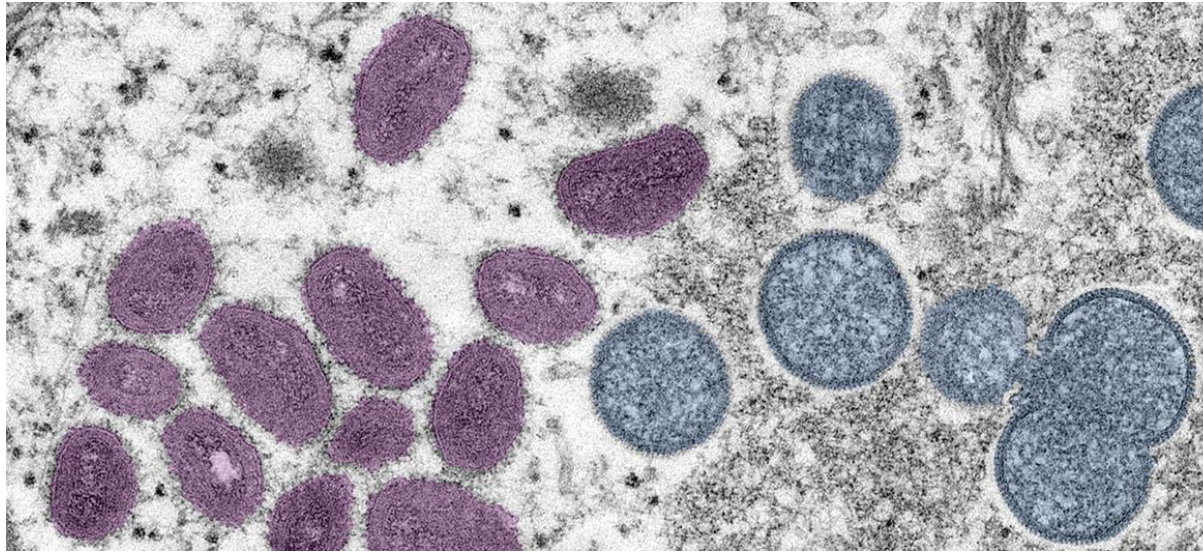


111年高雄市感染管制查核作業訓練研討會

猴痘的流行現況和疫苗施打



李欣蓉 醫師

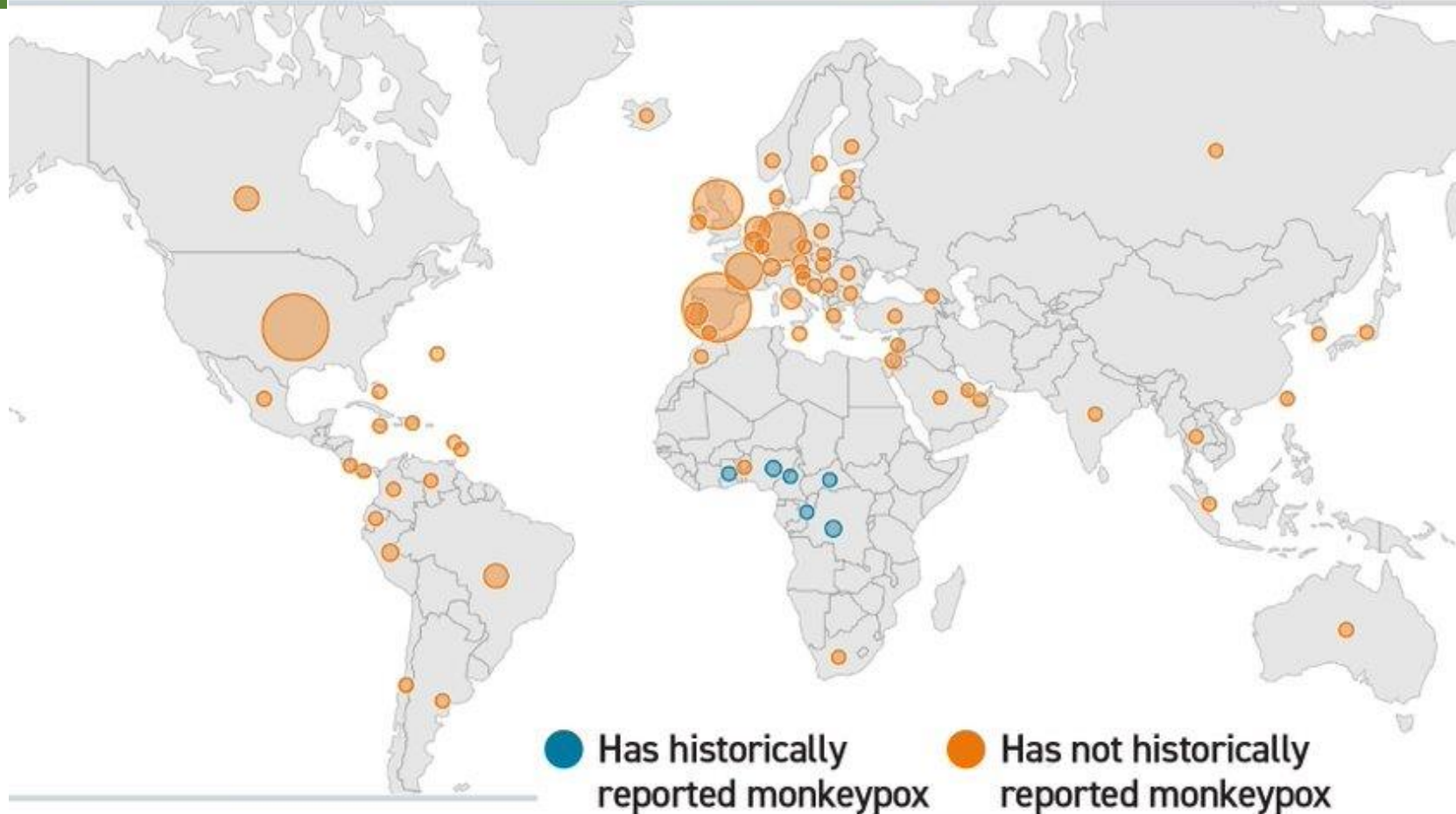
高雄榮民總醫院 感染科

2022年10月27日 11:10-12:00(線上會議)

