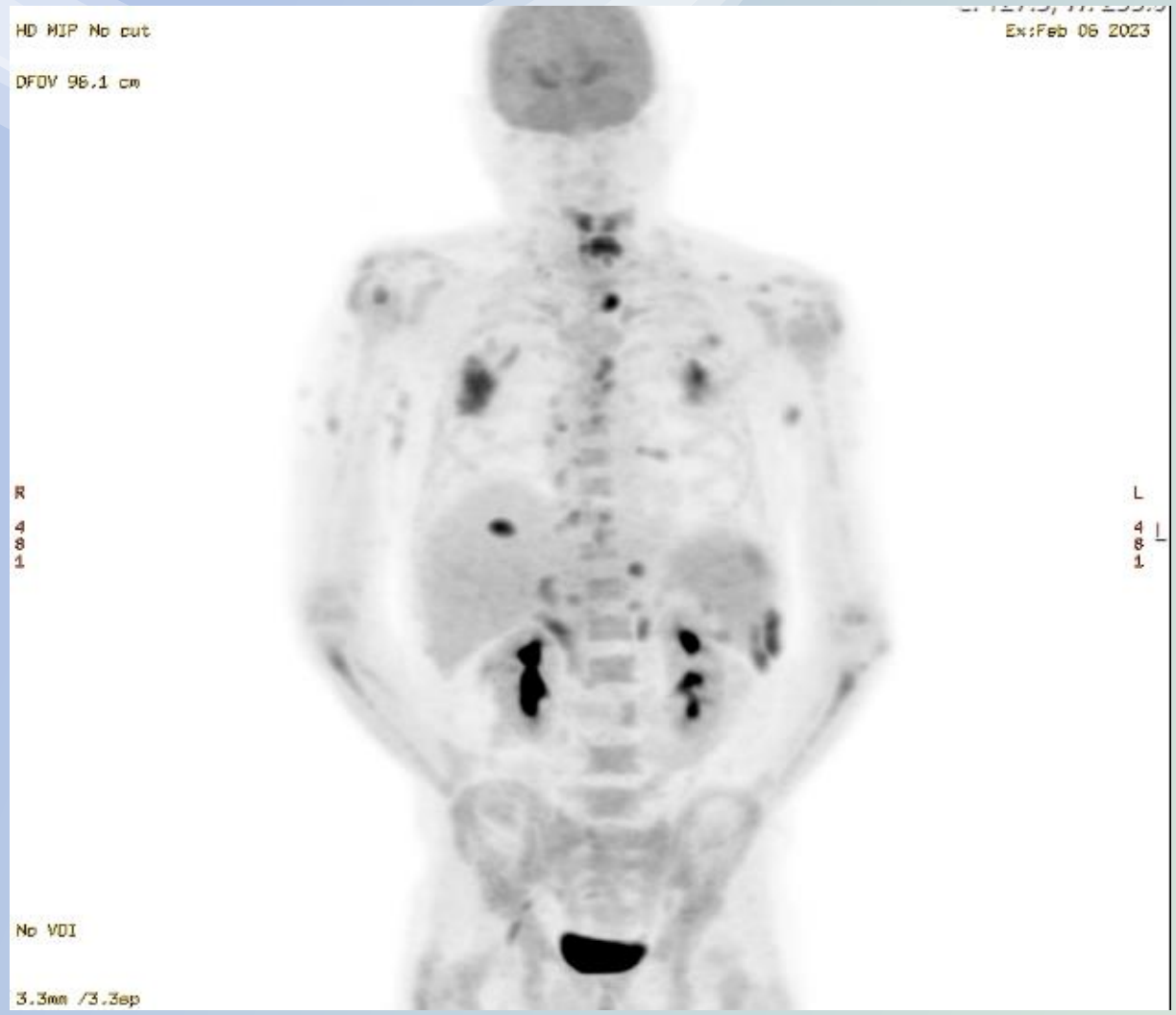
Gathering further history

- Patient still pyrexial with significant confusion (NEWS 6)
- Further patient history obtained and conversation had with RIPL team
- Retired. Previously employed by BAE Nuclear fuels.
- No information on insect bites/unpasteurised milk product consumption.
- Initially thought to have had no animal contact, however it later came to light that he had visited a **petting farm** in the UK in mid-December. UKHSA HPT notified.
- HPT notified APHA and environmental health. Farm in question currently closed until spring. EHO to follow up to ensure adequate hygiene practices in place. Note: Q-fever is not a reportable disease in animals.

Laboratory exposures

- Patient in hospital for 15D prior to positive Coxiella serology result.
- Multiple samples sent to lab during this period (including multiple BCs, stool and urine)
- Very low infectious dose (1-10 organisms).
- ACDP HG3 pathogen.
- Risk assessment completed by Microbiology / DIPC (with help from RIPL).
- Risk of exposure deemed VERY LOW.
- No further action other than processing Blood cultures at CL3.

Further imaging



- PET-CT performed which showed uptake in multiple organ systems.
- ?metastatic disease ?related to Q-fever diagnosis
- Considered for RIPL Q-fever MDT.

