Public Health England

Rabies post-exposure management

Kevin Brown
Virus Reference Department

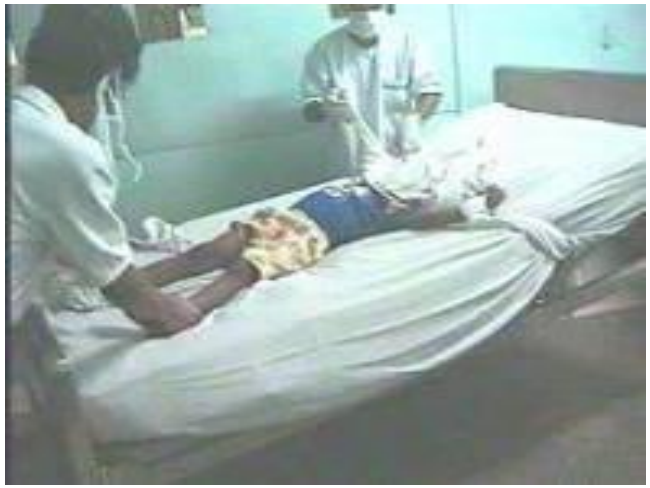
Why is rabies important?

A. Highest case-fatality rate of any infectious disease
B. Estimated to kill 50, 000 -70,000 humans / year
C. Kills an estimated 100 children each day
D. Annual global burden of canine rabies is estimated to be approximately $124 billion
E. All of the above

Public Health England

Why is rabies important?

- Highest case-fatality rate of any infectious disease
- Human deaths reported in >150 countries
- Is entirely preventable through vaccination
- Estimated to kill 50, 000 -70,000 humans / year
- Kills an estimated 100 children each day



- Annual global burden of canine rabies is estimated to be approximately $124 billion
- Elimination of dog rabies has been demonstrated over large geographic areas
- This could lead to the global elimination of the major source of human rabies

Public Health England

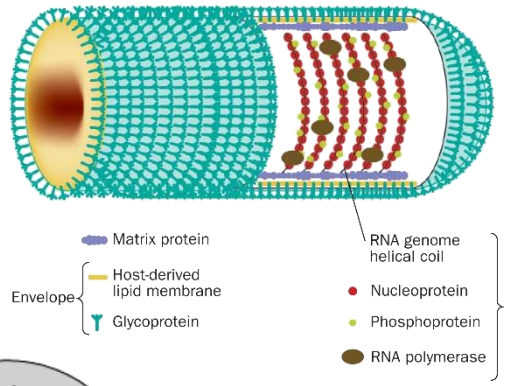
Rabies - background

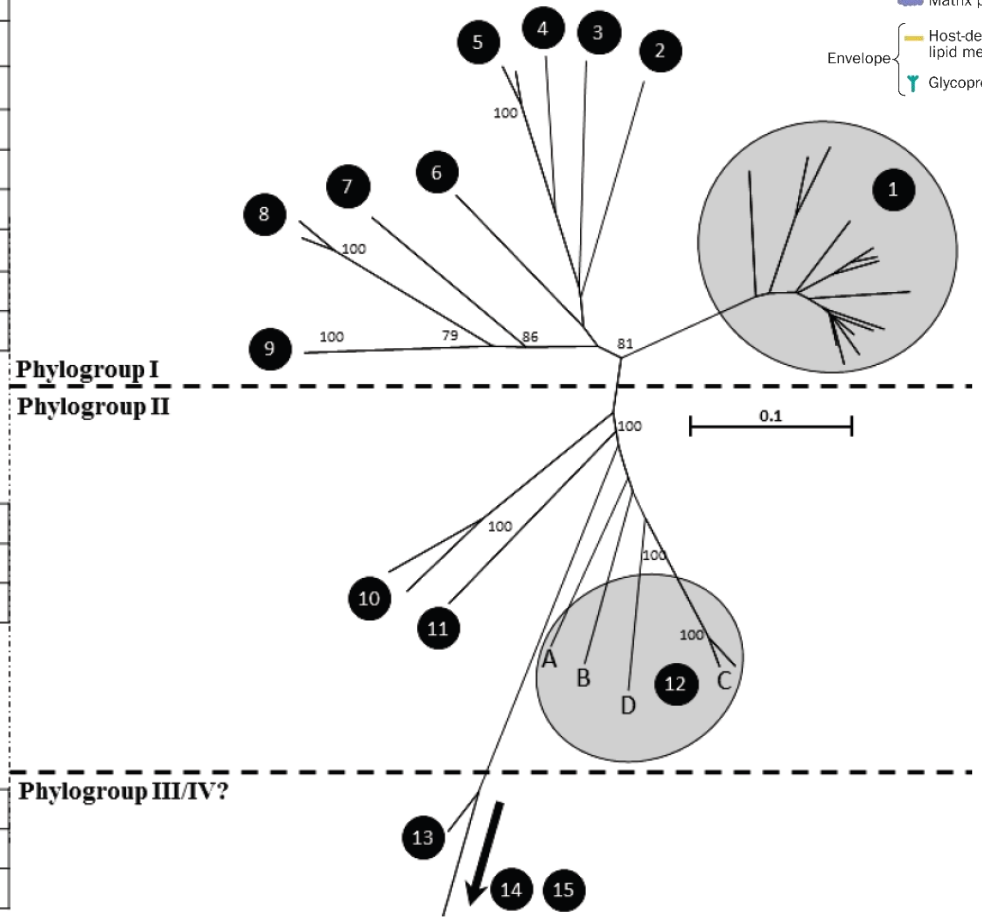
- An acute viral encephalomyelitis caused by infection with classic rabies virus or number of related Lyssaviruses
- Spread to people through infected saliva via bites or scratches from rabid animals (in particular dogs)
- Although effective post-exposure treatment (PET) is available, once clinical symptoms develop rabies is almost invariably fatal
- Domestic dog = single most important reservoir (responsible for > 99% rabies deaths)
- All mammals appear susceptible – major reservoirs carnivores (dogs, foxes, racoons, skunks etc) and bats
- Control of rabies in animals mainstay for prevention human rabies (control of stray dogs, vaccination of domestic dogs/wildlife)

Public Health England

Lyssaviruses

No.	Virus	Distribution
1	RABV	Global
2	ARAV	Eurasian
3	KHUV	Eurasian
4	BBLV	European
5	EBLV-2	Europe
6	ABLV	Australia
7	IRKV	Eurasian
8	EBLV-1	European
9	DUVV	African
10	MOKV	African
11	SHIBV	African
12	LBV	African
13	WCBV	Eurasian
14	IKOV	African
15	LLEBV	European

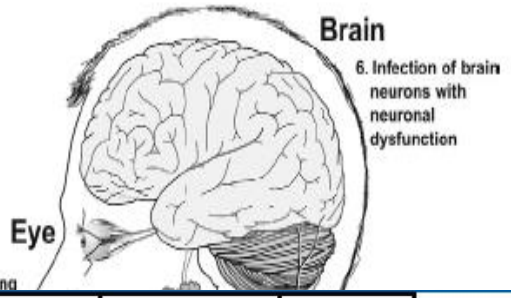




Banyard et al Viruses 2014
Warrell and Warrell Lancel 2004

Public Health England

Pathogenesis of rabies infection



Infection	Incubation period (5 days to > 2 years)	Prodrome (0-10 days)	Acute neurologic period (2-7 days)	Coma (5-14 days)	Death

Spread and replication of virus in the absence of appropriate PEP

US median incubation period is ~35 days

Vaccine induced humoral immune response

Zone of PEP mediated virus neutralization at the site of infection

CNS virus

Salivary glands virus

Virus present at entry site

Passive immunity - HRIG

Rabies virus concentration

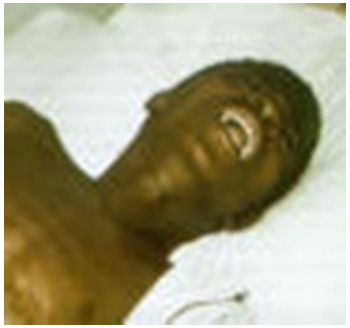
Antibody response

0 3 7 14 28 Days post-exposure

Jackson AC, 'Rabies' (2013) 3rd ed. P300
CDC Rabies time course

Human rabies in the UK

- 173 human cases in the 19th Century
- 27 classical rabies human deaths reported since 1902
  - dog / cat bites were the main source of infection
  - all infected abroad in rabies endemic areas
  - none had received post-exposure prophylaxis
- One case as a result of EBLV-2 in 2002
  - bat contact & no pre-exposure immunisation or PET



Public Health England

Rabies diagnosis in the UK

- Queries about possible human rabies 1/month
  - Local risk assessment (ID/virology)
  - Call duty virologist at VRD for risk assessment and advice re testing
  - Testing is done at APHA, Weybridge on behalf of PHE
  - Testing generally needs to be discussed with VRD before APHA will test
  - Guidance available at