演講大綱

- 猴痘的國際流行現況
- 猴痘的臨床表現、處置及預後
- 猴痘的感染管制措施
- 猴痘的藥物治療
- 猴痘的預防-疫苗

MONKEYPOX UPDATE



As of July 26, **19,188** confirmed or probable monkeypox cases have been identified in **76** countries, including **3,591** in the US.

Global Cases
19,188

US Cases
3,591

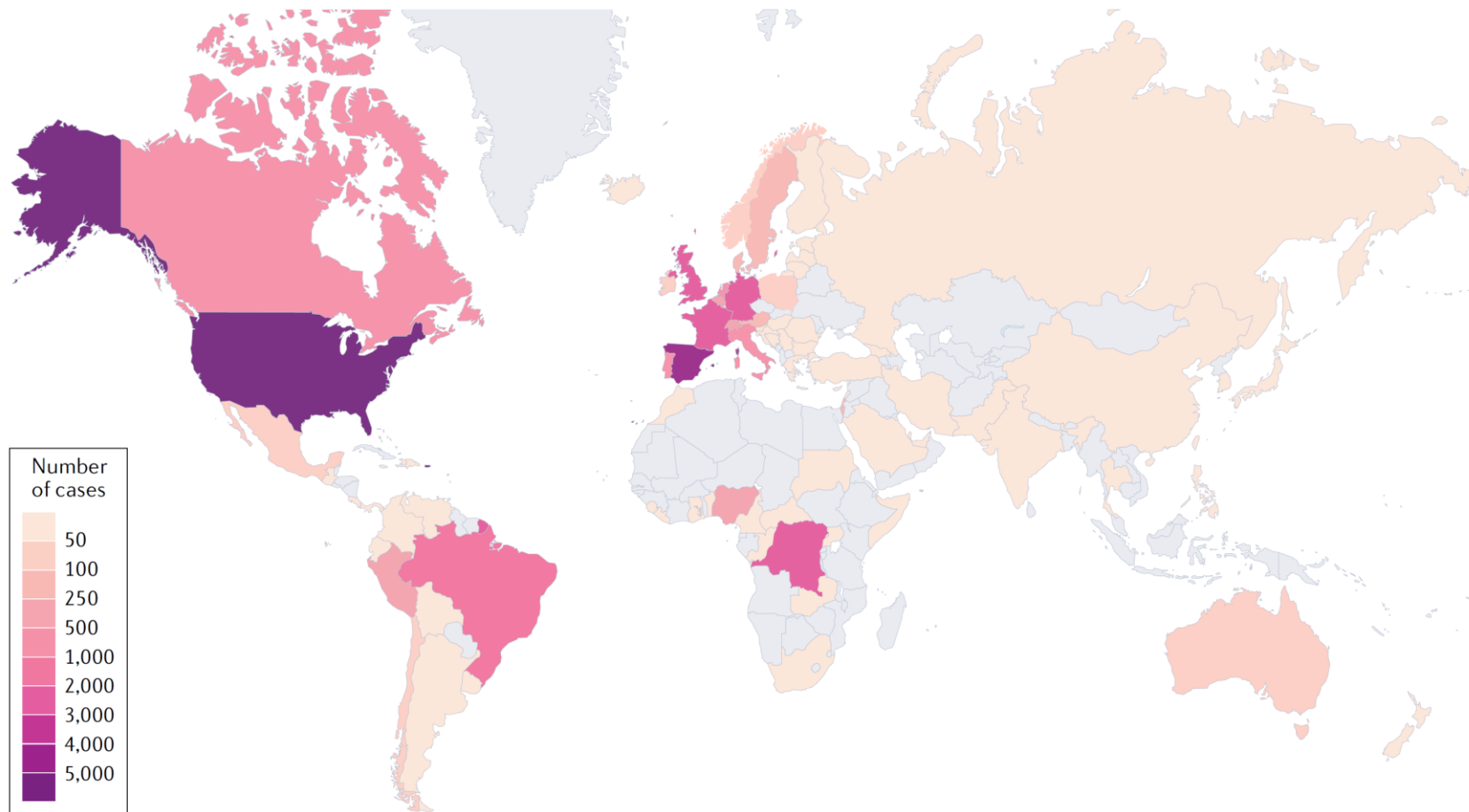
www.cdc.gov/Monkeypox

WHO declared **Public Health Emergency of International Concern (PHEIC)** on July 23, 2022.