RIPL follow up

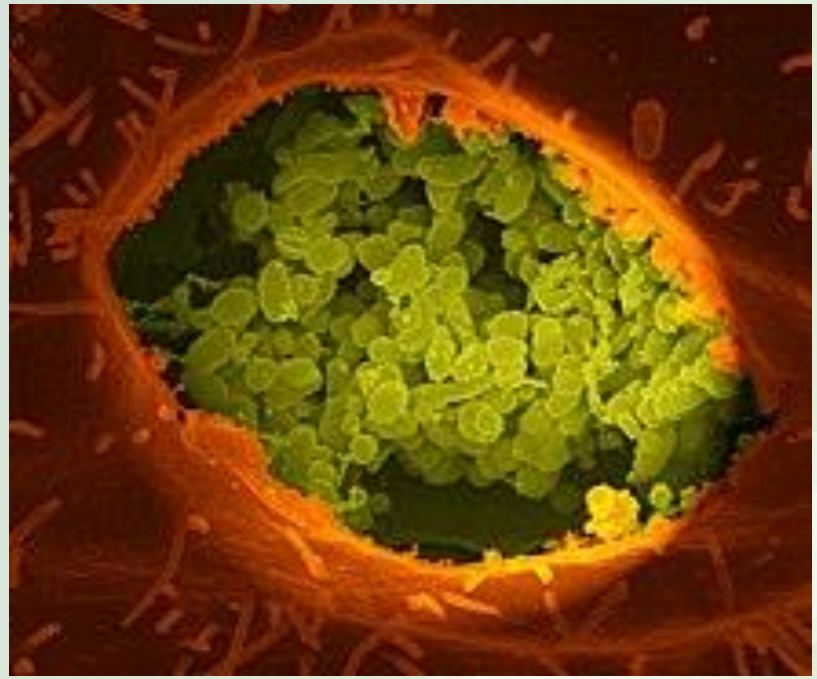
- Further serology results:
- Phase 1 IgG negative
- Phase 1 IgA negative
- **Phase 2 IgG POSITIVE titre 1:5120**
- **Phase 2 IgM POSITIVE titre 1:10240**
- It is the absence of phase 1 antibodies that rules out chronic Q fever. Lab results clearly point towards infection in the last few weeks. Previous theory of reactivation of previous infection now very unlikely.
- If PET-CT findings result of Q-fever, then this is a **highly atypical** presentation.
- Advice: Continue DOXYCYCLINE treatment. No requirement for second agent (Chloroquine). Recommended to investigate alternative causes of lesions to delineate other pathology.

Case conclusion / current state of play

- Discharged with safety netting on the 17th February.
- Routine weekly blood monitoring.
- Follow up in 2 weeks
- On DOXYCYCLINE until next review.
- Currently awaiting US neck and biopsy of subcutaneous lesion if possible.
- Fever generally settling, still spiking but less severe and less frequent
- Still on DOXYCYCLINE until after US scan.
- Still concerns re: cancer possibility.

Coxiella burnetii:

- Obligate, intracellular, pleomorphic GNB
- Genus *Coxiella* morphologically similar to rickettsia
- Highly resistant to environmental stresses e.g. desiccation, heat, disinfectants. The bacterium exhibits a biphasic life cycle, forming a resistant, spore-like small cell variant.
- *C. burnetii* causes disease (sometimes) and abortion in animal hosts e.g. cattle, sheep, goats.
- Causative agent of Q-fever in humans – ZOONOSIS.



Q-fever

- ~50% of infected individuals develop non-specific, flu-like symptoms: High fever, rigors, severe headache, myalgia, malaise, nausea, pharyngitis, non-productive cough, diarrhoea, abdominal/chest pain, lymphadenopathy.
- Symptoms typically resolve within 2-weeks.
- Complications of Q-fever can include:

- Pneumonia or granulomatous hepatitis (severe)
- Myocarditis
- CNS complications
- Post Q-fever fatigue syndrome
- **Chronic Q-fever (5%)**
- Endocarditis.
- In pregnancy: Premature birth, LBW or miscarriage. Chronic infections can put pregnancies at risk.

Q-fever

Incubation period:

- 2-3 weeks (may range from 2-40 days)

Incidence:

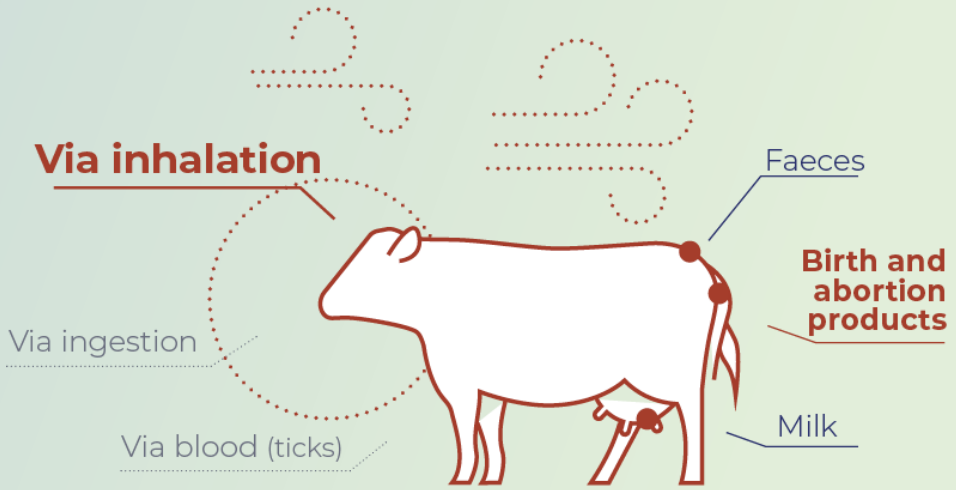
- 50-100 human cases per/year in the UK (HSE stats) – likely under-reported.

At risk groups:

- Agriculture workers
- Abattoir workers, meat processing plant workers, butchers.
- Veterinarians
- Laboratory workers (if working with high-risk specimens).