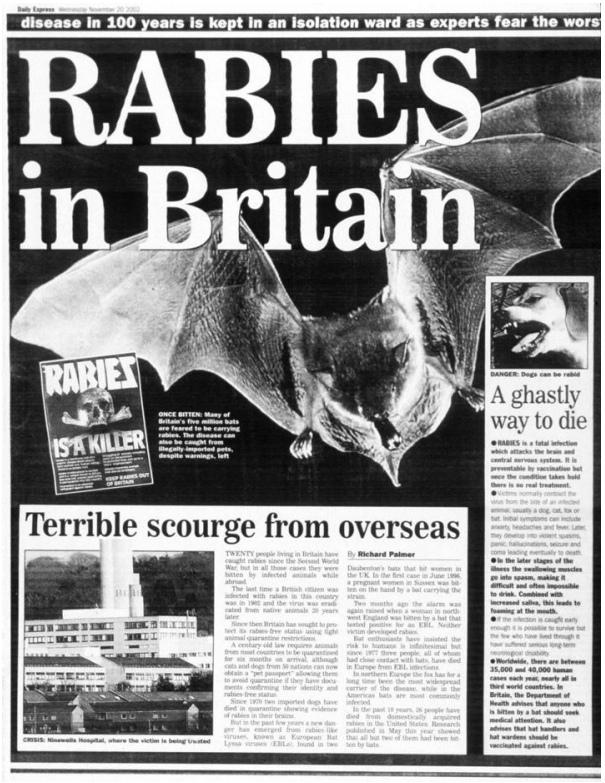
    http://www.nhs.uk/Conditions/Rabies/Pages/introduction

    https://www.gov.uk/government/publications/human-rabies-public-health-management-of-a-suspected-case

Public Health England

Human rabies case Scotland 2002

1st indigenous case of human rabies in UK for 100 years



disease in 100 years is kept in an isolation ward as experts fear the wors

RABIES in Britain

RABIES IS A KILLER

ONCE BITTEN: Many of Britain's five million bats are feared to be carrying rabies. The disease can also be caught from illegally imported pets, despite warnings, left

DANGER: Dogs can be rabid

A ghastly way to die

Terrible scourge from overseas

By Richard Palmer

CRISIS: Ninewells Hospital, where the victim is being treated

- Tragic death of bat conservationist
- EBLV2 identified as cause
- Despite recommendation had not been vaccinated
- Increased numbers of submissions for passive bat surveillance
- Enhanced awareness in the bat community and public (press)
- EBLV2 found in Daubenton bats
- Not found in pipistrelles

No other human cases of EBLV2 (so far)

Public Health England

Human rabies cases in the UK

- 28 cases in UK since 1902 (26 from infection abroad)
- Median age 35 years, M>F
- Majority from dog bites in Indian subcontinent

Year	Country of exposure	Age	Sex	Animal involved
2001	Phillipines	55	M	Dog
2001	Nigeria	52	F	Dog
2002	UK	55	M	Bat
2005	India	37	F	Dog
2009	South Africa	35	F	Dog
2012	India	58	F	Dog

- Common elements – none received PET before presentation

Public Health England

PHE Rabies & Ig Service (RIgS)

- Public Health England manages the service on behalf of Department of Health in England:
  - Pre exposure vaccine for occupational risk groups
    - Risk groups are currently under review
  - Post exposure treatment
  - Diagnosis and public health management of human rabies
- Separate arrangements exist for Wales, Scotland and Northern Ireland

Public Health England

Current Green Book Recommendations

Continuous

- Laboratory workers routinely working with rabies virus

Frequent

- **People who regularly handle bats**
- **Persons who regularly handle imported animals,** e.g.:
  - at animal quarantine stations
  - at zoos
  - at animal research and acclimatisation centres
  - at ports where contact with imported animals occurs, e.g. certain HM Revenue and Customs offices
  - as carrying agents authorised to carry imported animals
  - as veterinary and technical staff in animal health*
- **Animal control and wildlife workers, veterinary staff or zoologists who travel regularly in rabies enzootic areas**
- **Health workers in rabies enzootic areas** who will be at risk of direct exposure to body fluids or tissue from a patient with confirmed or probable rabies

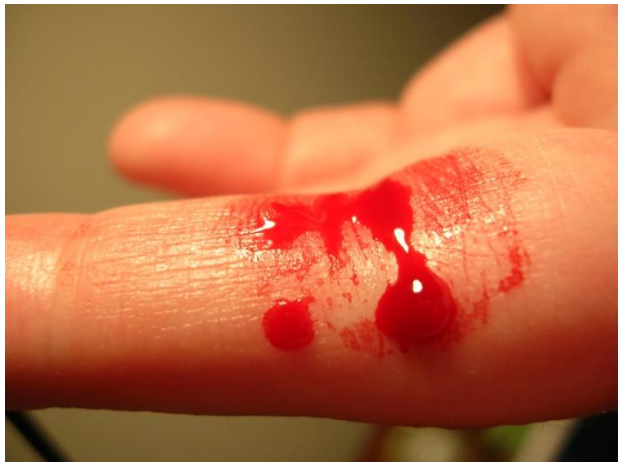
Infrequent

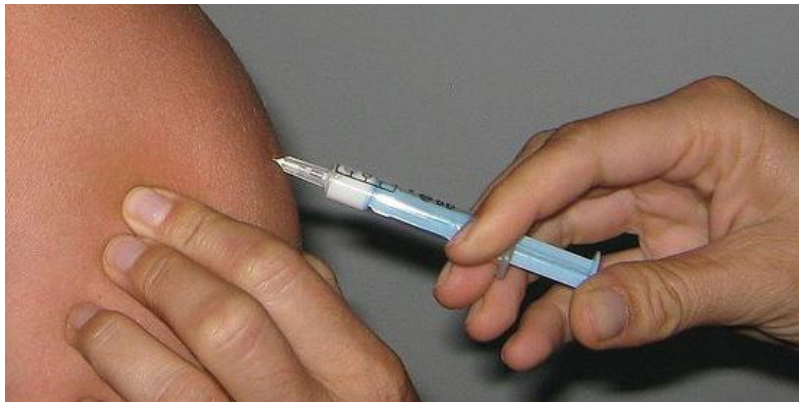
- **Travellers** to rabies enzootic areas especially if
  - post exposure medical care and rabies biologics at the destination are lacking or in short supply or
  - they are undertaking higher risk activities such as cycling or running or
  - they are living or staying for more than one month.

Public Health England

Post exposure treatment (PET)

- There are two key aspects to the management of potential rabies exposures:
  - Wound care: immediate and thorough wound cleansing, using soap and water, detergent, or water alone. Suturing of wounds should be avoided.
  - Risk assessment of exposure and post-exposure treatment if indicated





Public Health England

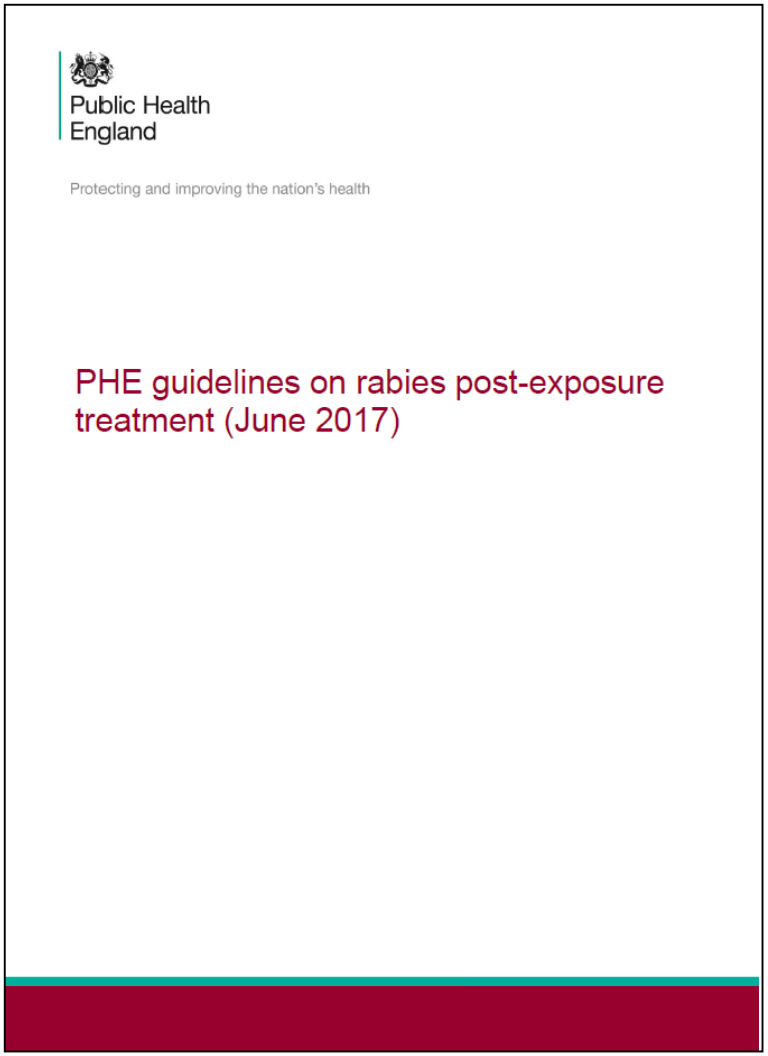
Post exposure treatment (PET)