CS332385 07/27/2022

Global monkeypox outbreak (May-Aug,2022)



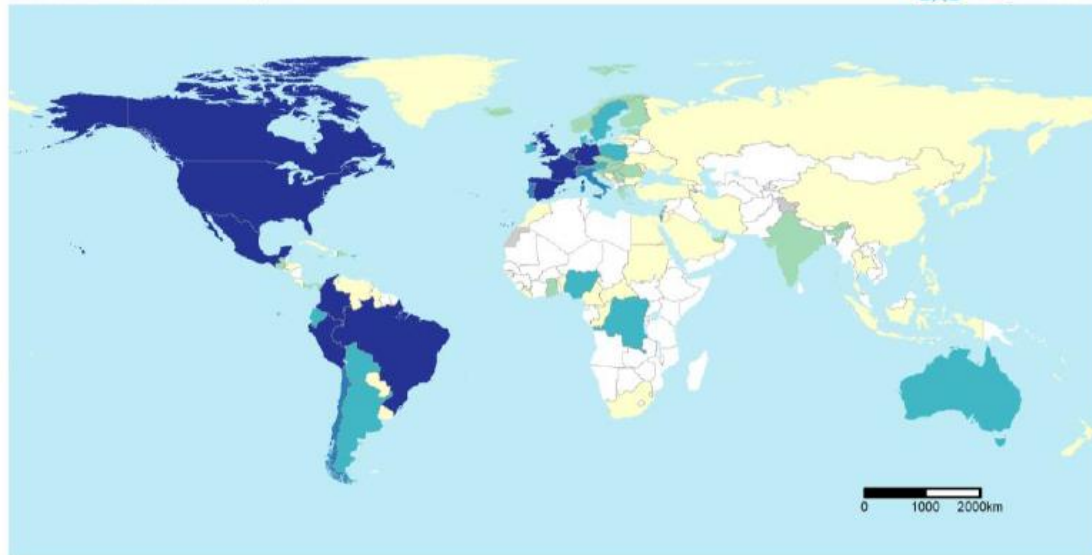
- July 23, 2022, WHO declared monkeypox outbreak a **Public Health Emergency of International Concern (PHEIC)**
- July, 2022: 16,000 cases and 5 deaths, 75 countries
- May-Aug, 2022 (< 4 months): over 48,000 cases, and 13 deaths.

Fig. 1 | **Geographical distribution of confirmed and suspected monkeypox cases during the outbreak between May and August 2022.** Data presented as of 5 August 2022 were obtained from [Global.health](https://www.global.health). Diagram generated with Datawrapper.

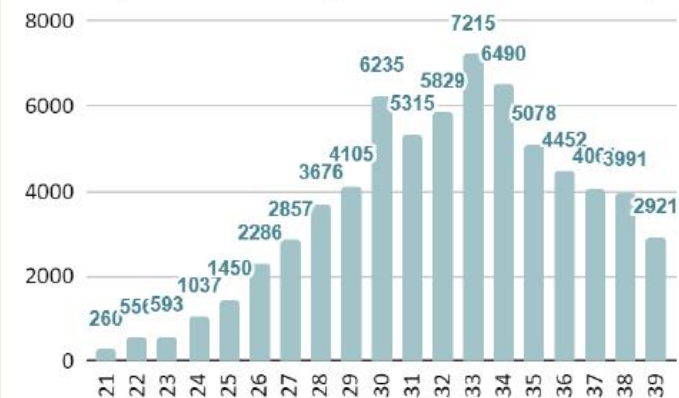
■國際疫情概況

- 全球截至2022年10月2日累計105國68,501例確診，其中美洲區域(28國42,833例)新增病例仍多惟略趨緩，歐洲區域(44國24,694例)已趨緩；美國報告25,850例占全球總數37.7%。
- 目前已知15國家累計30例死亡(奈及利亞7/迦納4/西班牙3/美國2/巴西2/中非共和國2/喀麥隆2/秘魯1/墨西哥1/比利時1/厄瓜多1/捷克1/印度1/蘇丹1 /古巴1)。

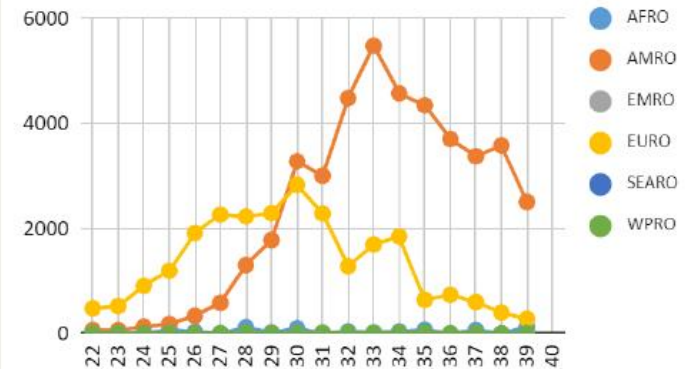
Confirmed cases of Monkeypox
from 1 Jan 2022, as of 28 Sep 22



Weekly New Cases (2022.5.23起統計迄今)



Weekly New Cases (by regions)



History of monkeypox outbreaks

1970-1979

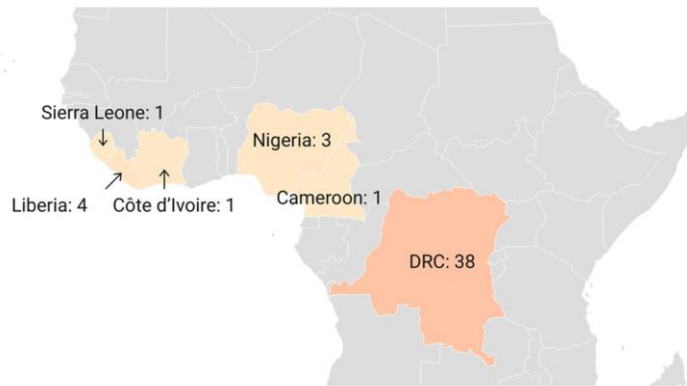


Fig 2. Number of confirmed, probable, and/or possible monkeypox cases between 1970-1979.