Q-fever (Transmission)

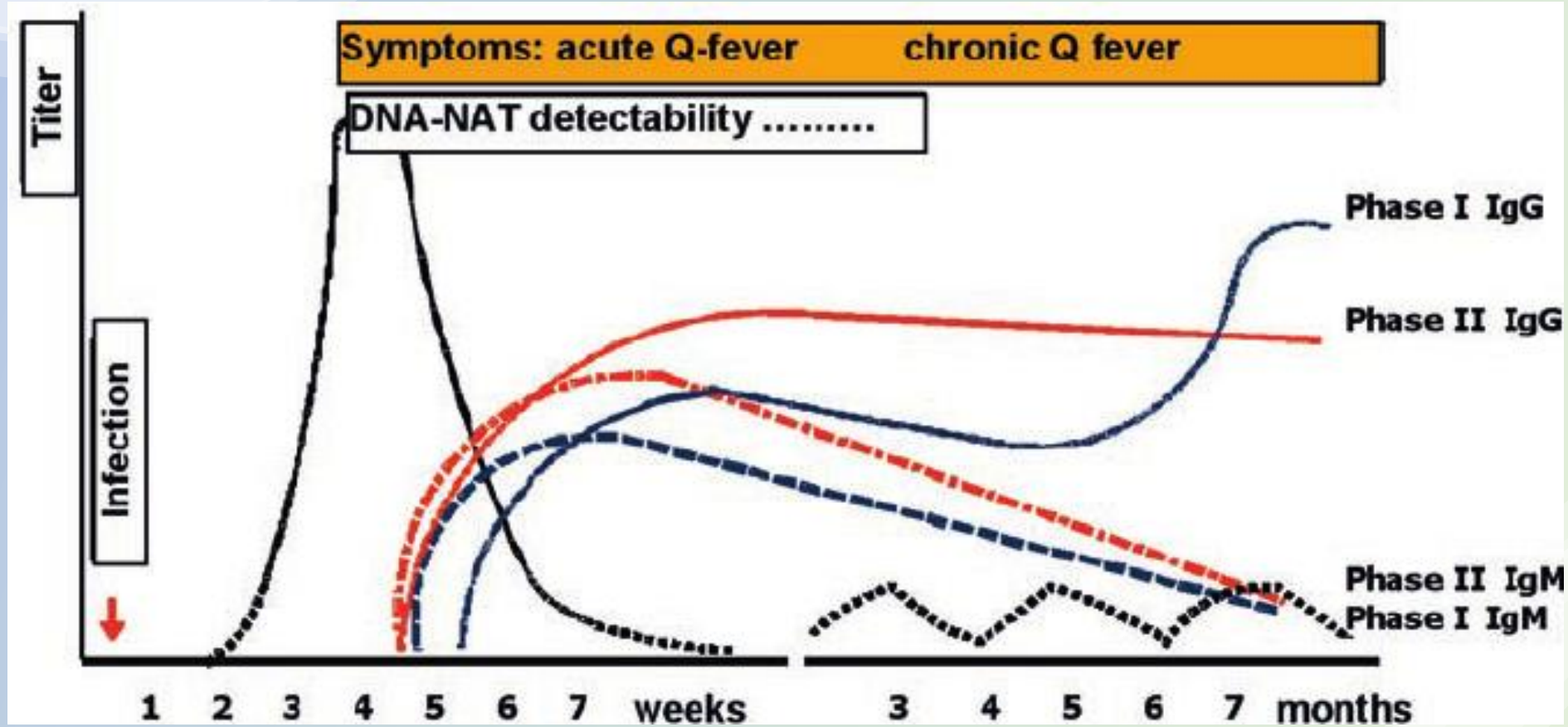
- Cases are sporadic. Outbreaks are rare and unpredictable.
- Q-fever has an exceptionally low infectious dose (1-10 organisms).
- The most common route of transmission is via inhalation of resistant spore-like form on dust particles contaminated with afterbirth, blood, urine or stool of infected animals.
- Direct contact with farm animals, especially sheep, cattle and goats or animal skin, fur, wool or pelts.
- Entry via broken skin.
- Consumption of unpasteurised milk (disputed).
- Tick bites (rare) have also been implicated.
- Windborne spread from nearby agricultural premises can cause urban outbreaks (rare).



Q-fever (Diagnosis)

- Diagnosis of Q-fever is clinically challenging.
- Good patient history taking is important (relevant exposures, occupational information).
- Other clinical evidence to support Q-fever diagnosis: prolonged fevers with low platelet count, normal leucocyte count AND elevated liver enzymes = suggestive, but not diagnostic
- Laboratory testing for Q-fever is performed by the Rare and Imported pathogens laboratory at Porton down.
- **Serology**: Serial titration of sera and detection of *C. burnetii* antibodies by IF.
- **PCR:** Molecular assays can be performed on whole blood, serum and biopsy material. Blood should ideally be obtained within the first 2-weeks of symptoms
- **Chronic Q-fever** – infection is confirmed by an elevated phase I IgG >/=1:1024 and an identifiable focus (e.g. endocarditis). Tissue biopsies may be obtained for confirmation by PCR or immunohistochemistry.

Q-fever (Diagnosis)



Q-fever (Treatment)

- First line treatment for acute Q-fever is DOXYCYCLINE (100mg BD) for 1-2 weeks. In pregnancy, Co-trimoxazole may be selected instead. Treatment results in a reduction in symptom duration, however most infections will resolve without treatment.
- Chronic infection requires a much longer course (several months of DOXYCYCLINE +/- chloroquine). The RIPL run an MDT with cardiology, infectious disease expert input which may help to inform treatment duration decisions.

Q-fever (Prevention)

- No vaccine available in UK for Q-fever.
- Difficult to prevent animals becoming infected – no formal control programme or vaccines for livestock in the UK.
- Since Q-fever is mainly an occupational disease linked to rural environments, targeted prevention/control measures are most effective for specific occupational groups and environments:

- Restricting access to potentially infected animals.

- Safe disposal of animal birth products.

- Should avoid contact with cattle, sheep, goats and cats while the animals are pregnant (pregnant women, immunocompromised, those with congenital or acquired heart valve disease or vascular grafts).

- Hand washing, protective clothing e.g. gloves/goggles, clean cuts/grazes immediately and cover with waterproof dressing.

