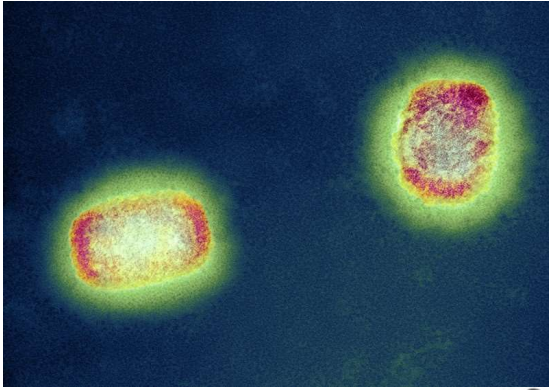




Monkeypox

謝思民
台大醫院感染科主治醫師



About Monkeypox

typical inverted terminal repeat conserved housekeeping genes typical inverted terminal repeat



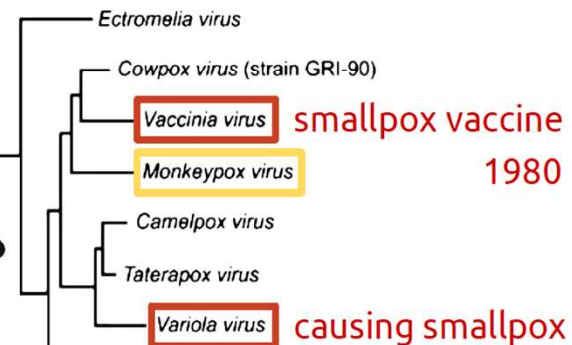
- **Bioinformatics** | poxviridae, orthopoxvirus
 - 197kb enveloped dsDNA with 33% GC, 190 coding sequences
 - challenges for reconstructing genome:
 - long (~ 6.5kb) inverted tandem repeat, hard to resolve into individual copies
 - low GC results in long poly-A/T homopolymeric tracts
 - local tandem repeats scattering
 - potential within-host diversity within/between lesions
 - slow evolutionary rate: 47 bp per year (TC > TT or GA > AA by APOBEC3 protein?)

- **First identification** | (animal) crab-eating macaques, 1958; (human) Congo, 1970

- **Main clades** | Congo Basin & West African

(CB)

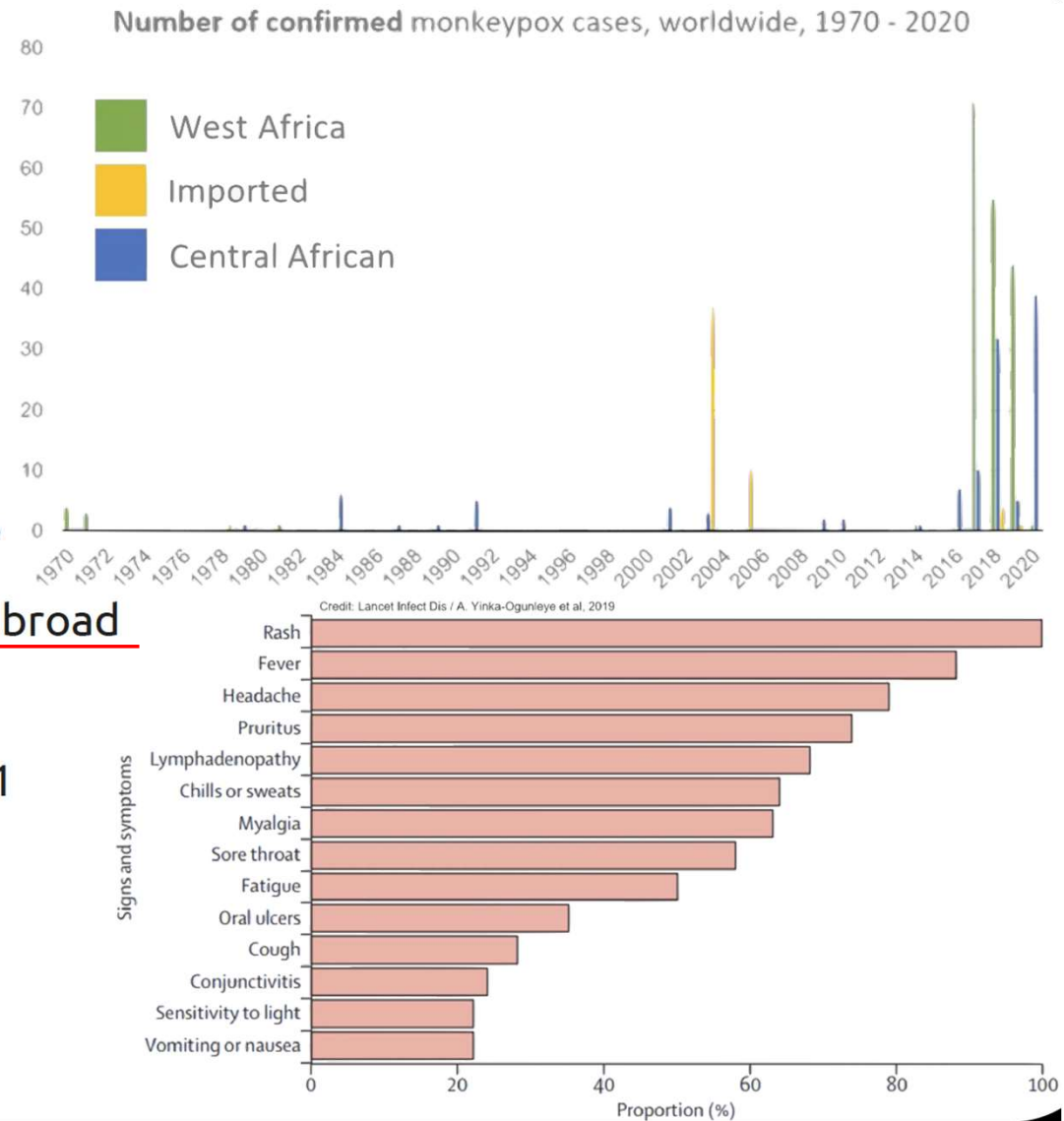
(WA)