- Prompt PET (rabies vaccine +/- HRIG) highly effective in preventing disease
- PHE issues ~2000 courses PET/year: 85-90% for returning travellers, 10-15% for UK bats
- Most calls go direct to RIgS office at Colindale
  - 10% direct to issuing centres or HPTs
- Issuing centre issues are only for local pick up
- All vaccine/HRIG that is mailed out should be sent from Colindale
- Colindale is responsible for stock reports and annual reports to DH on use of vaccine/HRIG

Rabies Issuing Centres
Birmingham
Cambridge
Leeds
Liverpool
Manchester
Newcastle
Norwich
Oxford

Public Health England

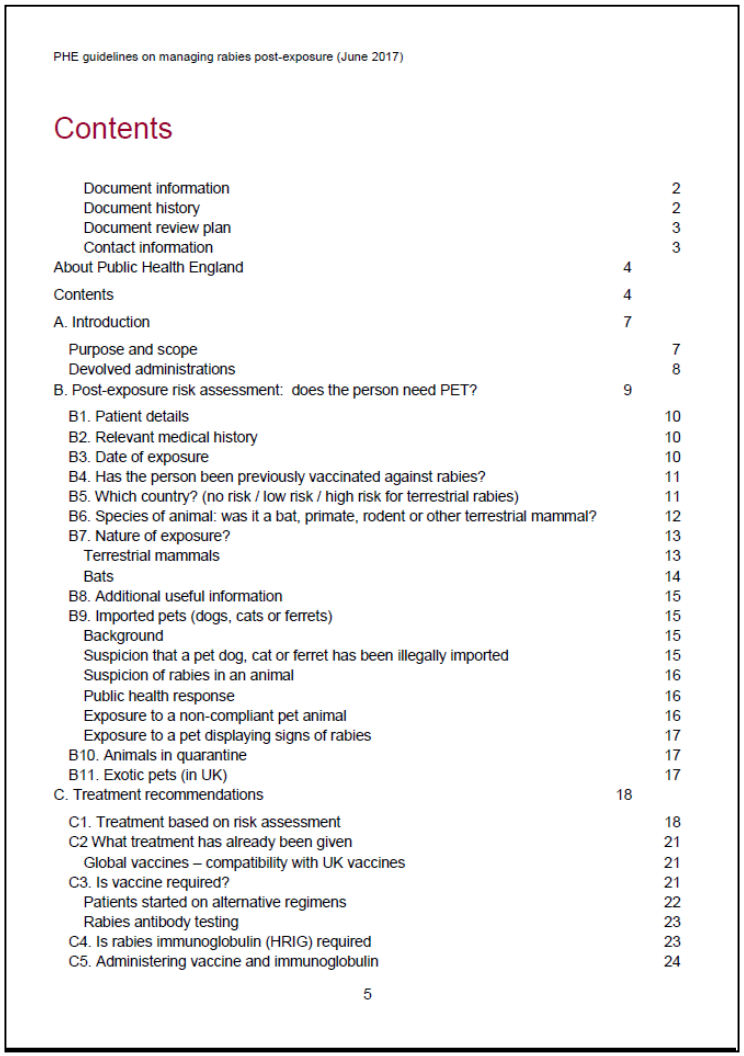
Rabies PET guidance



Public Health England

Protecting and improving the nation's health

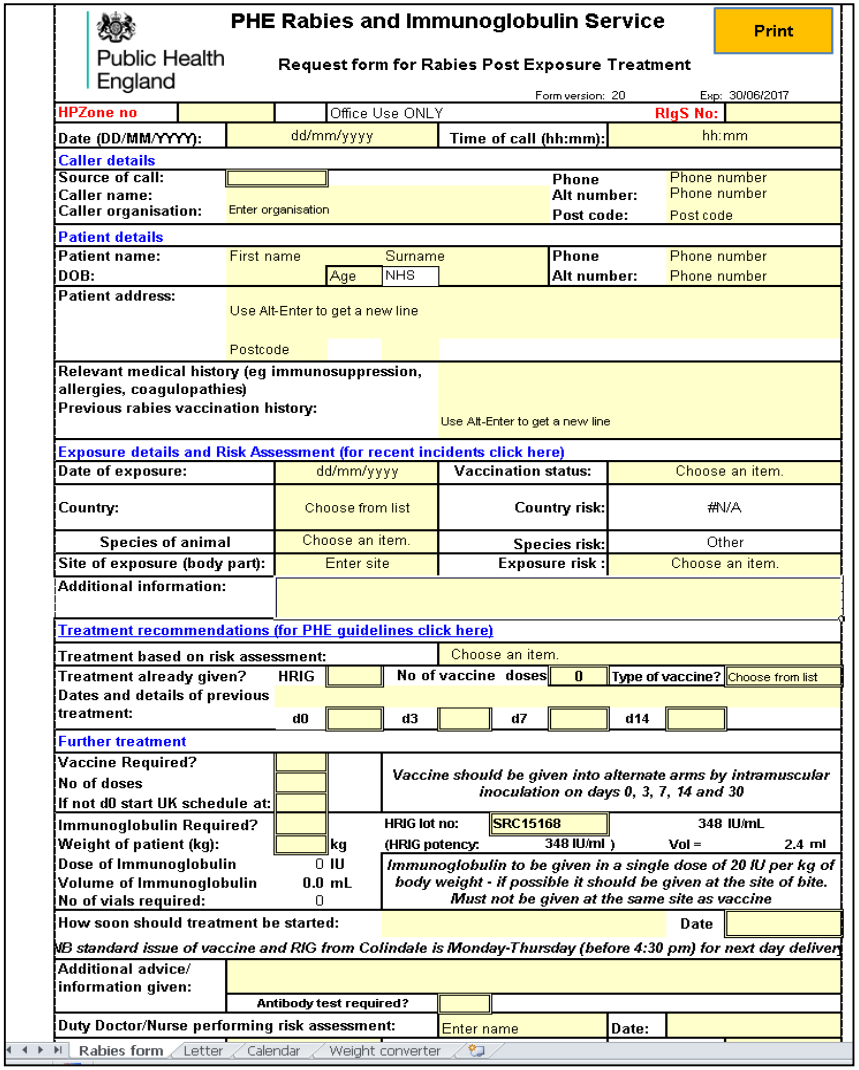
PHE guidelines on rabies post-exposure treatment (June 2017)



Contents

Document information 2
Document history 2
Document review plan 3
Contact information 3
About Public Health England 4
Contents 4
A. Introduction 7
Purpose and scope 7
Devolved administrations 8
B. Post-exposure risk assessment: does the person need PET? 9
B1. Patient details 10
B2. Relevant medical history 10
B3. Date of exposure 10
B4. Has the person been previously vaccinated against rabies? 11
B5. Which country? (no risk / low risk / high risk for terrestrial rabies) 11
B6. Species of animal: was it a bat, primate, rodent or other terrestrial mammal? 12
B7. Nature of exposure? 13
Terrestrial mammals 13
Bats 14
B8. Additional useful information 15
B9. Imported pets (dogs, cats or ferrets) 15
Background 15
Suspicion that a pet dog, cat or ferret has been illegally imported 15
Suspicion of rabies in an animal 16
Public health response 16
Exposure to a non-compliant pet animal 16
Exposure to a pet displaying signs of rabies 17
B10. Animals in quarantine 17
B11. Exotic pets (in UK) 17
C. Treatment recommendations 18
C1. Treatment based on risk assessment 18
C2 What treatment has already been given 21
Global vaccines – compatibility with UK vaccines 21
C3. Is vaccine required? 21
Patients started on alternative regimens 22
Rabies antibody testing 23
C4. Is rabies immunoglobulin (HRIG) required 23
C5. Administering vaccine and immunoglobulin 24

Risk assessment form



PHE Rabies and Immunoglobulin Service

Public Health England

Request form for Rabies Post Exposure Treatment

Print

Form version: 20 Exp: 30/06/2017

HPZone no | Office Use ONLY | RIgS No:

Date (DD/MM/YYYY): dd/mm/yyyy | Time of call (hh:mm): hh:mm

Caller details

Source of call: | Phone: Phone number

Caller name: | Alt number: Phone number

Caller organisation: Enter organisation | Post code: Post code

Patient details

Patient name: First name Surname | Phone: Phone number

DOB: Age NHS | Alt number: Phone number

Patient address: Use Alt-Enter to get a new line

Postcode

Relevant medical history (eg immunosuppression, allergies, coagulopathies)

Previous rabies vaccination history: Use Alt-Enter to get a new line

Exposure details and Risk Assessment (for recent incidents click here)

Date of exposure: dd/mm/yyyy | Vaccination status: Choose an item.

Country: Choose from list | Country risk: #N/A

Species of animal: Choose an item. | Species risk: Other

Site of exposure (body part): Enter site | Exposure risk : Choose an item.

Additional information:

Treatment recommendations (for PHE guidelines click here)

Treatment based on risk assessment: Choose an item.

Treatment already given? HRIG | No of vaccine doses: 0 | Type of vaccine? Choose from list

Dates and details of previous treatment: d0 | d3 | d7 | d14

Further treatment

Vaccine Required?