Useful resources

- Q-fever infections in humans: sources, transmission, treatment (GOV.UK). Available at: https://www.gov.uk/guidance/q-fever
- Q-fever: good practice for farmers (GOV.UK). Available at: https://www.gov.uk/government/publications/q-fever-good-practice-for-farmers
- Q-fever (HSE). Available at: https://www.hse.gov.uk/agriculture/zoonoses-data-sheets/q-fever.pdf
- Q-fever: Information for healthcare providers. Available at: https://www.cdc.gov/qfever/healthcare-providers/index.html
- Rare and Imported pathogens laboratory (RIPL) user manual. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1073757/SPATH039-RIPL-user-manual-April-2022-version-26.pdf

NHS
Manchester University
NHS Foundation Trust

Case Based Discussion

Manchester University NHS Foundation Trust

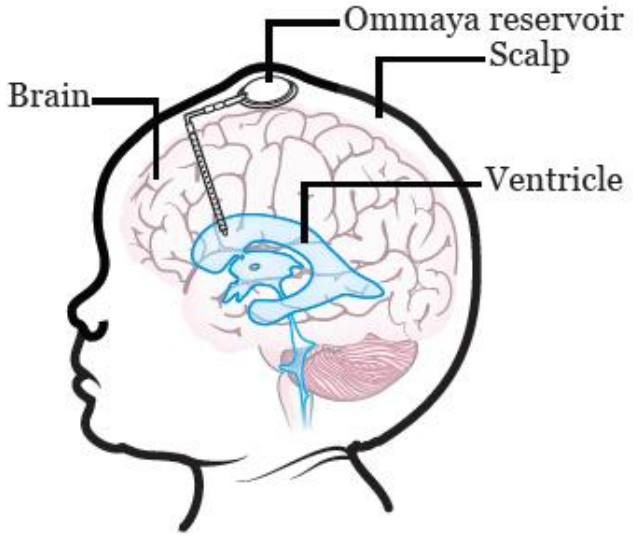
Presented by: Adam Hawker
Trainee Clinical Scientist in Microbiology

Clinical Presentation

- 7-year-old male
- Presented to local emergency department 8/1/23 with a potential viral illness
- Red blister-like rash, fluid filled vesicles
- Patient had status epilepticus which required the patient to be intubated
- High oxygen demand, desaturation to low 70s
- Noradrenaline and Adrenaline administered
- Ceftriaxone, Clindamycin and Aciclovir were started for Gram positive cover as well as viral infection
- The patient was transferred from the local hospital to the tertiary Paediatric Intensive Care Unit

Previous Medical History

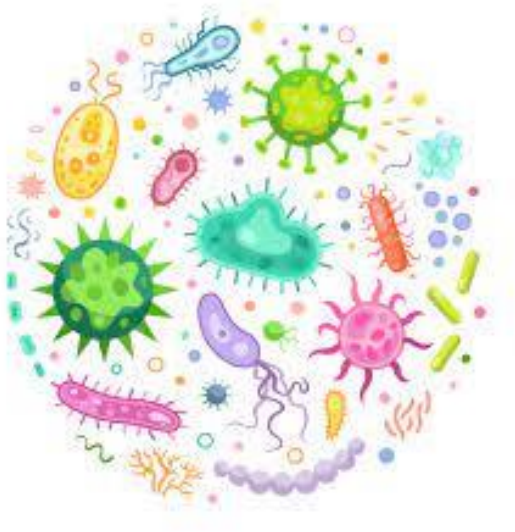
- Ex-premature at 29 weeks gestation
- Hydrocephalus
- Ommaya Reservoir Placement which was later changed to a ventriculoperitoneal (VP) shunt
- E. coli meningitis November 2015
- Epilepsy
- Cerebral Palsy
- Bilateral dislocated hips in December 2020 with reconstructive surgery required



What investigations would you request?

What further medical history questions might you ask?