Historical outbreak

- **2003 USA** | animals transported from central Africa
 - 34 cases w/ rash > raised lesion > pustule for 2-3 wks
 - 3 cases w/o symptoms were vaccinated (protective factor)
 - no confirmed HHT
 - clinical symptom: fever + rash + LAP
- **2017 Nigeria** | west African clade going abroad
 - 183 cases w/ 9 deaths
 - Israel: 1 case in 2018
 - UK: 4 cases in 2019 & 3 cases in 2021
 - Singapore: 1 case in 2019

2022/05/06 UK spreading in Europe



NEWS | 23 June 2022

Monkeypox in Africa: the science the world ignored

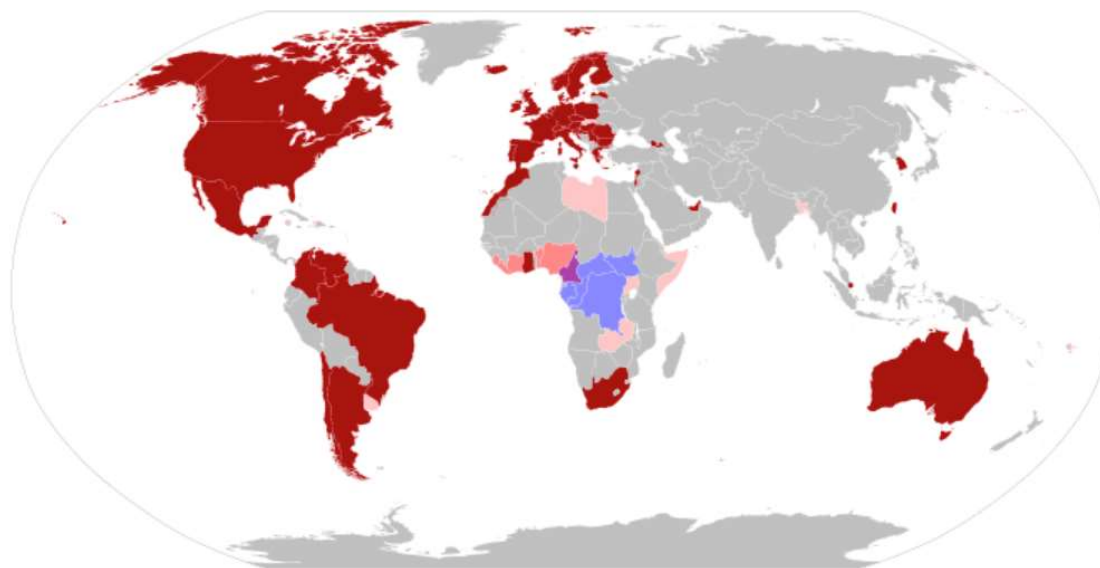
African researchers have been warning about monkeypox outbreaks for years. As vaccines are deployed globally, they worry they will be left behind.

Monkeypox cases rising in Africa

Decade	Confirmed cases caused by the viral strain that emerged in <u>Central Africa</u>	Confirmed cases caused by the viral strain that emerged in <u>West Africa</u>
1970–79	38	9
1980–89	355	1
1990–99	520	0
2000–09	92 10,027 suspected*	47
2009–19	85 18,788 suspected*	195

CA





猴痘病毒全球傳播地圖

-  西非演化支地方性流行
-  中非演化支地方性流行 Severe but endemic
-  兩種演化支同時存在
-  2022年西非演化支爆發 Mild but epidemic
-  疑似病例

Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus

西非演化支的突變株？

Received: 27 May 2022

Accepted: 20 June 2022

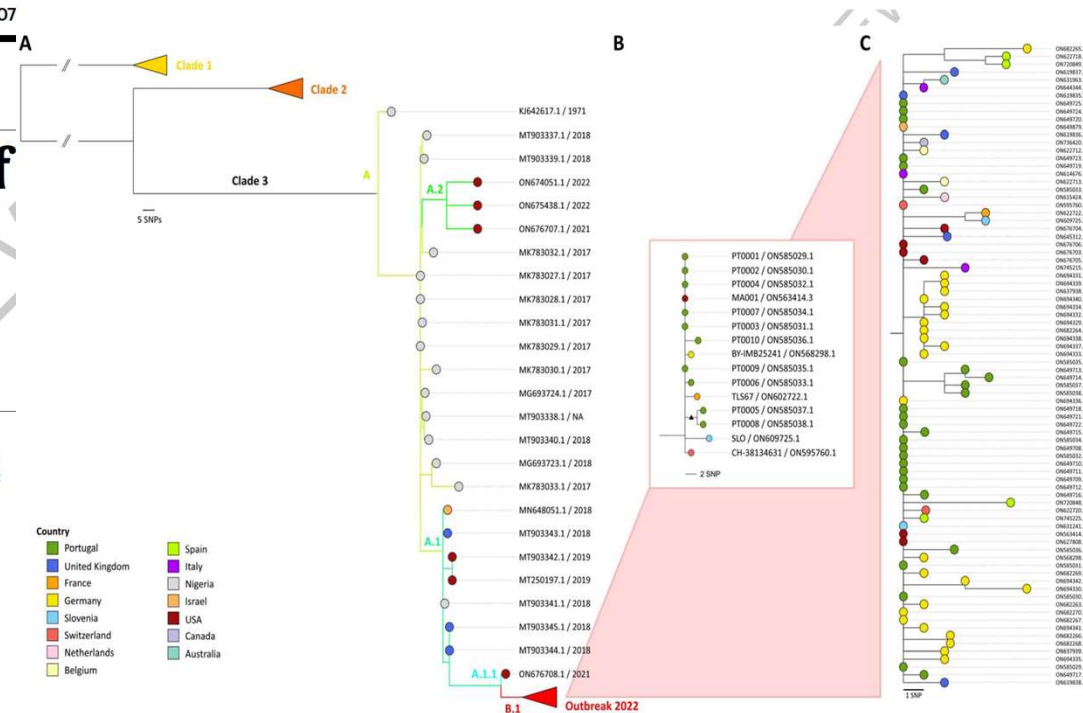
Accelerated Article Preview

Published online: 24 June 2022

Joana Isidro, Vítor Borges, Miguel Pinto, Daniel Sobral, João Dourado Santos, Alexandra Nunes, Verónica Mixão, Rita Ferreira, Daniela Santos, Sílvia Duarte, Luís Vieira, Maria José Borrego, Sofia Nuncio, Isabel Lopes de Carvalho, Ana Pelerito, Rita Cordeiro & João Paulo Gomes

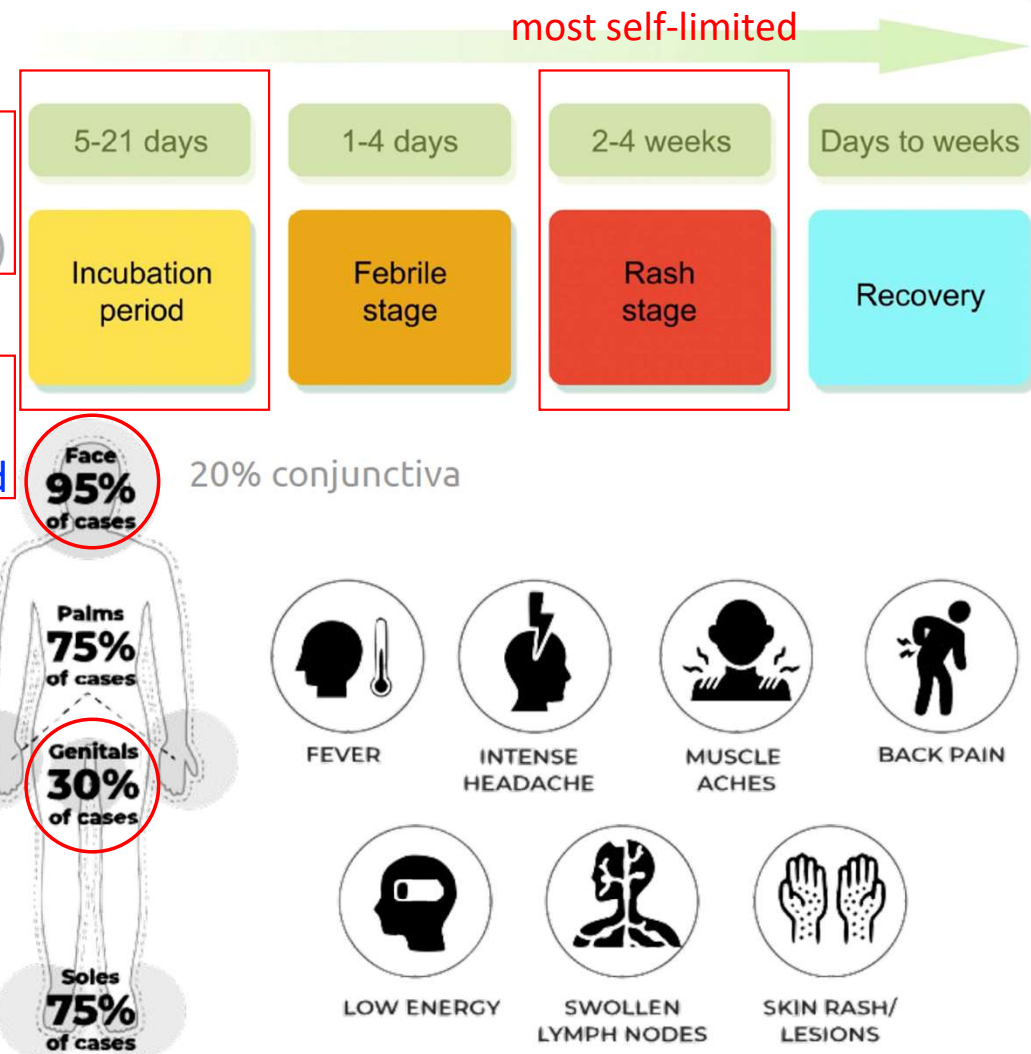
Abstract / Introductory paragraph

The largest monkeypox virus (MPXV) outbreak described so far in non-endemic countries was identified in May 2022¹⁻⁶. Here, shotgun metagenomics allowed the rapid reconstruction and phylogenomic characterization of the first MPXV outbreak genome sequences, showing that this MPXV belongs to clade 3 and that the outbreak most likely has a single origin. Although 2022 MPXV (lineage B.1) clustered with 2018-2019 cases linked to an endemic country, it segregates in a divergent phylogenetic branch, likely reflecting continuous accelerated evolution. An in-depth mutational analysis suggests the action of host APOBEC3 in viral evolution as well as signs of potential MPXV human adaptation in ongoing microevolution. Our findings also indicate that genome sequencing may provide resolution to track the spread and transmission of this presumably slow-evolving dsDNA virus.