No of doses

If not d0 start UK schedule at:

Vaccine should be given into alternate arms by intramuscular inoculation on days 0, 3, 7, 14 and 30

Immunoglobulin Required?

Weight of patient (kg): kg

HRIG lot no: SRC15168 348 IU/mL

(HRIG potency: 348 IU/ml) Vol = 2.4 ml

Dose of Immunoglobulin 0 IU

Volume of Immunoglobulin 0.0 mL

No of vials required: 0

Immunoglobulin to be given in a single dose of 20 IU per kg of body weight - if possible it should be given at the site of bite. Must not be given at the same site as vaccine

How soon should treatment be started: Date

NB standard issue of vaccine and RIG from Colindale is Monday-Thursday (before 4:30 pm) for next day delivery

Additional advice/ information given:

Antibody test required?

Duty Doctor/Nurse performing risk assessment: Enter name | Date:

Rabies form | Letter | Calendar | Weight converter

Enables risk assessment to be done as collect information
Drop down lists for many key questions

Automatically provides a letter and dates for vaccine and HRIG if needed

The Royal College of Pathologists
Pathology: the science behind the cure

What are the key questions to ask as part of a PET risk assessment

A. Country
B. Species
C. Site of body
D. Date of birth
E. Date of event
F. Vaccine status of animal
G. Vaccine status of patient

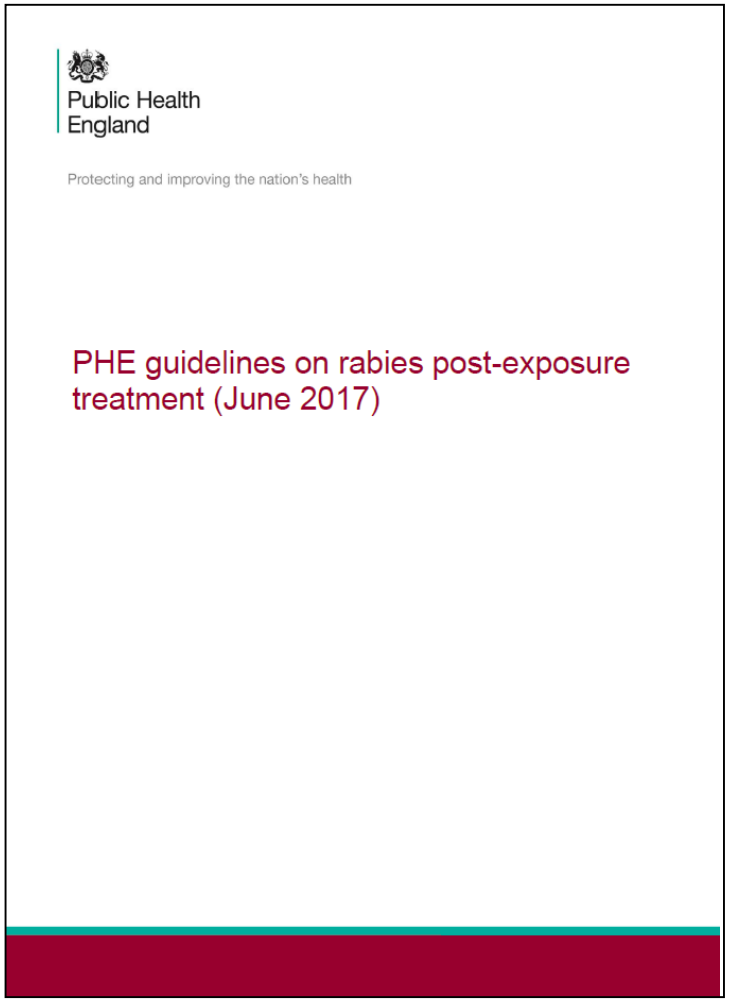
Public Health England

Risk assessment – key questions

- Where (country)
- What (type of animal/bat)
- How (type of exposure)

Also need to know:

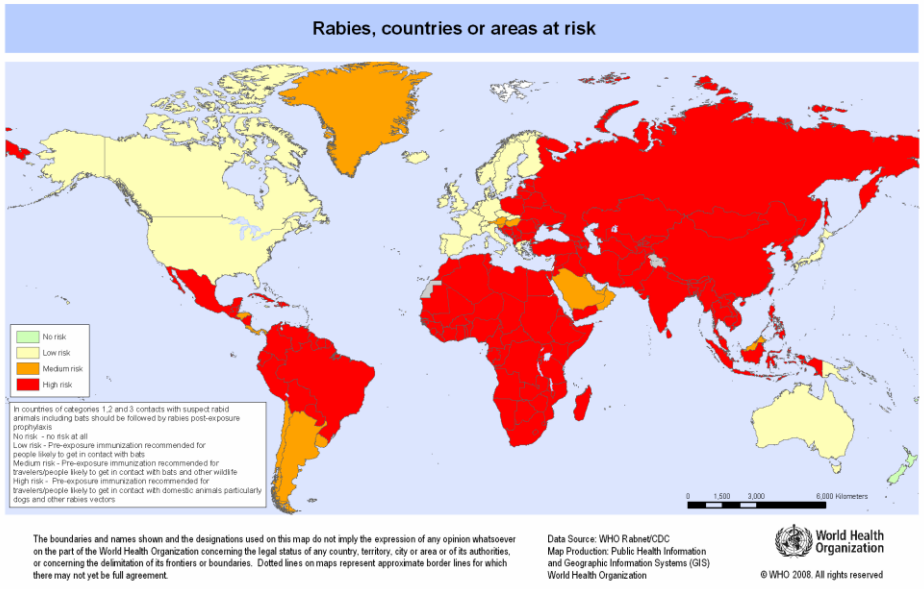
- When
- Previous vaccination
- Treatment already received
- Whether animal can be observed



Public Health England

Which country?

- All countries divided into no risk/low risk/high risk categories depending on presence of rabies in wild/domestic animals
- Drop down list of country risk on PHE website
- All countries considered high risk for bat exposures



Public Health England

What animal?

Was it a terrestrial mammal or a bat?

Bats

- May persistently carry rabies/related lyssaviruses without signs of disease
- In the UK are the ONLY reservoir of lyssavirus

Dogs and cats

- Animals shedding virus in saliva are in the terminal stage of disease
- If animal is well/behaving normal 15d after biting incident it will not have rabies

Rodents or Primates

- The risk is low, therefore rodent or primate bites in high risk countries should be treated with vaccine alone (ie cat II exposure)
- Only exception is severe monkey bites to head or neck

Further information

- Was the animal behaving normally?

Public Health England

What type of exposure?

Category	Terrestrial Mammal: Categories of exposure (Adapted from WHO)
I	Touching or stroking animals
II	Licks of the skin or other contact with saliva (e.g. feeding animals) Minor scratches, bruising or abrasions without bleeding Minor bites without breaking of the skin (covered areas of arms, trunk, and legs) All bites, licks and scratches from rodents and primates
III	Single or multiple transdermal bites or scratches, licks on broken skin Major bites (multiple or on face, head, finger or neck) Contamination of mucous membrane with saliva (i.e. licks)

Category	Bats: Categories of exposure (Adapted from WHO)
I	No physical contact: i.e. no direct physical contact with the bat's saliva or neural tissue, or if the person was protected by a barrier capable of preventing such contact, such as a boot, shoe, or appropriate protective clothing
II	Uncertain physical contact: (may be common with bat exposures): i.e. where there has been no observed direct physical contact but this could have occurred, a child found in a room with a bat, or in the UK a grounded or aggressive bat found in a room of a sleeping (or intoxicated) person*.
III	Direct physical contact with bat's saliva or neural tissue Single or multiple transdermal bites or scratches & bruising Minor bites without breaking of the skin (covered areas of arms, trunk, and legs) Major bites (multiple or on face, head, finger or neck) Contamination of mucous membrane with saliva or bat droppings/urine

Public Health England

Immune status

Fully immunised: At least three documented doses of rabies vaccine (either a complete primary pre-exposure course or as part of a five dose post exposure course) or documented rabies antibody (VNA) titres of at least 0.5 IU/ml.

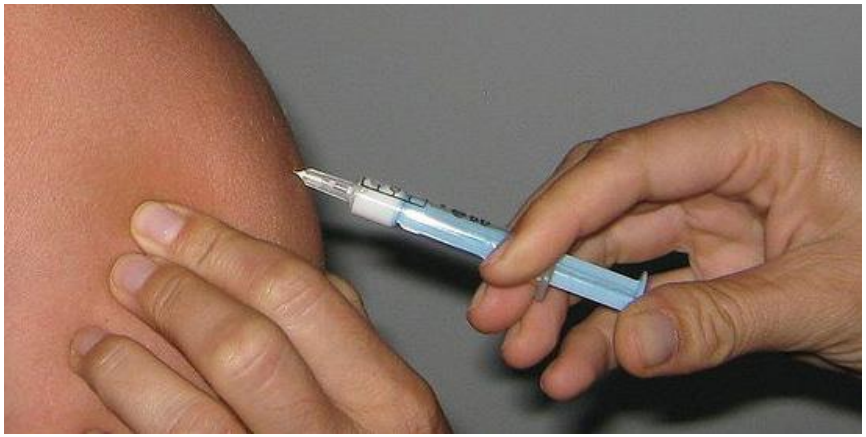
Partially immunised: person who has had incomplete/inadequate primary vaccination course, or VNA never >0.5 IU/ml

Non immune: Person who has never received pre- or post-exposure immunisation with rabies vaccine, or has had incomplete / inadequate primary vaccination course. If the person is immunosuppressed, treat as though non immune and consider testing antibody levels post vaccination.