1980-1989

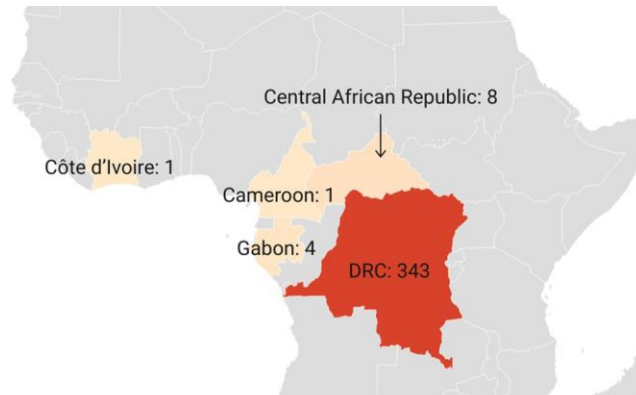


Fig 3. Number of confirmed, probable, and/or possible monkeypox cases between 1980-1989.

1990-1999



Fig 4. Number of confirmed, probable, and/or possible monkeypox cases between 1990-1999.

2000-2009



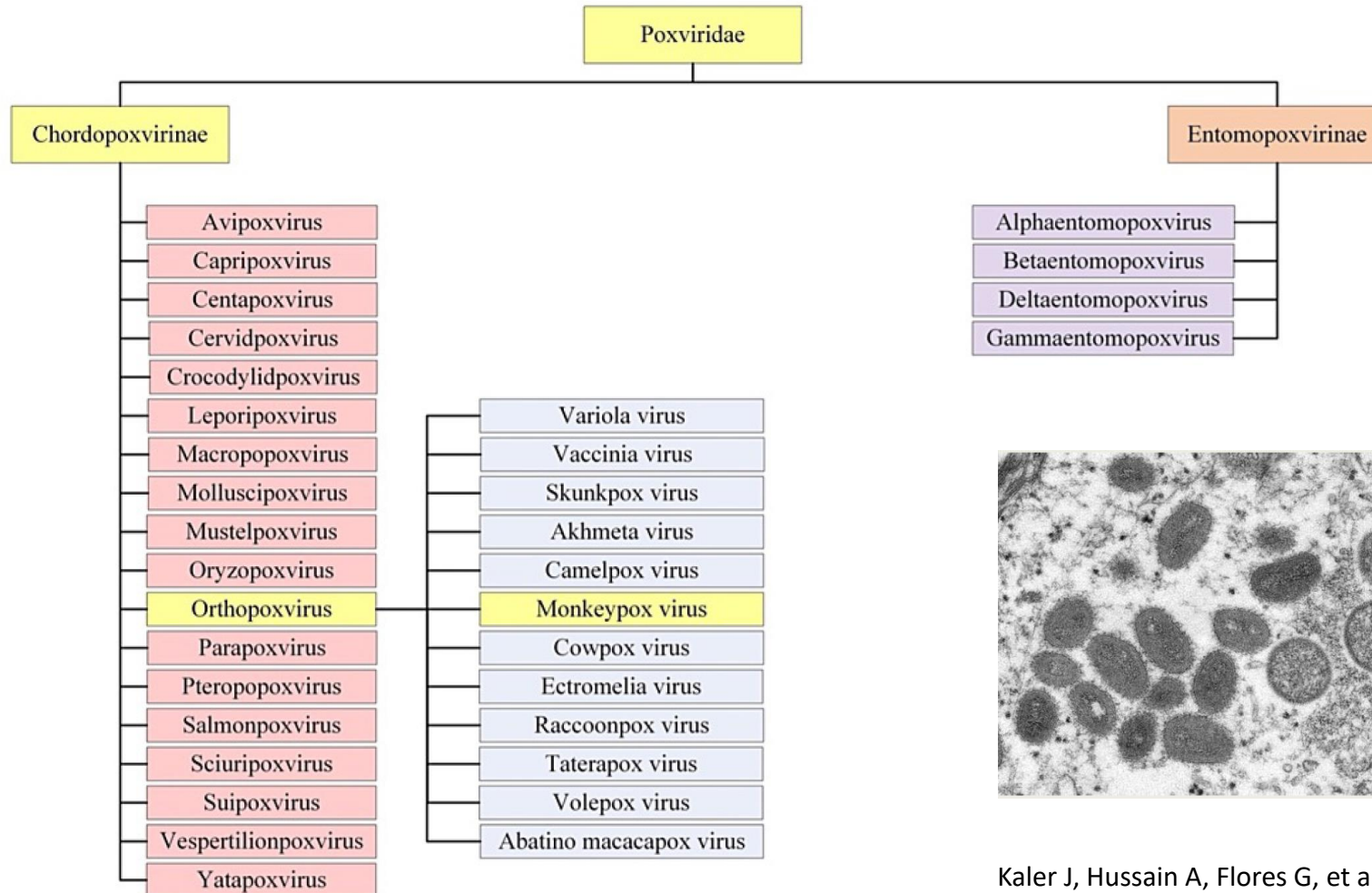
Fig 5. Number of confirmed, probable, and/or possible monkeypox cases between 2000-2009. [6,18,46,58,69] *

2010-2019



Fig 6. Number of confirmed, probable, and/or possible monkeypox cases between 2010-2019. [7,8,15,18,29,30,32,33,35,47-49,55-56]