Symptoms **Typical**

- **Febrile stage** | 1-3 d
 - fever, headache, fatigue
 - LAP (distinct from smallpox/chickenpox)
 - enanthem appears toward the end
- **Skin eruption stage** | > 5 d
 - 1-3 d after fever
 - rash over face or extremities: **widespread**
 - blood detected only at the beginning
 - producing antibodies
- **Mortality** | 0-11%, higher in children & pregnant women & immunosuppressed
- **Complications**
 - bacterial infection of eyes (4%) or skin (20%)
 - dehydration due to diarrhea/vomit (7%)
 - abscess with airway obstruction
 - bronchopneumonia
 - encephalitis/sepsis (<1%)

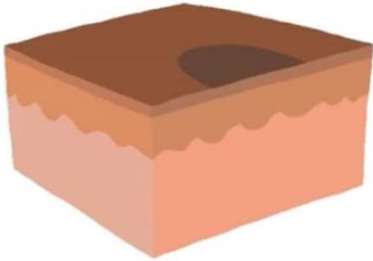


Symptoms | rash 皮膚病灶

can be itchy or painful / thick yellowish vesicle / umbilicated or hemorrhagic lesion / abscess

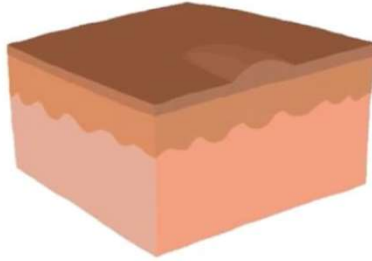
Macule

斑疹



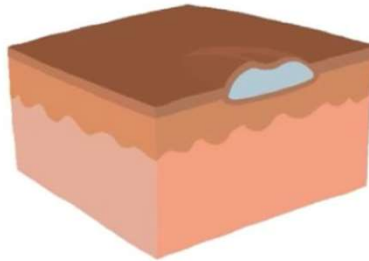
Papule

丘疹



Vesicle

水疱



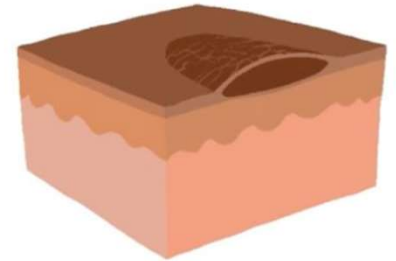
Pustule

膿疱



Crust

結痂



2022 UK outbreak



UK Health
Security
Agency

Research and analysis

Investigation into monkeypox outbreak in England: technical briefing 1

Published 10 June 2022

- Characteristics of the confirmed population
 - **London residents** (81%, 224/276)
 - **Male** (99% 311/314)
 - **38 y/o** (IQR 32-44)
 - **GBMSM** (99%, 151/152) (the remains declined the disclosure)
 - **Recent foreign travel** within 21 d prior to symptom onset (22%, 75/336); mostly **within Europe** (79%, 59/75)
- Rapid sexual health questionnaires
(55%, 45/82 cases with known/suspected GBMSM sexual transmission till 05/25) (symptom onset 04/08-05/20)
 - cisgender men, **gay** (89%, 40/45), **bisexual** (9%, 4/45)
 - **NO foreign travel** (69%, 31/45)
 - **Sex during incubation period** (98%), **group sex** (44%, 20/45)
 - **Sexually transmitted infection history** (60%, 27/45)
 - **> 10 sexual partners in previous 3 m** (44%, 20/45)
 - **Sexual activity other than place of residence**
 - other cities (30%, 13/45)
 - abroad (20%, 9/45)
 - with men who aren't UK residents (24%, 11/45)

2022/05/06-06/08 confirmed cases

Devolved administrations Confirmed cases

England	320
Northern Ireland	2
Scotland	11
Wales	3
Total	336

Region of residence Total confirmed

East of England	10
East Midlands	3
London	224
North East	2
North West	11
South East	15
South West	2
West Midlands	6
Yorkshire and Humber	3

Unknown* 44 **320-44 = 274**

Total 320



Who are at risk from 2022 Monkeypox?

- 此波猴痘疫情自5月中於英國爆發以來，全球累計50國報告至少3,598例確診 (6/24)
- 其中以歐洲及美洲病例數最多，累計病例前五名為英國、德國、西班牙、法國及葡萄牙
- 猴痘傳播對象具侷限性: 多與確診個案有親密接觸或不安全性行為。確診者的同住家人，及照顧確診者的醫護人員，若無適當防護措施，亦有風險

Atypical presentations in 2022 Monkeypox have been noted

- Skin lesions: may be limited over genital and/or perineal area, rather than face and/or widespread
- Skin lesions may appear before obvious fever and lymphadenopathy

IMAGES IN CLINICAL MEDICINE

Monkeypox Genital Lesions

Rita Patrocinio-Jesus, M.D., D.T.M.H., and Francesca Peruzzi, M.D.