Public Health England

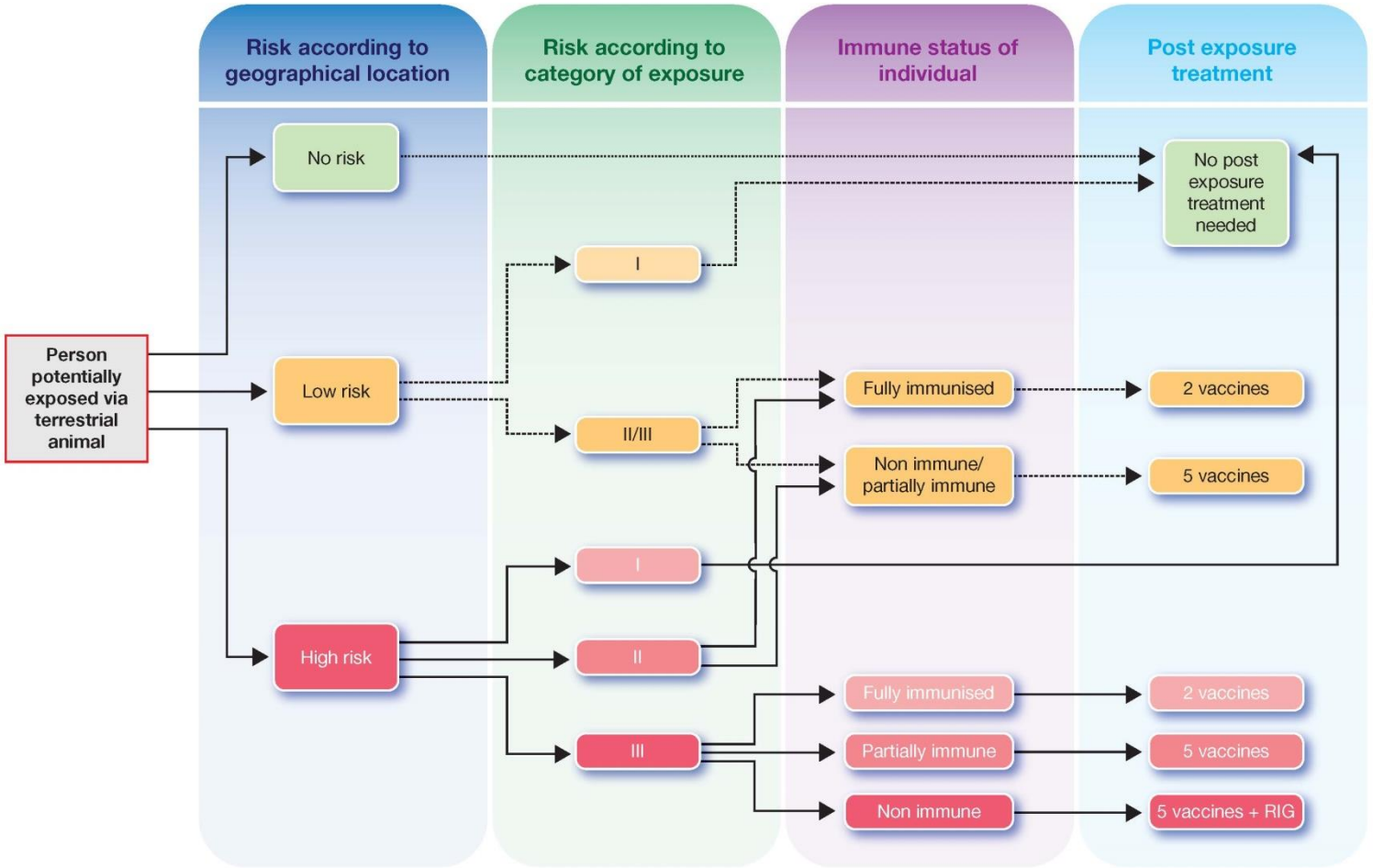
Post exposure treatment

- Post exposure treatment for rabies includes rabies vaccine +/- human rabies immunoglobulin (HRIG)
- UK schedule is five dose of rabies vaccine given on D 0, 3, 7, 14, and 28-30 days (if previously vaccinated D 0 and 3-7)
- HRIG is given on D0
- The mainstay of rabies post exposure prophylaxis is rabies vaccine as the antibody induced by vaccination is much greater than that by HRIG.
- D 0 is first day of vaccine NOT day of bite