Taxonomy and Classification of Monkeypox within *Poxviridae* Lineage



猴痘病毒屬痘病毒科(Poxviridae) ·
正痘病毒屬(Orthopoxvirus)。

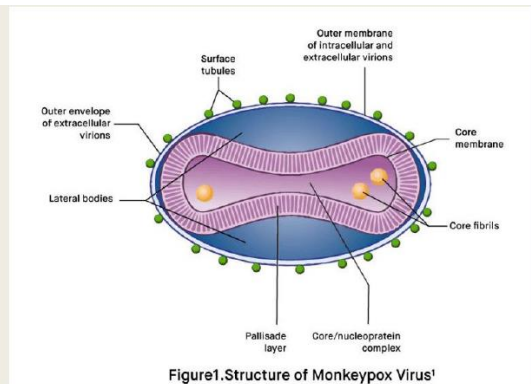
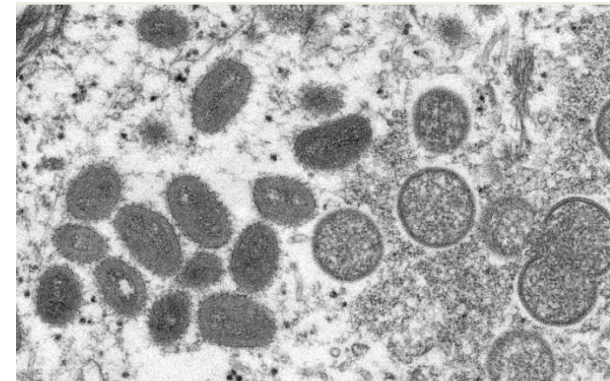


Figure1. Structure of Monkeypox Virus¹

Kaler J, Hussain A, Flores G, et al. Cureus 2022 July 03; 14(7): e26531.
USCDCpublichealthimagelibrary.Availableat:<https://phil.cdc.gov/details.aspx?pid=22664>
VitrosensBiotechnology.Availableat:<https://vitrosens.com/what-is-monkeypox-virus/>

Monkeypox cases by Virus Clade

Table 2. Number of Cases per Clade¹.

Decade	Central African Clade (N)	West African Clade (N)	Total Cases
1970–1979	38	9	47
1980–1989	355	1	356
1990–1999	520	0	520
2000–2009	92 confirmed 10,027 suspected ²	47	139 10,027
2009–2019	85 confirmed 18,788 suspected ²	195	280 18,788

¹ The five cases from Cameroon are not included in this table, as clade was not reported in any of the articles and WHO reported that Cameroon is the only country in which both clades have been detected [[12](#)].

² Suspected cases are from the Democratic Republic of the Congo, as number of suspected cases rather than confirmed cases were primarily reported. Suspected cases for other countries are not reported since testing of suspected cases was generally undertaken.

Case Fatality Rate of Monkeypox

Table 3. Pooled case fatality rate in confirmed, probable, and/or possible monkeypox cases.

Countries/Clade	Case Fatality Rate	95% CI ¹
All countries ²	78/892 = 8.7%	7.0%– 10.8%
Central African clade ³	68/640 = 10.6%	8.4%– 13.3%
West African clade ⁴	9/247 = 3.6%	1.7%– 6.8%
West African clade, African countries only	9/195 = 4.6%	2.1%– 8.6%

¹ Exact binomial method (Clopper-Pearson).

² The five cases from Cameroon are included in the “all countries” case fatality rate (CFR) calculation, but not in the calculation of CFR by clade, since WHO reported that Cameroon is the only country in which both clades have been detected [12]. The CFR without the inclusion of Cameroon is also 8.7% (77/887).

³ Central African clade includes the following countries: Central African Republic, Democratic Republic of the Congo, Republic of the Congo, and South Sudan.

⁴ West African clade includes the following countries: Côte d’Ivoire, Liberia, Nigeria, Sierra Leone, Israel, Singapore, United Kingdom, and United States.

Monekypox outbreak 2022

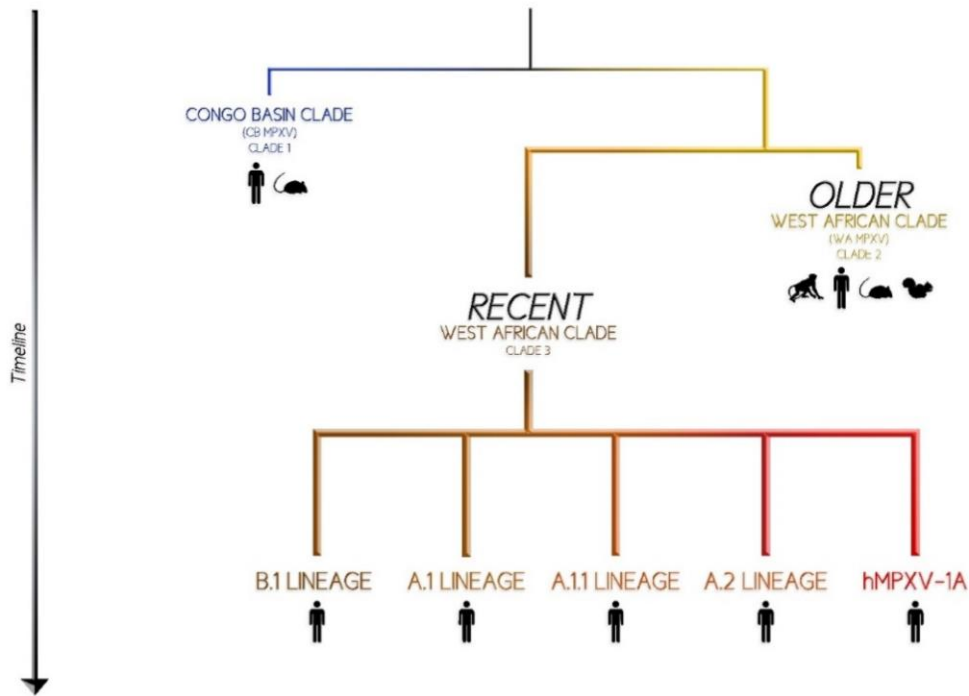


Figure 1. "Where does MPXV come from?" a graphical representation.

猴痘病毒可分為第一分支(I)病毒和第二分支(II)病毒，其中第二分支(II)病毒包括IIa和IIb兩子分支，後者即目前全球疫情主要流行株。

Tiecco G. Viruses **2022**; 14: 94.