June 15, 2022

DOI: 10.1056/NEJMicm2206893





	傳統型猴痘*	2022 猴痘
演化支	剛果(中非)演化支 Congo Basin (CB) 為主	有基因變異的西非演化支 West Africa (WA)
主要傳播途徑	1. 無防護的直接接觸黏膜或皮膚病灶 2. 長時間的飛沫或大量的體液暴露 3. 直接接觸感染猴痘的動物	1. 不安全的性行為 2. 無防護的密切接觸或親密行為 (例如，同住家人的相處)
主要感染患者	不限	20-50 歲男性
臨床表現	1. 發燒期 (1-3 天)：發燒，肌肉痠痛，淋巴結腫大。 2. 皮疹期 (2-4 週)：斑疹，丘疹，水疱，膿疱，結痂；可能會大面積散佈，尤其是臉部，軀幹，四肢	1. 發燒期 (1-3 天)：較不明顯；可能與皮疹期一起出現。 2. 皮疹期 (2-4 週)：斑疹，丘疹，水疱，膿疱，結痂；通常侷限於生殖器或會陰部週邊
死亡率	10% 左右	目前 < 0.1%
預防措施	1. 前往猴痘病毒動物流行地區時，避免接觸齧齒類動物和靈長類動物及生病或死亡動物。 2. 所有食物必須完全煮熟後才能食用。 3. 避免與猴痘病患密切接觸，或接觸時應佩戴適當防護裝備。	1. 避免與陌生人親密接觸或發生不安全性行為。 2. 繼續保持良好的防疫習慣 (維持手部衛生及戴口罩)。 3. 若曾至流行地區，如出現疑似症狀，回國入境時請主動告知機場檢疫人員，並儘速就醫並告知醫師旅遊史與接觸史。

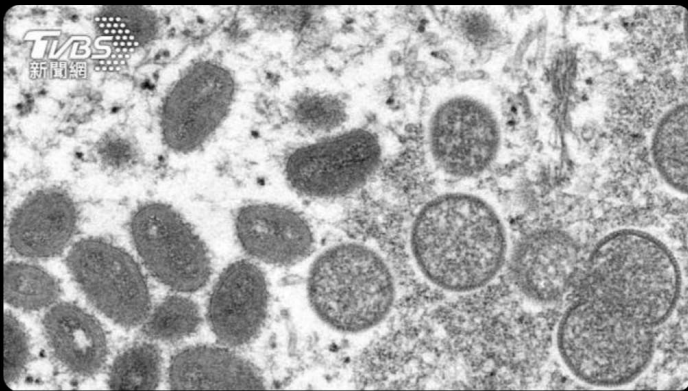


猴痘燒進亞洲！南韓、新加坡出現首起確診

柯幸宜

2022年6月22日 週三 下午9:24

猴痘病例持續延燒世界各國，現在亞洲也被攻破，包括新加坡、南韓都出現確診。雖然台灣上周也有通報疑似案例，但證實是虛驚一場。疾管署副署長莊人祥也在今天指揮中心記者會上表示，今天或明天可能就會將猴痘列為法定傳染病。



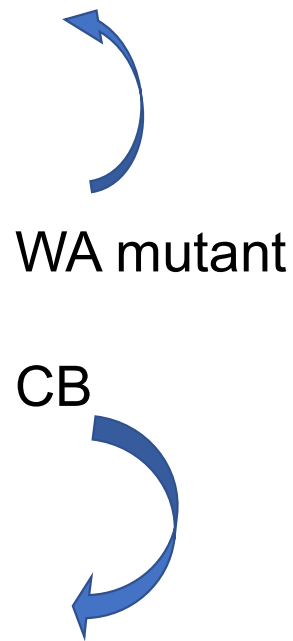
猴痘今起列第二類法定傳染病 疑似病例24小時內通報

2022/06/23 14:36

讚 127



猴痘疫情也從歐洲擴散到亞洲，因應未來可能出現病例，我疾病管制署今天公告「猴痘」為第二類法定傳染病，若有病例需在24小時內通報。（取自世衛官網）





即時 熱門 要聞 娛樂 運動 全

獨／防猴痘侵台 我國著手檢驗天花疫苗「隨時可開打」

2022-06-24 12:22

短期內若食藥署檢驗通過，當有緊急需求時，國內的第一代天花疫苗儲備可能派上用場。



即時 熱門 要聞 娛樂 運動 全

衛生福利部疾病管制署
Taiwan Centers for Disease Control



首頁 > 新聞稿

猴痘 (monkeypox) 全球確診病例已經超過3200例，世界衛生組織 (WHO) 緊急開會評估是否將猴痘列為「國際公共衛生緊急事件 (PHEIC)」。我國昨將猴痘列為第2類法定傳染病，據了解，國內也將啟動採購天花第三代疫苗及抗病毒藥物計畫，防止猴痘疫情侵台。

猴痘正於多個國家流行，多與有症狀病例密切身體接觸有關。根據美國疾病管制與預防中心 (CDC) 數據，天花疫苗對於猴痘病毒的有效性高達85%，而WHO指出，猴痘病毒與天花病毒一樣，屬於正痘病毒的一種，為罕見的人畜共通傳染病。

今年首例「猴痘」境外移入
確診個案，籲請自流行地區
返國入境民眾留意相關疑似
症狀



發佈日期：2022-06-24

疾病管制署(以下稱疾管署)今(24)日公布我國首例境外移入猴痘確診個案，為南部20多歲本國籍男性，於今(2022)年1月至6月至德國就學，6月16日搭機返國，機場COVID-19檢驗陰性後返家進行居家檢疫，6月20日出現發燒、喉嚨痛、肌肉痠痛、紅疹、鼠蹊部淋巴腫大等症狀，於6月21、22日就醫，經醫師評估後，進行採檢及通報，檢體送疾管署昆陽實驗室檢驗，於今日確認陽性。