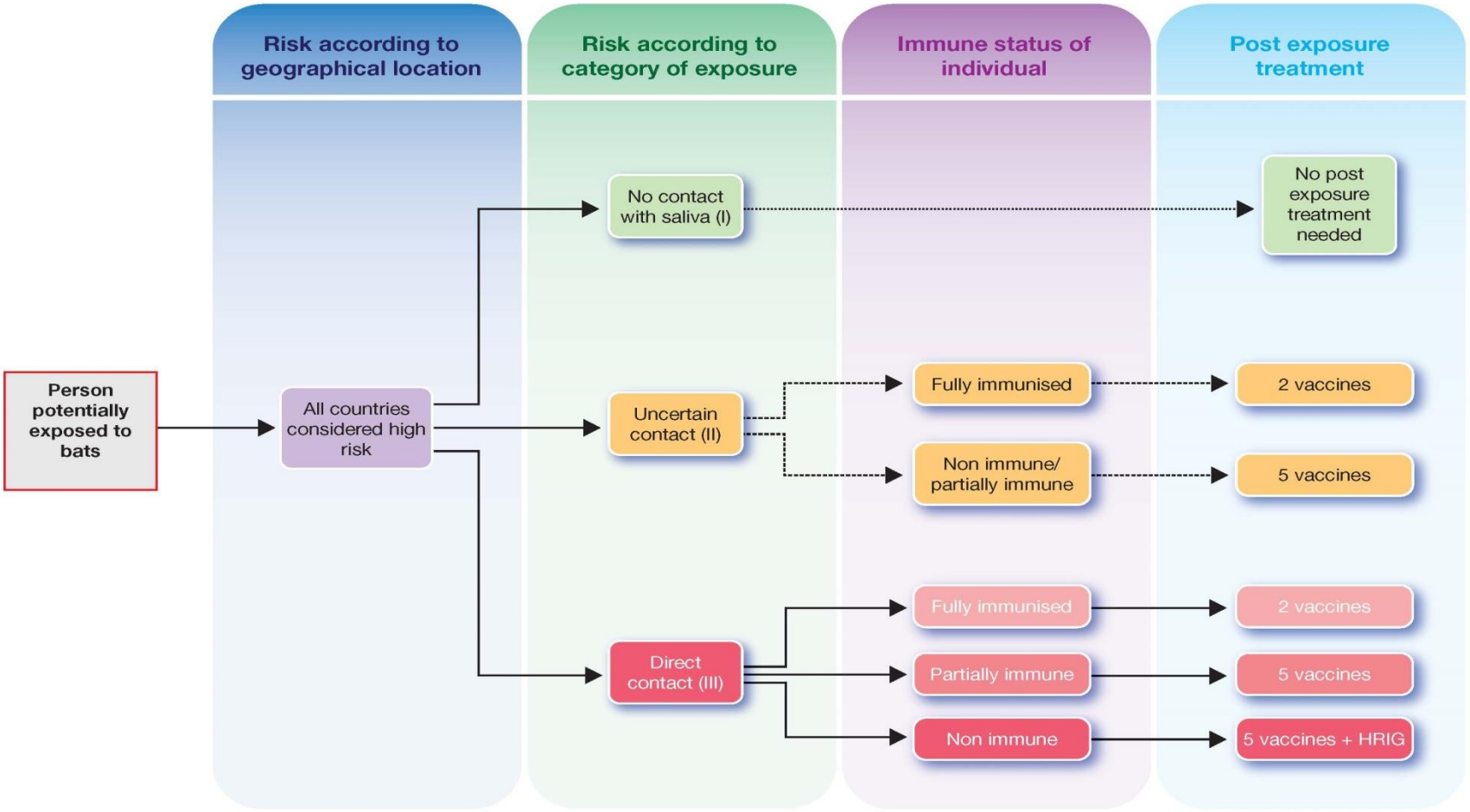
Public Health England

Terrestrial animals



Public Health England

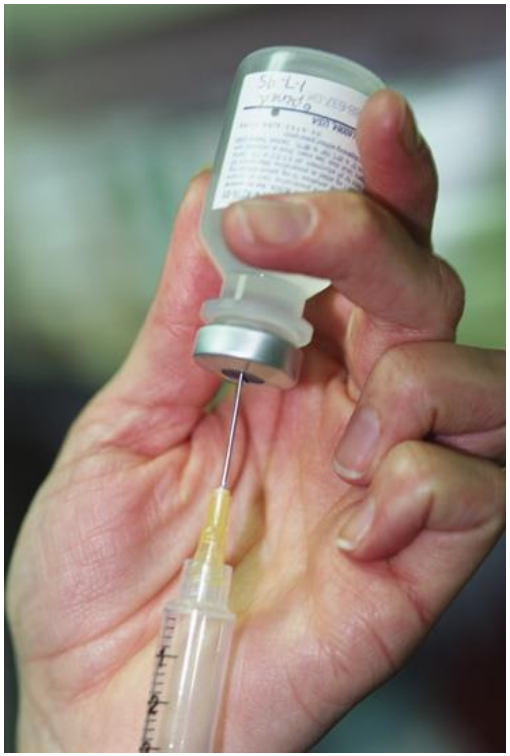
Bats



Public Health England

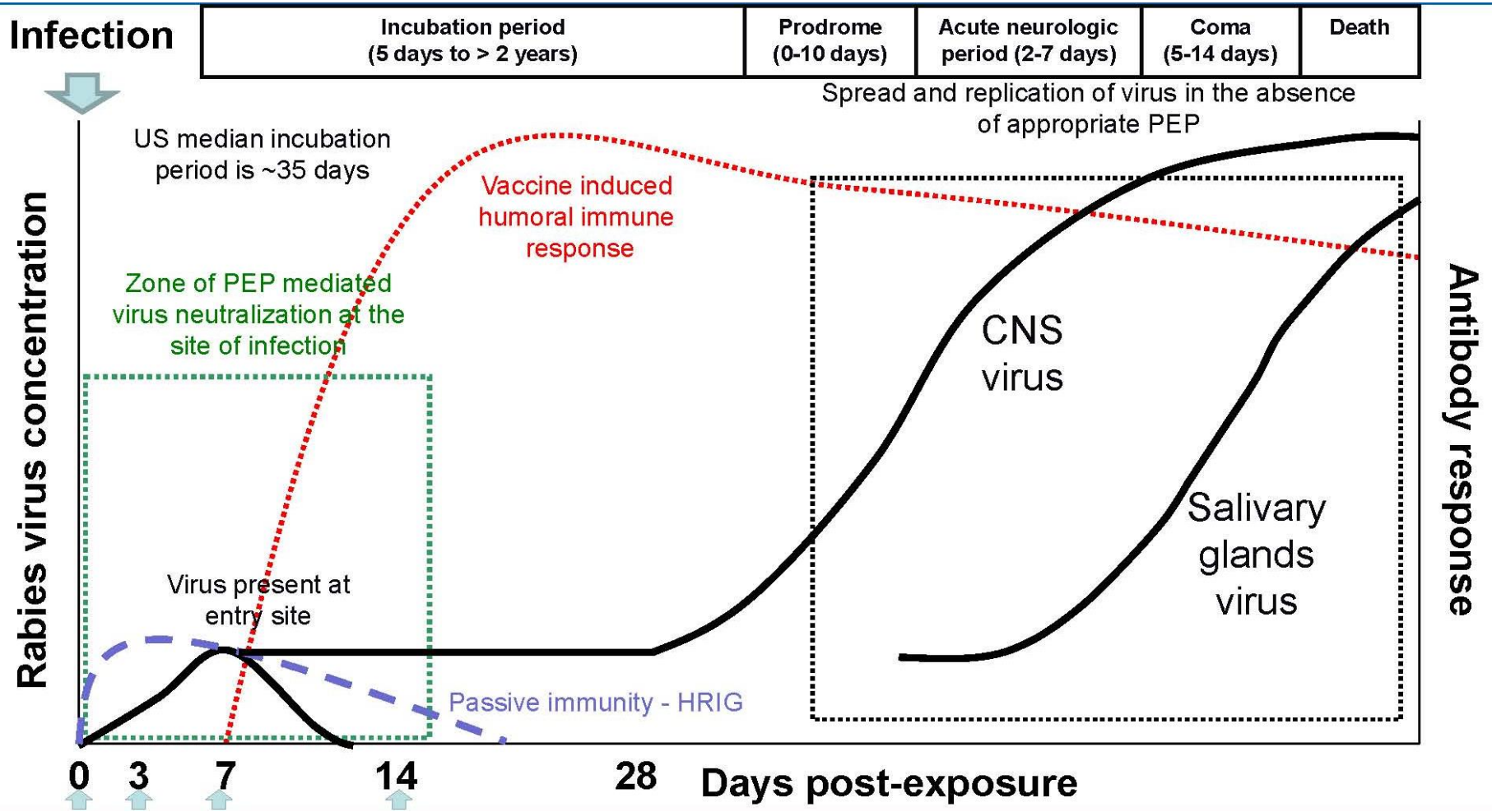
Rabies vaccine

- In the UK there are two vaccines licensed for intra muscular (IM) use:
  - human diploid cell vaccine (HDCV) (Rabies Vaccine BP)
  - purified chick embryo cell rabies vaccine (PCECV) (Rabipur).
- UK vaccines are interchangeable and compatible with most vaccines used in other countries – therefore can usually continue course started abroad



Public Health England

Post exposure treatment



The Royal College of Pathologists
Pathology: the science behind the cure

Human rabies immunoglobulin

A. Is given to all cat III exposures

B. Is given to all exposures in high risk countries

C. Dose is weight dependant

D. Is given to all non-immune cat III exposures in high risk countries

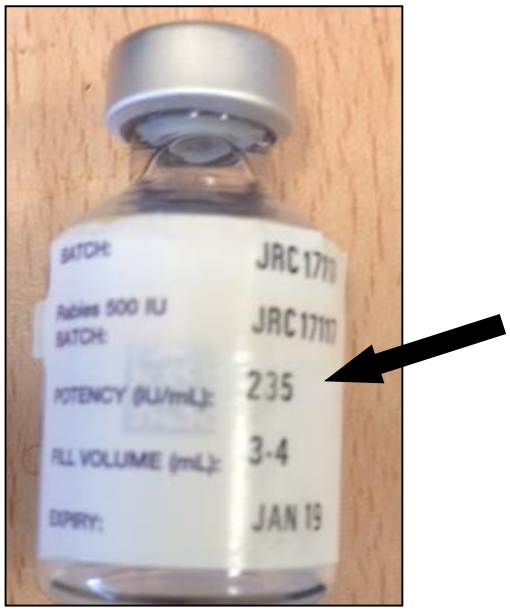
E. Is from patients who have recovered from rabies

F. Is the mainstay of rabies PET

Public Health England

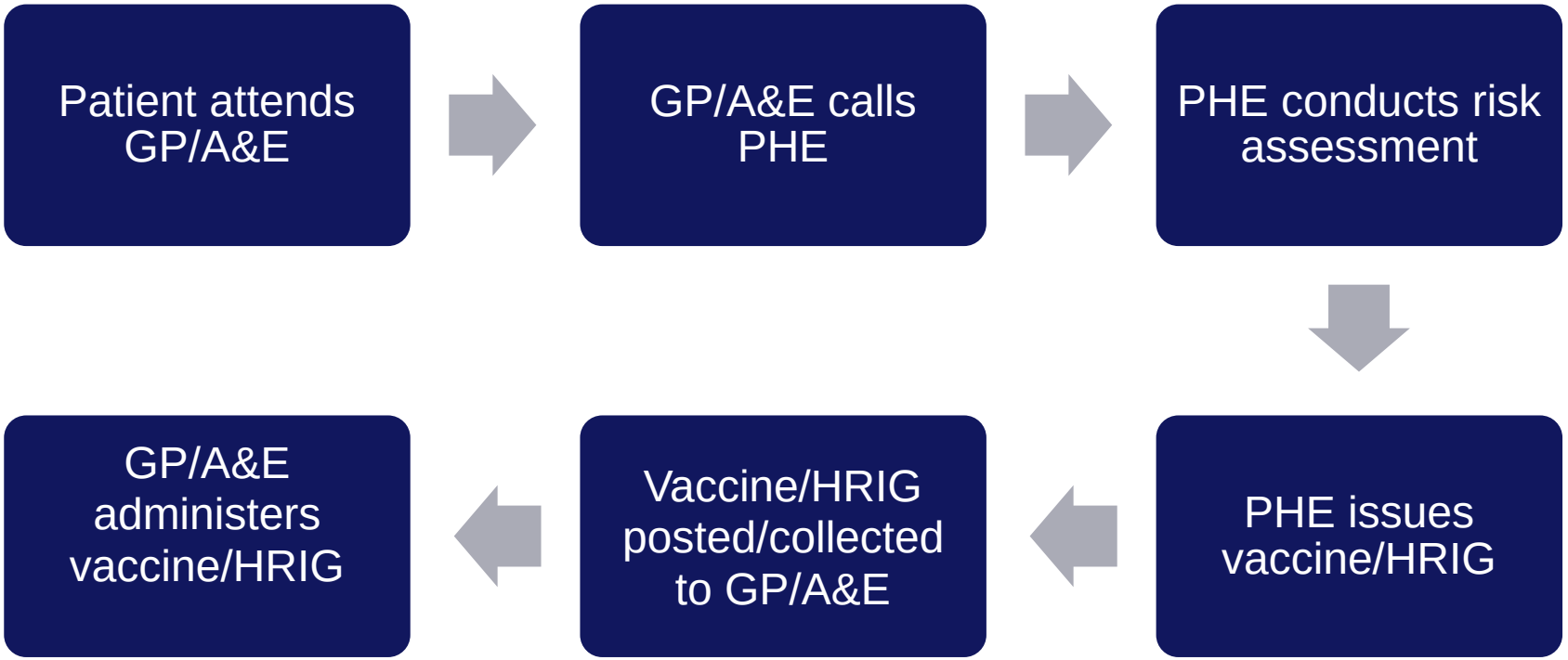
Human Rabies Immunoglobulin (HRIG)