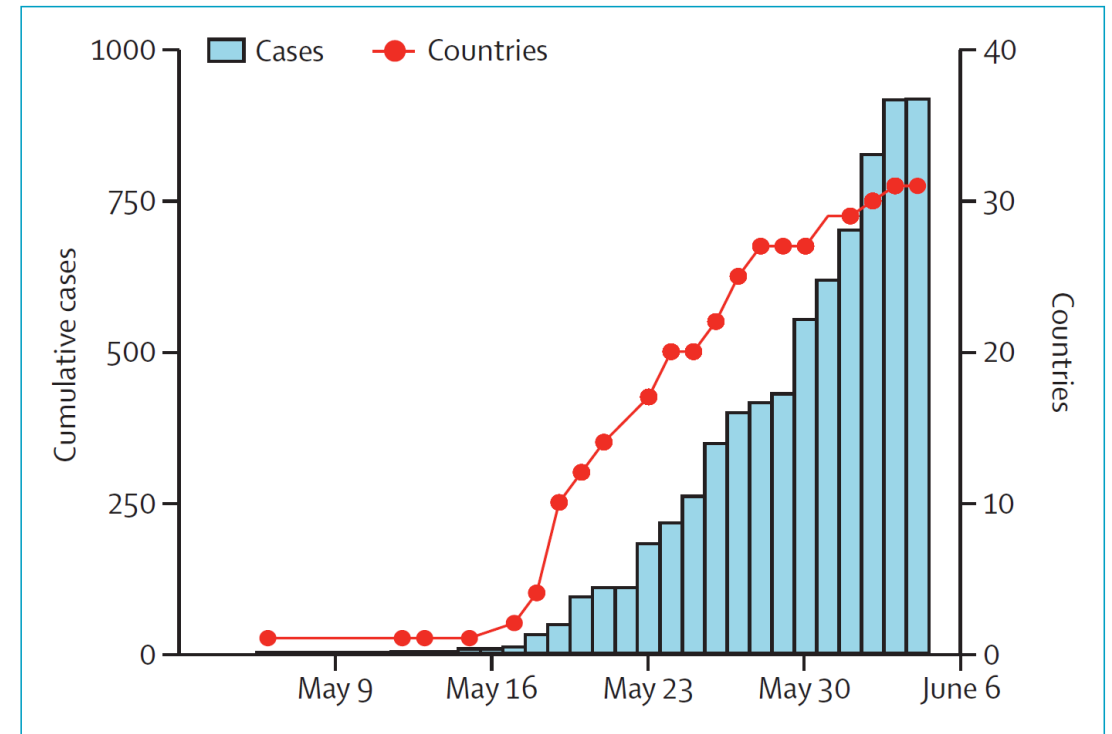


Figure: Rapid expansion of the 2022 monkeypox outbreak

Cumulative number of confirmed cases (by confirmation date) since the first reported case in the 2022 outbreak, and cumulative number of countries reporting confirmed cases.

Kraemer MUG. Lancet Infect Dis 2022 Jul;22(7):941-2.



Case Report

The first imported case of monkeypox in Taiwan

Shao-Tsung Huang ^a, Ying-Hsun Wu ^b, Hsi-Hsun Lin ^{c,d,e},
Jyh Yuan Yang ^f, Pei-Yu Hsieh ^f, Szu-Ju Chiang ^g,
Shang-Pin Wang ^g, Ya-Han Chan ^a, Li-Fen Lin ^h, Yueh-Ju Chen ⁱ,
Hung-Chin Tsai ^{e,h,i,j}, Yao-Shen Chen ^{e,i,j},
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Received 14 July 2022; received in revised form 21 August 2022; accepted 22 August 2022

KEYWORDS

Monkeypox;
Taiwan;
West African clade

Abstract The first imported case of monkeypox in Taiwan was diagnosed in an Asian man with HIV-1 infection and asymptomatic COVID-19, returning from Germany. Atypical presentations included asynchronous skin lesions, anogenital lesions and prominent inguinal lymphadenopathy. Whole genomic sequence alignment indicate that the Taiwan strain clustered together with human monkeypox virus West African clade B.1, currently circulating in Europe. Prompt diagnosis and infection control measures are crucial to mitigate the spread of monkeypox. Copyright © 2022, Formosan Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

中華民國111年6月23日衛授疾字第
1110100867號公告，新增「猴痘」為
第二類法定傳染病。



Atypical features

1. Presentation with only a few lesions
2. Genital, perineal and/or perianal areas
3. Different (asynchronous) stages of development
4. Appearance of lesions before the onset of fever and other constitutional symptoms

猴痘病例通報定義

■通報定義，具有下列任一條件：

- 符合臨床條件。
- 符合檢驗條件。

■臨床條件，需具下列條件：

- 皮膚病灶，如皮疹、斑疹、斑丘疹、水疱、膿疱等，且無法以其他已知病因解釋。
- 發燒($\geq 38^{\circ}\text{C}$)、畏寒/寒顫、出汗、頭痛、肌肉痛、背痛、關節痛、淋巴結腫大(如耳週、腋窩、頸部或腹股溝等處)等任一症狀。