接觸者匡列原則 (CDC, 6/24)

- 自個案發病後至隔離前，曾在無適當防護下，直接接觸感染者的呼吸道分泌物、皮膚或黏膜之民眾或醫療人員，皆應列為接觸者
- 對被匡列為接觸者的對象，不需隔離，但應進行健康監測至與確定病例最近一次接觸日後21天。健康監測應觀察是否有發燒、淋巴結腫大或皮膚出疹症狀。

醫療人員接觸者依暴露風險高低分類

1. 高風險接觸者：

- 曾在無防護狀況下與確診病患之皮膚、黏膜、體液或其汙染之物品接觸者
- 於病患執行會產生飛沫微粒 (aerosol) 之醫療措施時，未穿戴N95面罩與護目鏡/面罩，且位於同一空間或相距2公尺內。

2. 中風險接觸者：

- 曾與未戴口罩之病患共處一室(相距2公尺內)，累計超過三小時，且醫護人員未佩戴外科口罩以上等級防護裝備
- 醫護人員之衣物與病患皮膚、體液或床單曾有接觸，且未穿著隔離衣者。

國內24日出現首例境外移入猴痘確診個案，是一名自德國留學返台的25歲台南學生，目前匡列9名接觸者，引發民眾擔憂。而目前可接種的猴痘疫苗，分為傳統天花（俗稱「牛痘」）和新一代的猴痘疫苗，所以其實台灣有部份民眾早已有抗體，只要觀察身上2部位是否有「這疤痕」即可分辨。

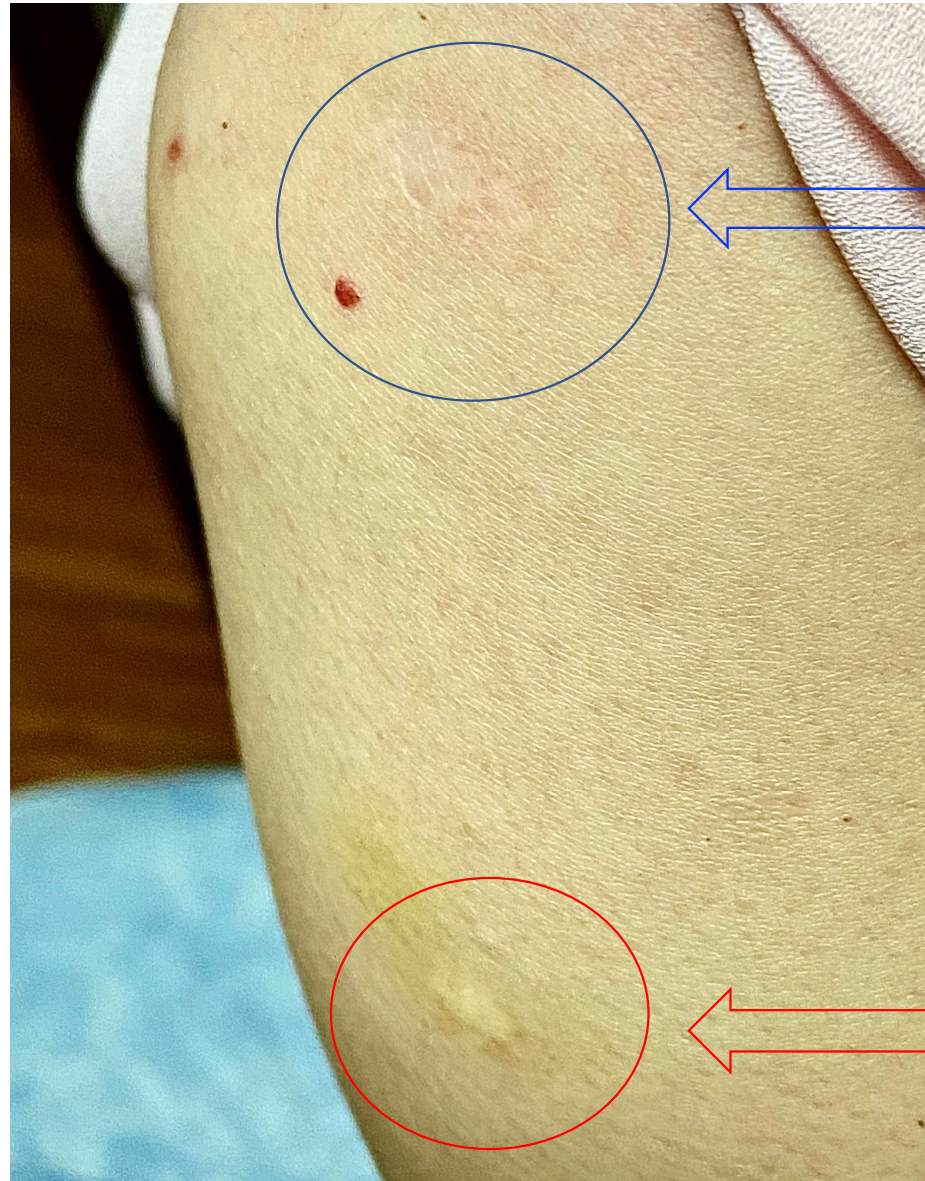


目前可接種的猴痘疫苗，分為傳統天花（俗稱「牛痘」）和新一代的猴痘疫苗。（圖 / TVBS）

根據《自由時報》報導，彰化縣衛生局長葉彥伯指出，民眾出生年68年次之前都有接種牛痘疫苗，多數人打的手臂上，少數打在大腿處，因此要分辨自己是否打過牛痘疫苗，只要看手臂或大腿處有無「凹下去的疤痕」就能得知；另外很多人的手臂同時留下2個疤痕，葉彥伯表示，一個是卡介苗疫苗，疤痕中心點凸起來；另一個才是牛痘疤痕，「凹下去，而且有放射狀的線條」。

Really?