- HRIG is made from the pooled plasma from immunised non-UK donors.
- It is used after high risk exposure to mop up live virus at the wound site and may give rapid protection.
- The mainstay of rabies post exposure prophylaxis is rabies vaccine as the antibody induced by vaccination is much greater than that by HRIG.
- HRIG should not be given to those who have started a course of PEP seven or more days ago, or have been fully immunised previously.
- It is weight-dependent (20IU/kg) and the dose must be calculated from the potency



Public Health England

Process for issuing PET vaccine and/or HRIG in England



Logistics

In most cases vaccine is administered by GP

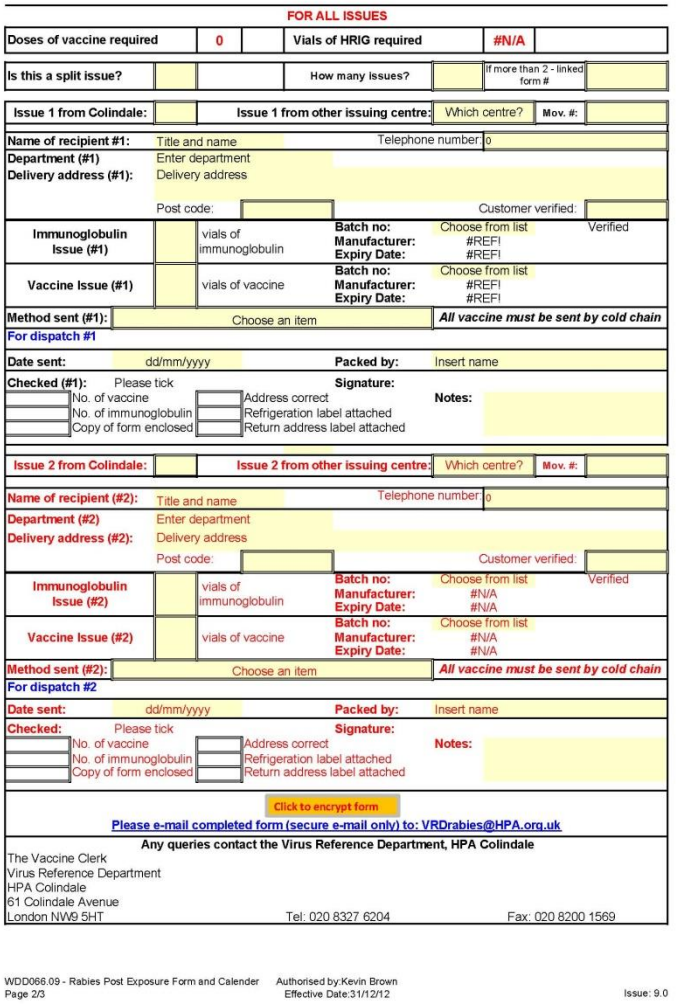
If original contact is hospital may need to send first doses of vaccine/HRIG to A&E

Can issue to two different sites if required

Use local vaccine if possible and RIgS will replace

Need information on where to send and who is responsible for receipt

RIgS will organise if vaccine is to be sent by mail



FOR ALL ISSUES

Doses of vaccine required	0		Vials of HRIG required	#N/A	
Is this a split issue?			How many issues?	If more than 2 - linked form #	
Issue 1 from Colindale:		Issue 1 from other issuing centre:	Which centre?	Mov. #:	
Name of recipient #1:	Title and name		Telephone number:	0	
Department (#1)	Enter department				
Delivery address (#1):	Delivery address				
	Post code:		Customer verified:		
Immunoglobulin Issue (#1)	vials of immunoglobulin	Batch no:	Choose from list	Verified	
		Manufacturer:	#REF!		
		Expiry Date:	#REF!		
Vaccine Issue (#1)	vials of vaccine	Batch no:	Choose from list		
		Manufacturer:	#REF!		
		Expiry Date:	#REF!		
Method sent (#1):	Choose an item		All vaccine must be sent by cold chain		
For dispatch #1					
Date sent:	dd/mm/yyyy	Packed by:	Insert name		
Checked (#1):	Please tick	Signature:			
No. of vaccine		Address correct	Notes:		
No. of immunoglobulin		Refrigeration label attached			
Copy of form enclosed		Return address label attached			
Issue 2 from Colindale:		Issue 2 from other issuing centre:	Which centre?	Mov. #:	
Name of recipient (#2):	Title and name		Telephone number:	0	
Department (#2)	Enter department				
Delivery address (#2):	Delivery address				
	Post code:		Customer verified:		
Immunoglobulin Issue (#2)	vials of immunoglobulin	Batch no:	Choose from list	Verified	
		Manufacturer:	#N/A		
		Expiry Date:	#N/A		
Vaccine Issue (#2)	vials of vaccine	Batch no:	Choose from list		
		Manufacturer:	#N/A		
		Expiry Date:	#N/A		
Method sent (#2):	Choose an item		All vaccine must be sent by cold chain		
For dispatch #2					
Date sent:	dd/mm/yyyy	Packed by:	Insert name		
Checked:	Please tick	Signature:			
No. of vaccine		Address correct	Notes:		
No. of immunoglobulin		Refrigeration label attached			
Copy of form enclosed		Return address label attached			

Click to encrypt form

Please e-mail completed form (secure e-mail only) to: VRDrabies@HPA.org.uk

Any queries contact the Virus Reference Department, HPA Colindale

The Vaccine Clerk
Virus Reference Department
HPA Colindale
61 Colindale Avenue
London NW9 5HT
Tel: 020 8327 6204
Fax: 020 8200 1569

WDD066.09 - Rabies Post Exposure Form and Calender Page 2/3
Authorised by:Kevin Brown
Effective Date:31/12/12
Issue: 9.0

Public Health England

RIgS hours

Working Hours (Mon-Fri 9am-5pm)

- RIgS team or local HPT can carry out risk assessment

OOH (Evenings 5pm-9am)

- Urgent but not a medical emergency
- Not necessary to issue overnight in most cases
- Exception is unimmunised/untreated category III exposures to head and neck from high risk countries
- Ask brief risk assessment questions to check if issue is necessary overnight
- Most cases can be referred to RIgS/duty doctor team next morning (after 9am)

OOH (Weekends and bank holidays 9am-5pm)

- Duty doctor or local issuing centres available for risk assessment
- PET can be issued from Colindale or local issuing centres
- Colindale will issue between 2-3pm, so all arrangements need to be made before 1pm that day

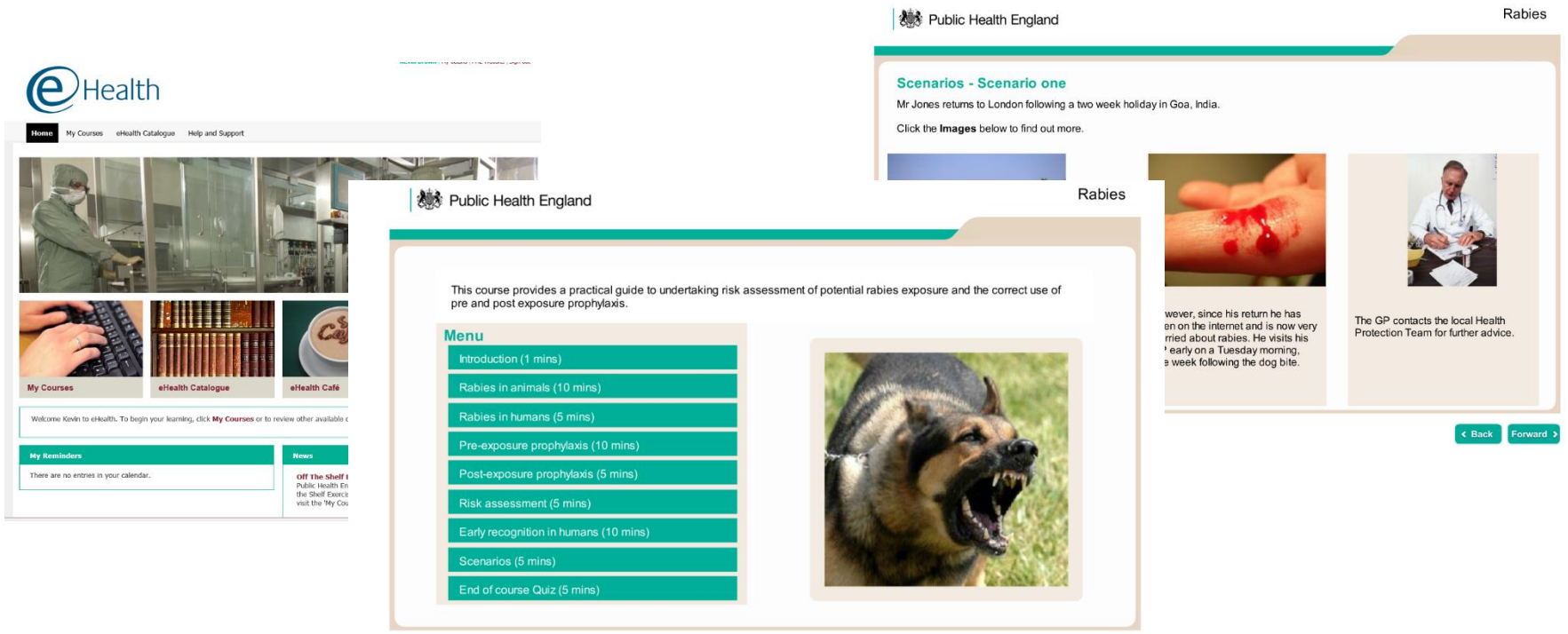
(Other immunoglobulins do not require issue overnight, with exception of diphtheria and botulinum antitoxins)