■檢驗條件，具有下列任一條件：

- 臨床檢體(如病患發病期內皮膚水疱、血液、咽喉擦拭檢體和結痂檢體)分離並鑑定出猴痘病毒。
- 臨床檢體猴痘病毒分子生物學核酸檢測或定序為陽性。

■流行病學條件，發病前21日內，具有下列任一條件：

- 曾經與確定病例或出現症狀的極可能病例有密切接觸。
- 具有猴痘確定病例報告之國家旅遊史。
- 具有野生動物或非洲特有外來種動物(含屍體)暴露史。

■疾病分類

- 極可能病例：符合臨床及流病條件。
- 確定病例：符合檢驗條件。

The Taiwan monkeypox strain

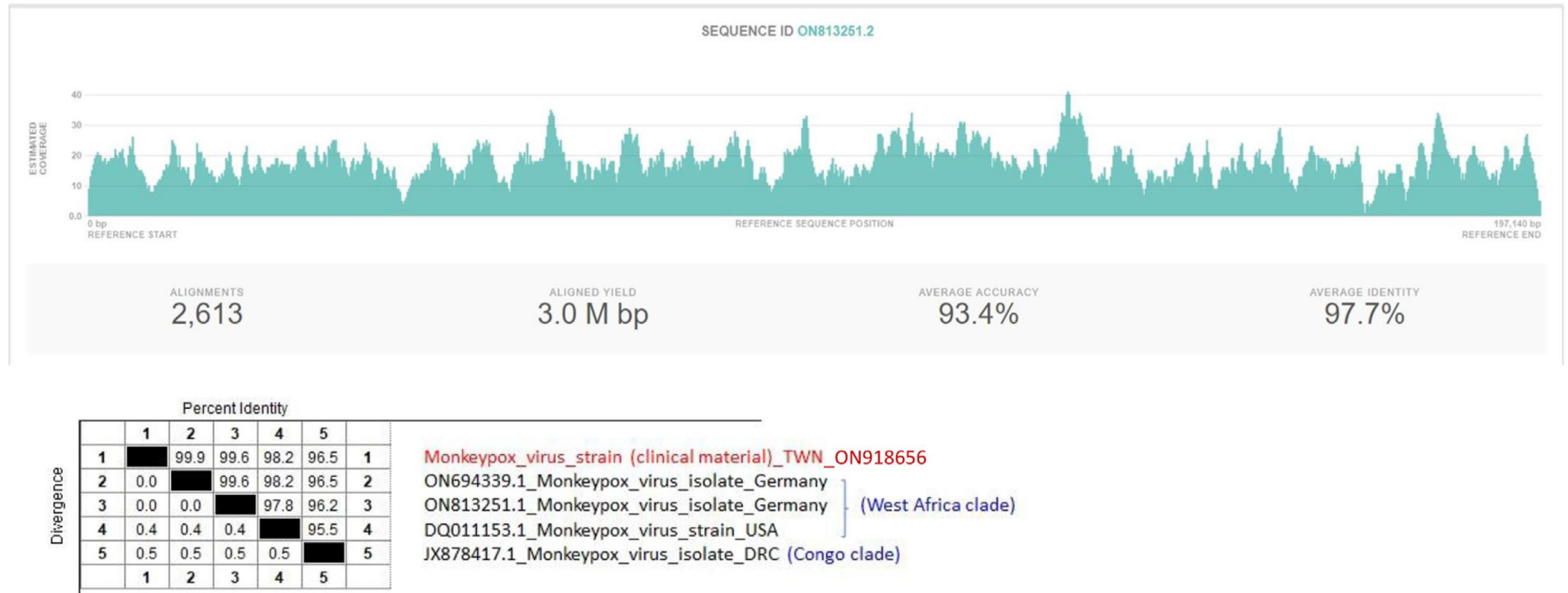
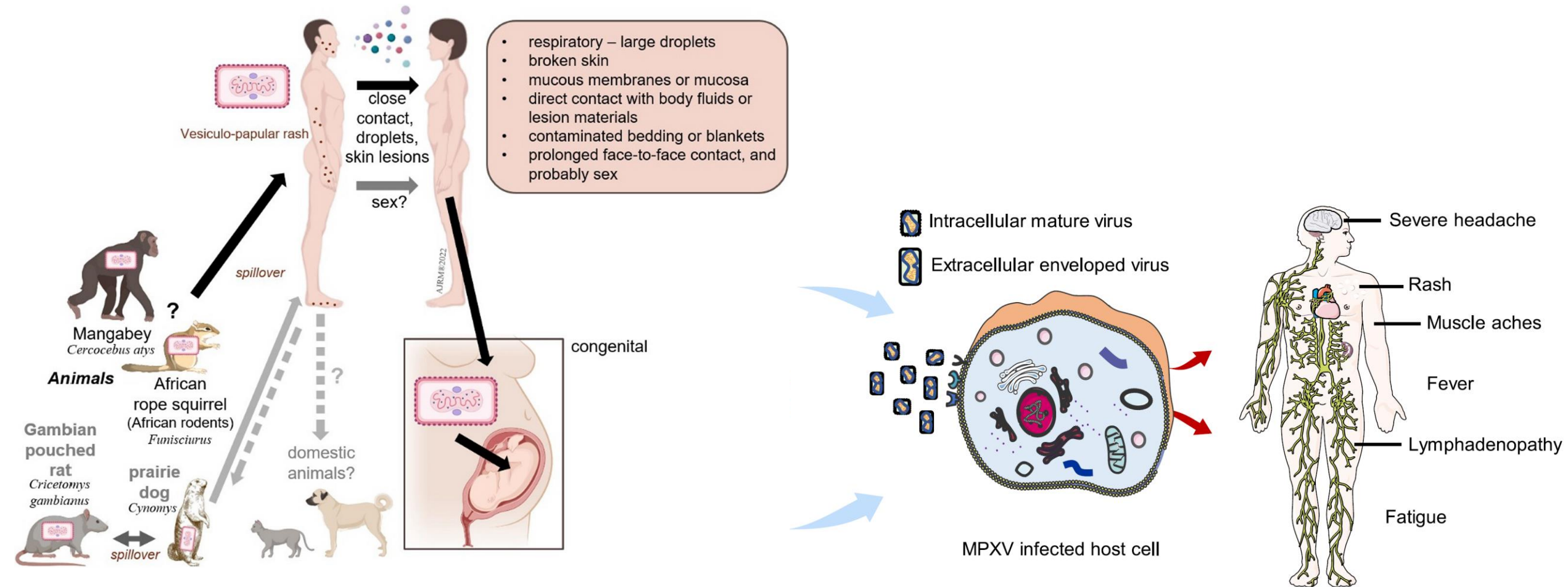