BCG scar

Vaccinia scar

MAJOR ARTICLE

Age Distribution for T Cell Reactivity to Vaccinia Virus in a Healthy Population

Szu-Min Hsieh, Sung-Ching Pan, Shey-Ying Chen, Pei-Fang Huang, and Shan-Chwen Chang

Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei

(See the editorial commentary by Bray on pages 90–1)

EDITORIAL COMMENTARY

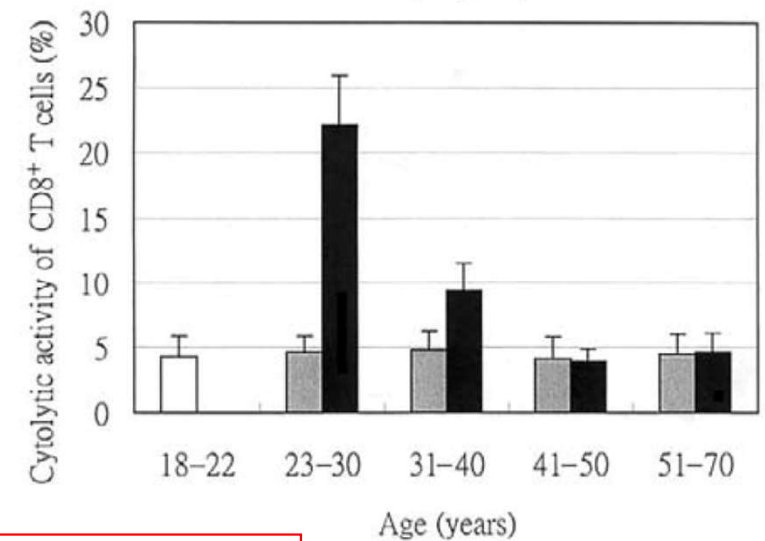
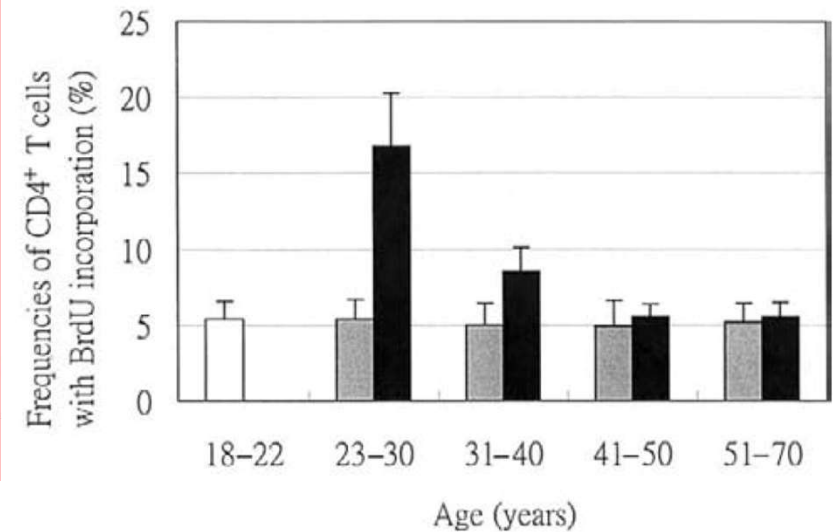
New Data in a 200-Year Investigation

Mike Bray

Biodefense Clinical Research Branch, Office of Clinical Research, Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

(See the article by Hsieh et al. on pages 86–9)

Clinical Infectious Diseases 2004;38:90–1



23 y/o = 1979 出生

Clinical and immunological responses to undiluted and diluted smallpox vaccine with vaccinia virus of Lister strain

Szu-Min Hsieh^a, Shey-Ying Chen^a, Gwo-Chang Sheu^b, Min-Nan Hung^a,
Wen-Hsiang Chou^b, Shan-Chwen Chang^{a,*}, Kwo-Hsiung Hsu^b

^a Division of Infectious Diseases, Department of Internal Medicine, National Taiwan University Hospital and College of Medicine,
National Taiwan University, No. 7 Chung-Shan South Road, Taipei 100, Taiwan, ROC

^b Center for Disease Control, Department of Health, Taiwan



Vaccinia-specific immune responses after vaccination with diluted or undiluted smallpox vaccine of Lister strain in vaccinia-naïve and non-naïve subjects

Subjects	Vaccine	Magnitudes of increase in T cell responses: median (range)		Rate of significant antibody responses (%) ^a
		CD4+	CD8+	
Vaccinia-naïve	Undiluted (n = 20)	5.2 (3.1–17.5)	4.8 (3.0–16.8)	100
	1:5 diluted (n = 37)	4.7 (2.7–21.3)	5.1 (3.2–15.3)	100
	1:10 diluted (n = 40)	5.0 (2.8–18.4)	4.7 (2.8–25.4)	100
Previously vaccinated	Undiluted (n = 35)	2.8 (1.8–10.3)	3.1 (2.1–10.5)	100
	1:10 diluted (n = 35)	3.0 (2.0–11.5)	2.9 (1.7–10.6)	100
	1:30 diluted (n = 52)	2.7 (1.6–12.8)	3.4 (1.8–11.9)	100

^a We defined the significant antibody response to vaccination as a positive seroconversion or a ≥ 4 -fold elevation of titer of vaccinia-specific antibody.