Initial test results



Meningococcal/Pneumococcal PCR: Negative

Rapid Covid/Flu A/Flu B/RSV: Negative

MRSA & CPE Screen: Negative

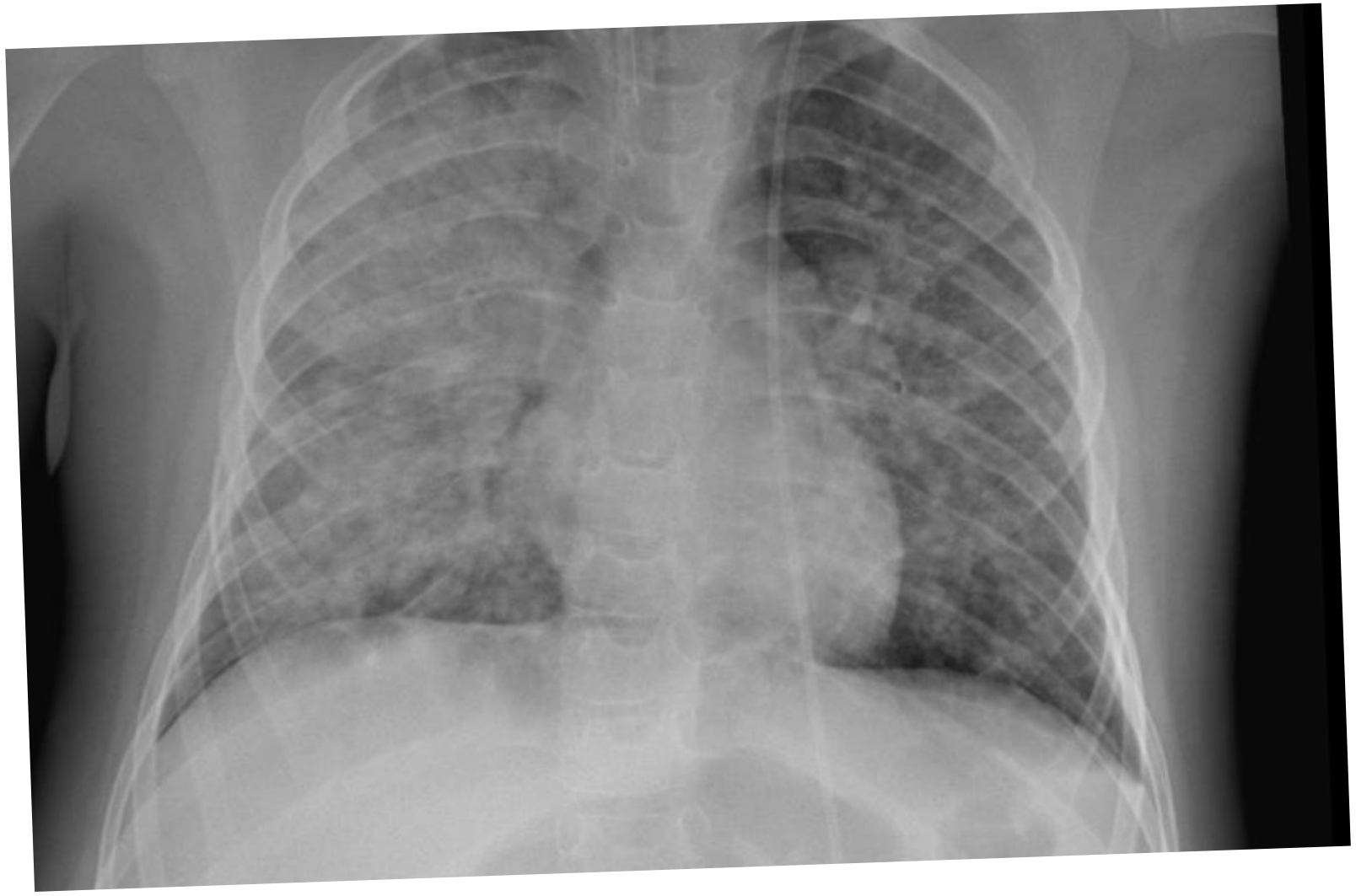
Urine MC&S (CSU): WBC<10 RBC 10-20, No Growth

Respiratory culture (ETA): No growth

C-reactive protein: 9

WCC: 20.8 Neutrophils: 13.3 Lymphocytes: 6.13

Chest x-ray: Diffuse airspace consolidation, more confluent in the right lung



Diagnosed with tonsilitis December 2022 – received 10 days oral Penicillin.

Returned to GP in early January 2023 with pyrexia and red ear – received a course of Amoxicillin.

The patient's sister is at home with suspected chickenpox with rash first developing mid-December 2022

Throat swab MC&S: No Pathogens Isolated

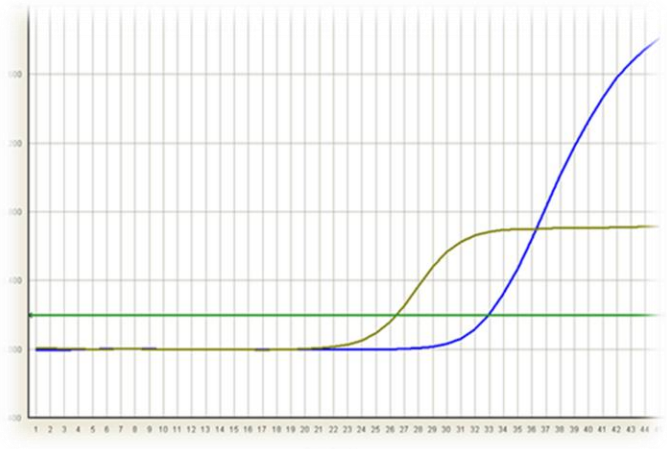
Anti-streptodornase = <100U/mL

Extended respiratory viral screen:

Negative for – Flu, RSV, Rhinovirus, Paraflu1/2/3, Adenovirus, Covid.

Positive for Metapneumovirus (CT 34)

Is Metapneumovirus fitting with this clinical case?