Public Health England

E-Learning

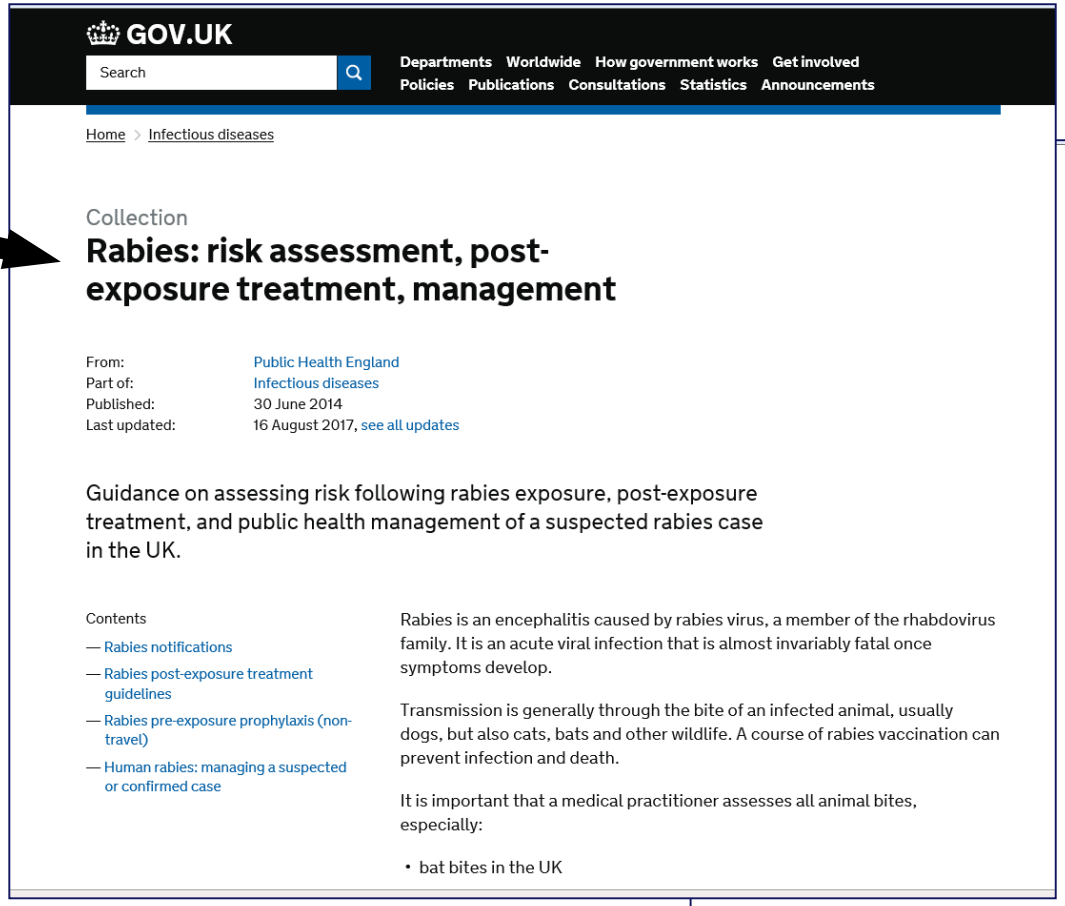
Rabies e-learning module available through eHealth

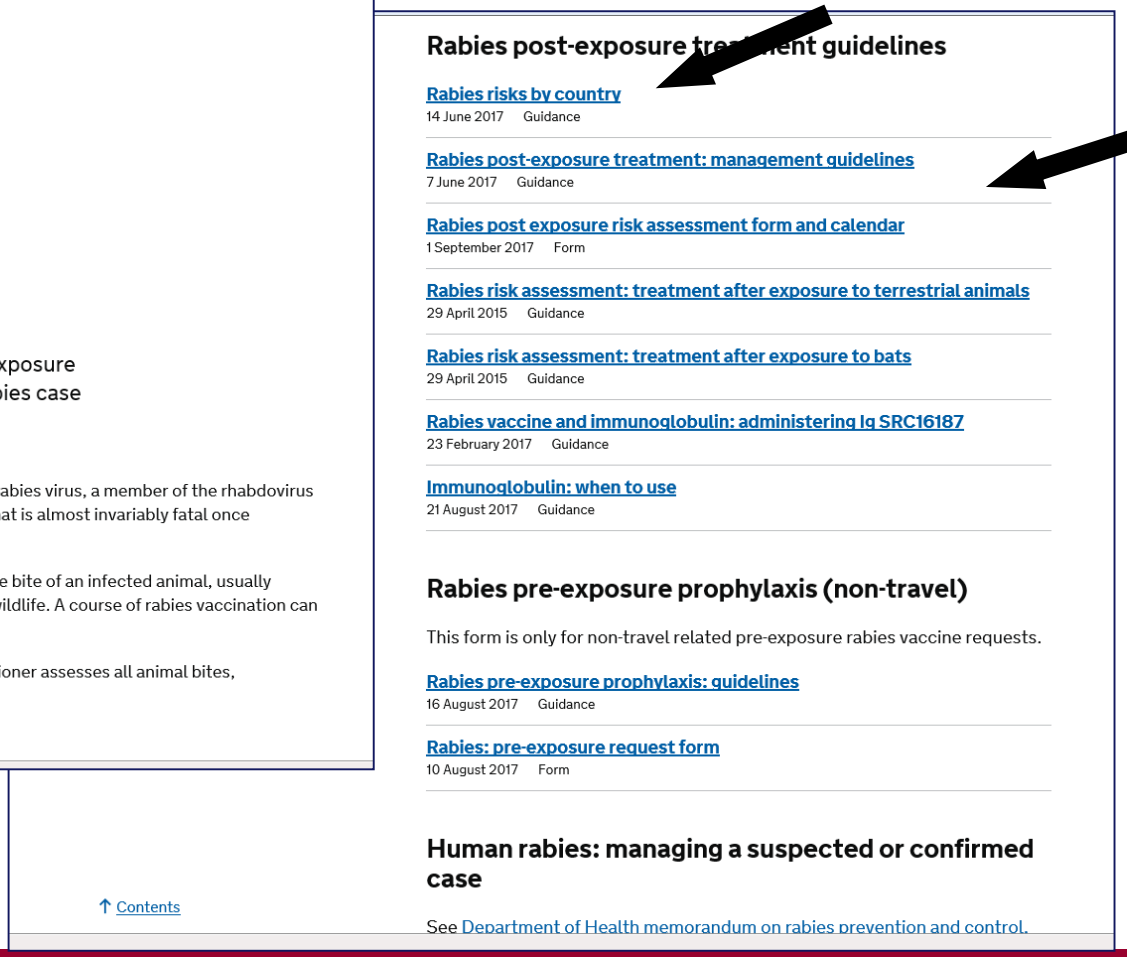
https://lms.kallidus.com/PublicHealthEngland



Public Health England

Guidance documents





Public Health England

Conclusion

- UK is rabies-free, but a rabies-related virus European bat lyssavirus (EBLV2) is found in some bats
- 6 human cases in UK since 2000 (5 imported,1 indigenous bat)
- Approximately 2000 individuals in England receive PET/year
  - 85-90% of these are returning travellers
  - 10-15% following exposure to UK bats
- Vaccine may be available locally and it may be quicker to suggest local vaccine is used.
- If local vaccine is used as d0 of PET, let RIgS team know the details the next working day and we can replace
- Concentrate on getting the first dose of vaccine to the patient as soon as possible, NOT the HRIG

Public Health England

Acknowlegements

Rabies and Immunoglobulin team
Katherine Russell

Amanda Dennis
Michelle Olphonce
Laryn Muzalewski

Michael Lattimore
Teresa Gibbs

Public Health England

Questions