Systemic reactions within 15 days after vaccination with diluted or undiluted smallpox vaccine in vaccinia-naïve and previously vaccinated subjects

Subjects	Vaccine	Age (years)	Fever	Headache	Muscle aches	Fatigue	LAP	Rash ^a
Vaccinia-naïve (<i>n</i> = 97)	Undiluted (<i>n</i> = 20)		4 (20%)	10 (50%)	8 (40%)	11 (55%)	13 (65%)	0
	1:5 diluted (<i>n</i> = 37)		4 (11%)	10 (27%)	10 (27%)	18 (49%)	25 (68%)	0
	1:10 diluted (<i>n</i> = 40)		8 (20%)	12 (30%)	17 (43%)	15 (38%)	21 (53%)	1 (3%)
	<i>P</i> -value ^b		0.50	0.19	0.34	0.39	0.37	0.49
Previously vaccinated (<i>n</i> = 122)	Undiluted (<i>n</i> = 35)	24–40 (<i>n</i> = 20)	1 (5%)	4 (20%)	3 (15%)	5 (25%)	4 (20%)	0
		41–65 (<i>n</i> = 15)	0	2 (13%)	1 (7%)	4 (27%)	2 (13%)	0
	1:10 diluted (<i>n</i> = 35)	24–40 (<i>n</i> = 19)	1 (5%)	3 (16%)	5 (26%)	7 (37%)	3 (16%)	0
		41–65 (<i>n</i> = 16)	1 (6%)	1 (6%)	1 (6%)	3 (19%)	4 (25%)	0
	1:30 diluted (<i>n</i> = 52)	24–40 (<i>n</i> = 30)	2 (7%)	7 (23%)	12 (40%)	15 (50%)	10 (33%)	1 (3%)
		41–65 (<i>n</i> = 22)	1 (5%)	1 (5%)	4 (18%)	4 (18%)	5 (23%)	2 (9%)
	<i>P</i> -value ^b		0.80	0.79	0.08	0.57	0.40	0.13

^a Rash at sites other than vaccination sites.

^b *P*-values are the results of comparison between the undiluted, 1:10 diluted and 1:30 diluted groups (by χ^2 -test).

Prevention | smallpox vaccine



Vaccine (Manufacturer)	Licensed for smallpox (country, type, date)	Licensed for monkeypox (country, type, date)	Considerations
MVA-BN (Bavarian Nordic) 3rd generation	EU: Imvanex has been authorised under exceptional circumstances (2013) Canada: Full MA (2013) USA: Full MA (2019)	USA, full MA (2019) Canada, full MA (2019)	Very limited supply Liquid-frozen formulation, approved for use in the general adult population Two doses four weeks apart
LC16 (KM Biologics) 3rd generation	Japan - Full MA (1975) USA - EIND (2014)	No	Approved for use in infants and children (all ages) as well as adults (all ages)

Vaccine (Manufacturer)	Licensed for smallpox (country, type, date)	Licensed for monkeypox (country, type, date)	Considerations
ACAM20 (Emergent BioSolutions) 2nd generation	USA - Approved	USA - EIND for PEP	Approved for use in adults aged 18 – 64 years of age. Earlier production by Sanofi Pasteur approved in France.
Vaccinia, various strains* from national production 1st generation	Various countries Various national production (SEP), held by various countries	No	Regular potency testing recommended

- **2nd G** | use the same vaccinia virus vaccine strains employed for 1st G vaccine or clonal virus variants plaque-purified from traditional vaccine stock
- **3rd G** | more attenuated smallpox vaccine strains
- **Precaution use for replicating vaccine**
 - immunodeficiencies
 - immunosuppression therapy
 - atopic dermatitis
 - children
 - pregnant / breastfeeding women

US: Jynneos
EU: Imvanex

猴痘的預防及照護

疫苗與治療照護

- ★ 不建議大規模接種猴痘疫苗，國際間通常建議高暴露風險職業或高感染風險之密切接觸者可接種疫苗
- ★ 大多數病患的不需特殊治療，必要時，可提供輸液治療與維持營養等支持性療法，以減輕症狀和併發症
- ★ 目前有數種藥物可用於治療，但僅建議嚴重病患或免疫低下者使用 Tecovirimat, Cidofovir, Brincidofovir)

預防方法

- ★ 前往猴痘病毒動物流行地區時，避免接觸齧齒動物和靈長類動物及生病或死亡動物，所有食物必須澈底煮熟後才能食用
- ★ 避免與猴痘病患接觸，或接觸時應佩戴適當防護裝備
- ★ 如有任何疑似症狀，應及時就醫，並告知旅遊史與接觸史

擔心猴痘嗎？做到以下五點不用驚：

1. 避免與陌生人親密接觸或發生不安全性行為
2. 保持良好的防疫習慣（繼續維持手部衛生及戴好口罩）
3. 若曾至流行地區，如出現疑似症狀，回國入境時請主動告知機場檢疫人員，並儘速就醫，記得告知醫師旅遊史與接觸史
4. 若同住家人有疑似症狀或相關旅遊史，請做好飛沫/接觸防護，並提醒同住者儘快就醫
5. 醫護人員執行醫療業務時，無論新冠檢測是否陽性，請繼續確實遵守感控原則

**Thank you for
your attention!**