Urea and Creatine were significantly raised and demonstrated a stage 3 Acute Kidney Injury (AKI) 10/1 which had resolved by 14/1

4 days after first presenting to their local ED a blood sample was sent for Varicella-zoster virus (VZV) PCR:

- Positive CT 35
- IgM and IgG positive for VZV

Important to note that on testing the patient was 7 days post symptom onset i.e., rash development

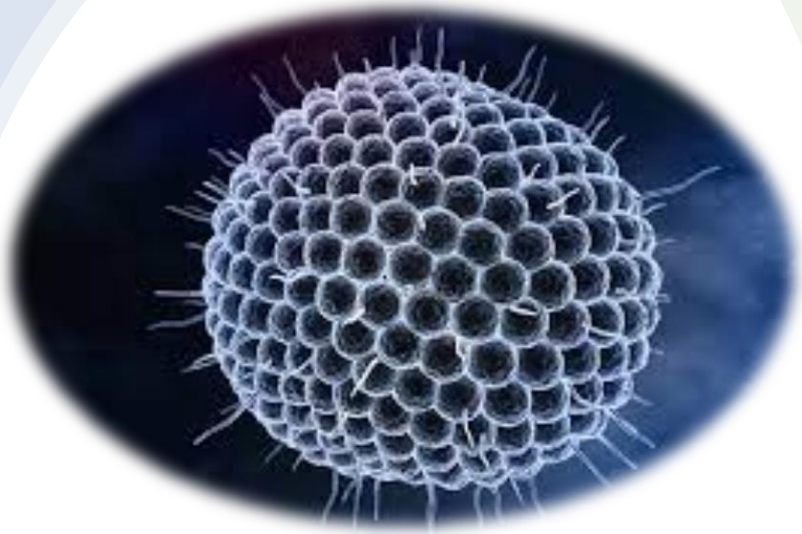
Ceftriaxone and Clindamycin stopped due to negative bacterial cultures

Aciclovir increased from 250mg/m^2 to 500mg/m^2 IV for a minimum of 10 days

MR head grossly unremarkable

Varicella-zoster virus

- Double stranded, linear DNA virus
- Part of the Herpesviridiae family
- Baltimore classification 1
- Lipid envelope with glycopeptides exposed
- Causes Chickenpox (Varicella) and Shingles (Herpes zoster)
- Active and latent stages of infection, latency occurs when the viral genome integrates into cells within the dorsal root ganglion.
- Antiviral resistance not common
- >90% of the population have seroconverted by the age of 20



What is Pneumonitis?

- A generalized term used to describe inflammation of the lung
- Can be caused by pathogens, allergens, aspiration and side effects from treatment e.g., chemotherapy and radiotherapy
- Acute symptoms: fever, chills, headache
- Chronic symptoms: dry cough, tight chest, appetite loss
- Pneumonia is a type of pneumonitis but is directly caused by infection, usually localized to a specific area of the lung

34

Varicella

NOTIFIABLE IN SCOTLAND AND NORTHERN IRELAND

The disease

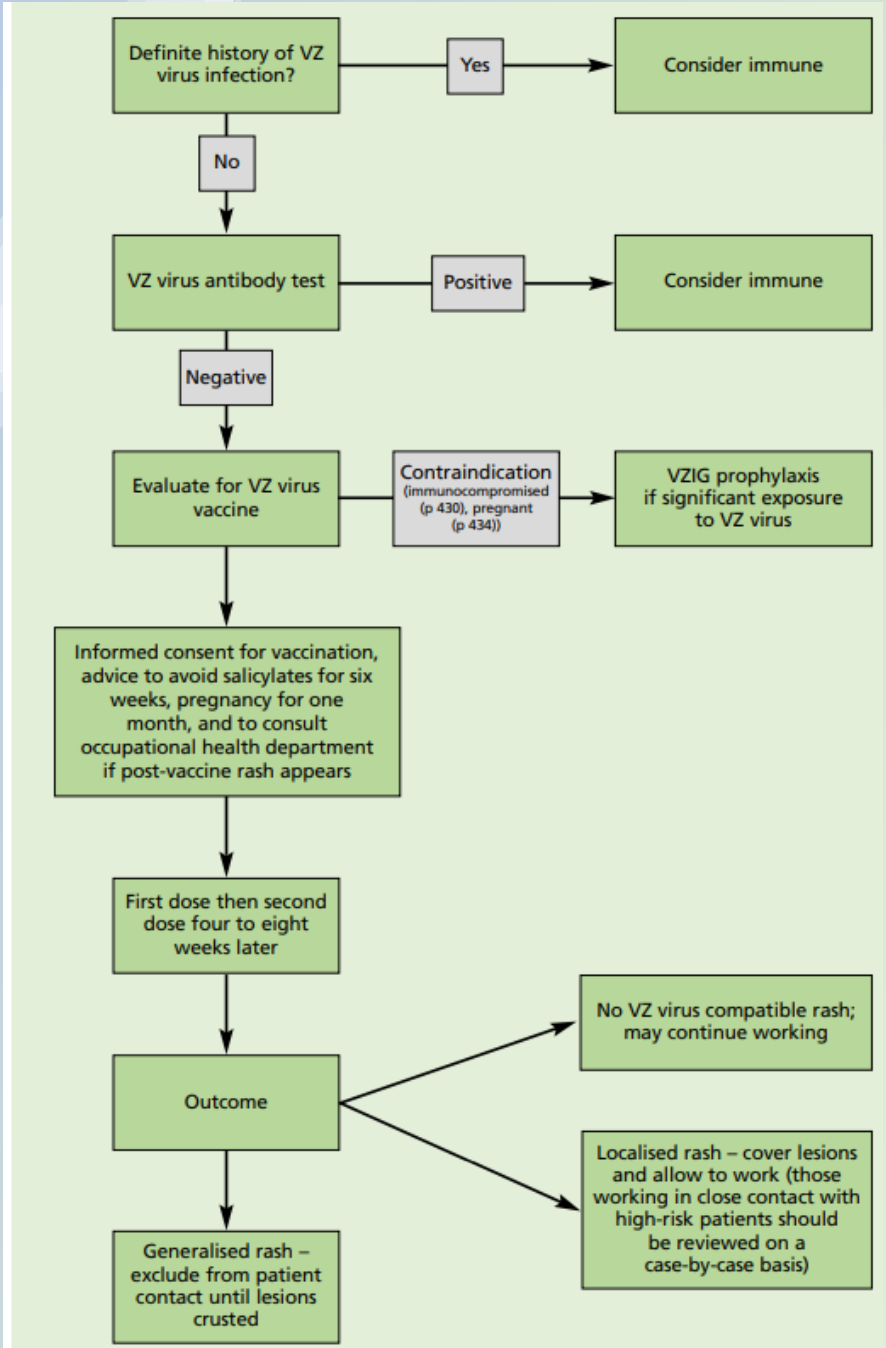


Figure 34.1 Procedure for vaccinating healthcare workers

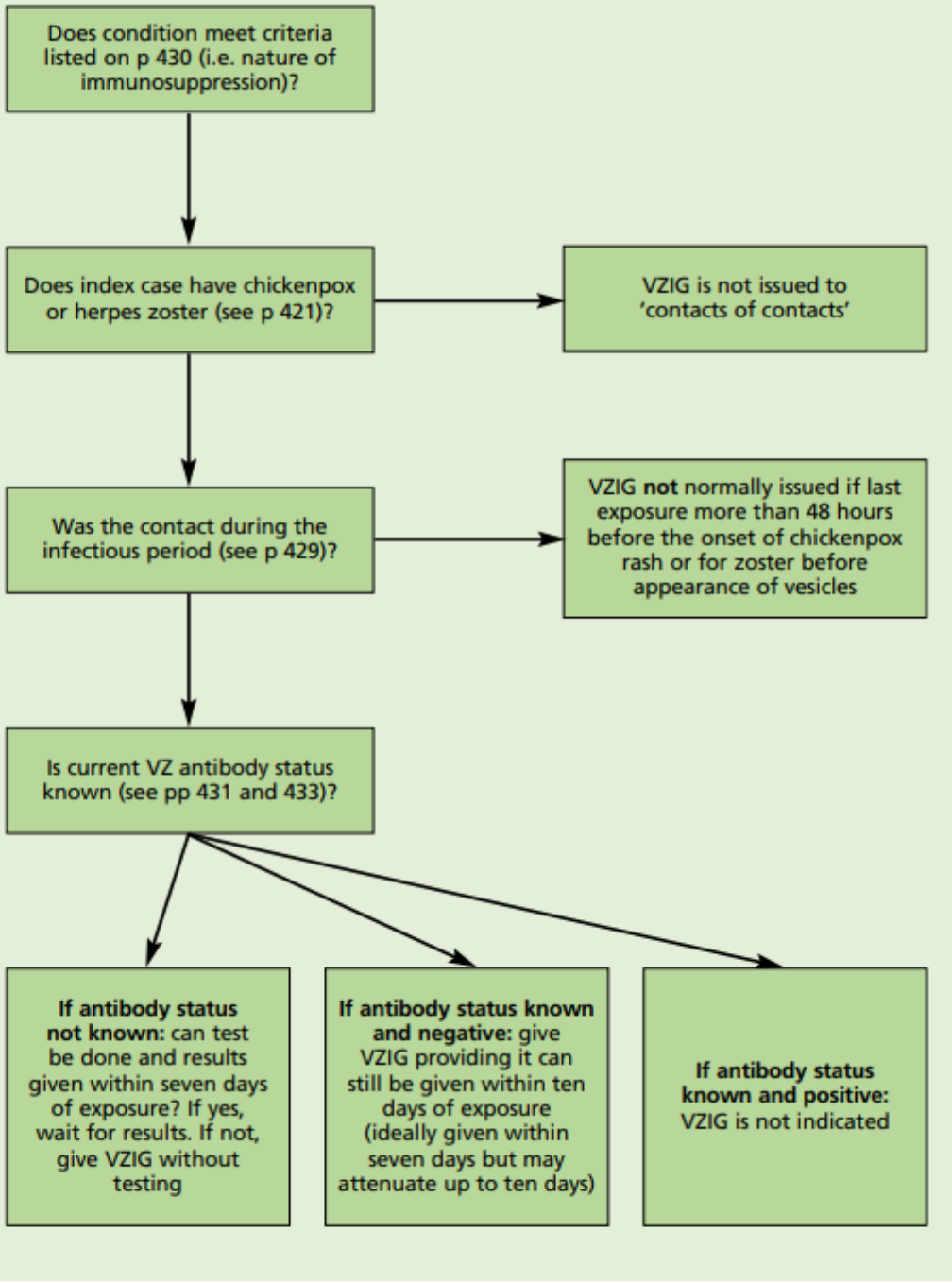


Figure 34.2 VZIG algorithm for immunocompromised patients who have been exposed to varicella zoster

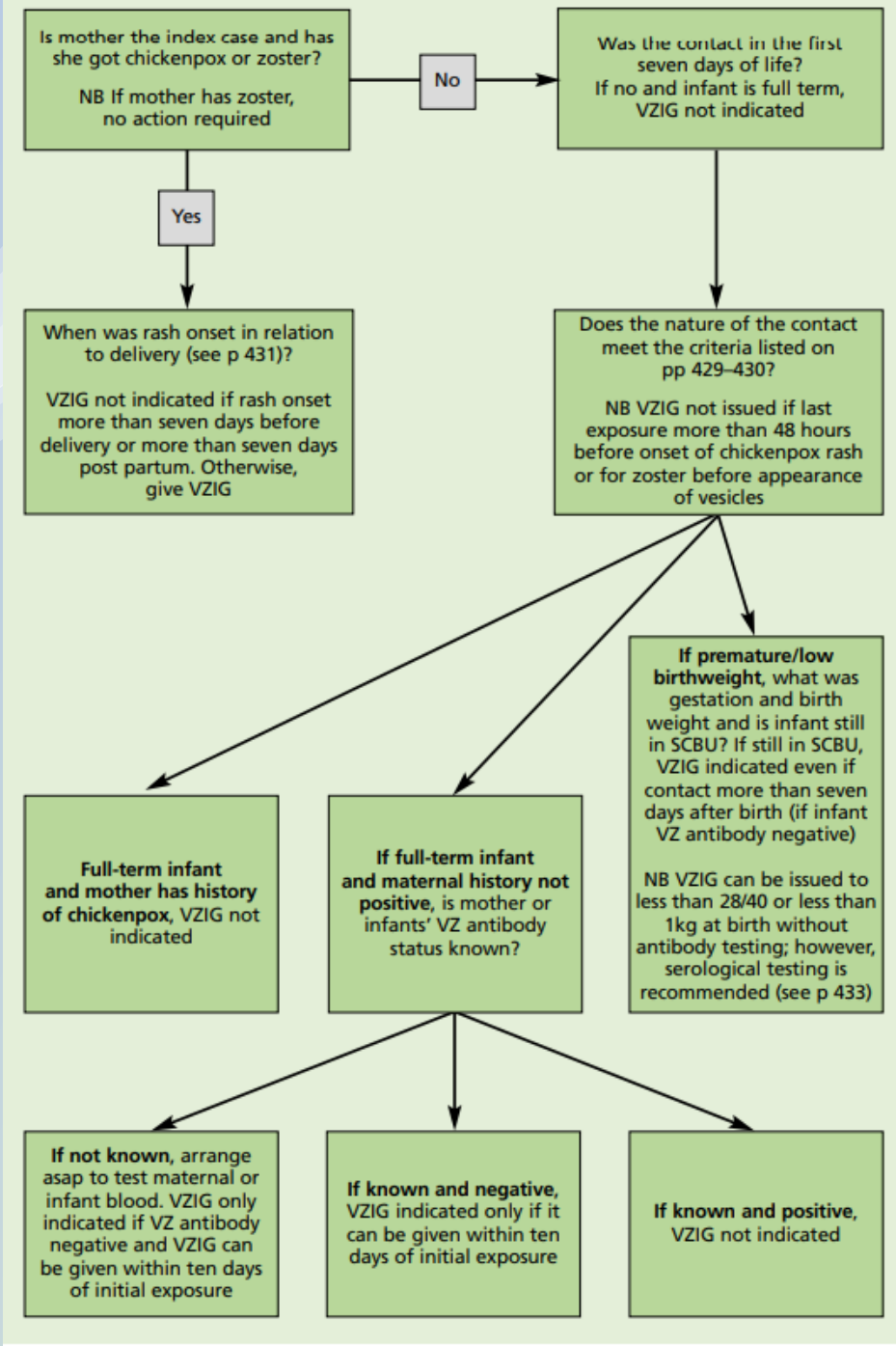


Figure 34.3 VZIG algorithm for neonates

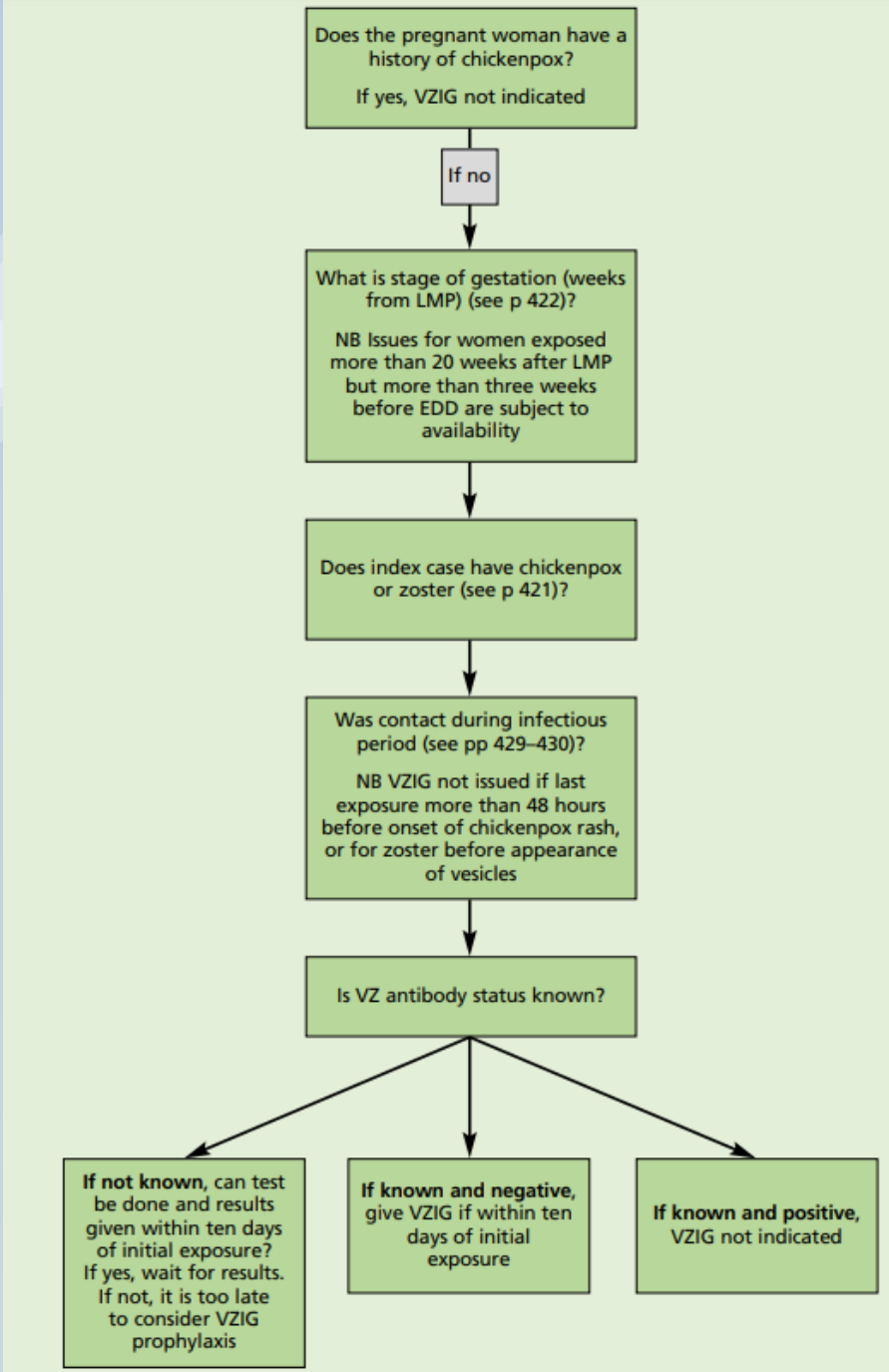


Figure 34.4 VZIG algorithm for pregnant women

UK Health Security Agency

Guidelines on post exposure prophylaxis (PEP) for varicella or shingles (January 2023)

Thank you for listening, are there any questions?

Closing remarks

- Appeal for presenters:
- Please contact: Callum Goolden (callum.goolden@lthtr.nhs.uk) if you have a case you would like to present or if you would like to gain some experience chairing meetings.

- Thank you all for attending!