Figure 2 Direct whole genome sequencing on the vesicular fluid sample by Oxford Nanopore MinION apparatus obtained 197,315 base pairs sequence. The results indicate that viral sequence shares high similarity with the “West African” monkeypox virus clade, including the European (Germany) and American lineages, rather than the “Central African” or Congo clade. The Taiwan monkeypox strain (MPXV/human/Taiwan/110-231642/2022) was submitted to GISAID (accession no. ON918656.1).

Monkeypox Transmission



主要由齧齒動物和靈長類動物傳播給人，屬人畜共通傳染病。
(如繩松鼠、松鼠、剛比亞巨鼠、睡鼠和靈長類動物)

Gong Q et al. *Virologica Sinica* 2022; 37:477-482.
Farahat et al. *Ann Clin Microbiol Antimicrob* (2022) 21:26

傳播方式和潛伏期

• 傳播方式

(一)人畜共通傳染：

- 直接接觸感染動物的血液、體液、損傷的皮膚或黏膜而被感染。
- 食用受感染的動物肉類也是一種危險因子。

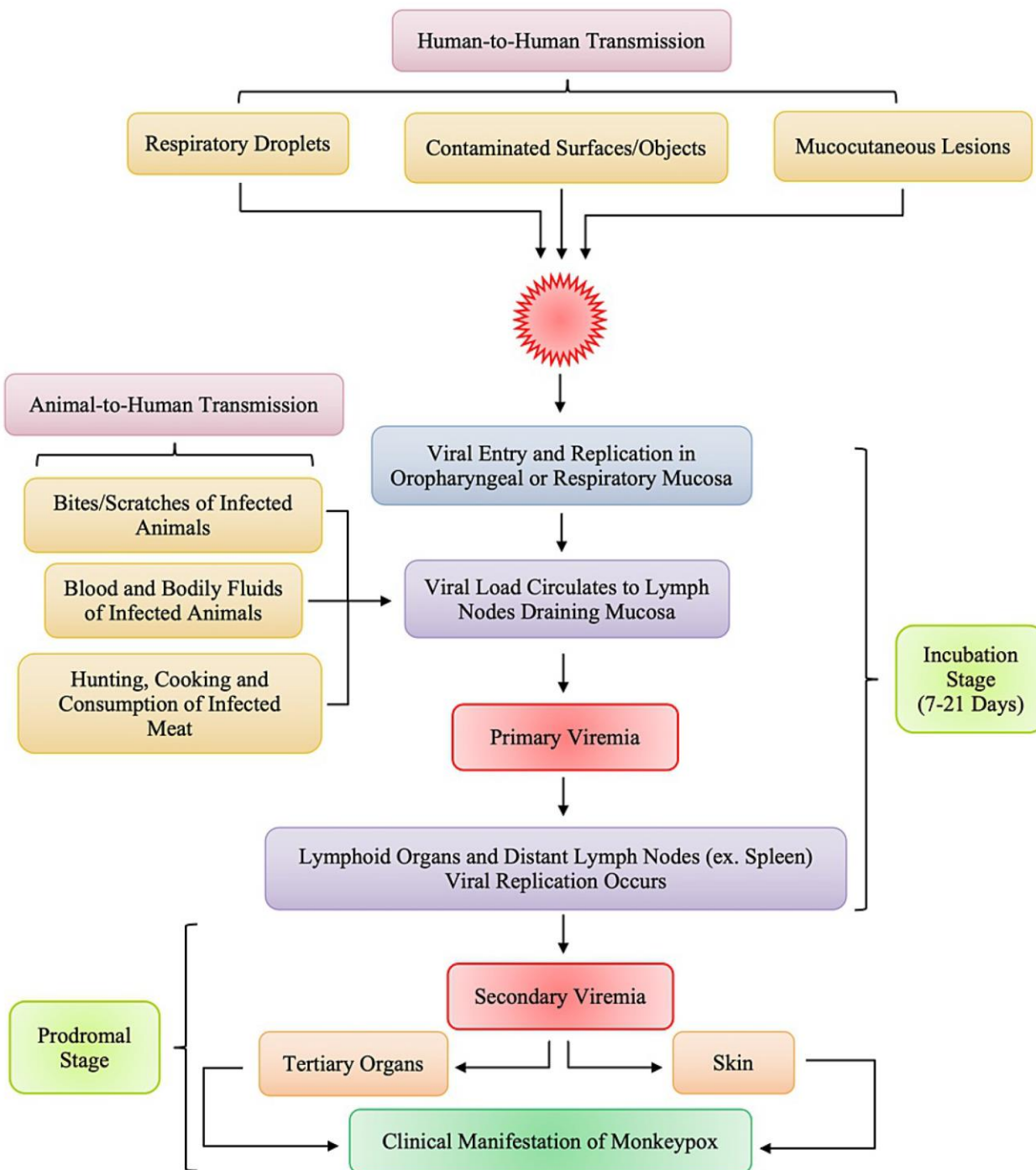
(二)人傳人：

- 接觸到感染者呼吸道分泌物、損傷的皮膚或黏膜或被污染物品而感染。
- 飛沫傳播需在長時間面對面接觸情境下較容易發生，因此醫護人員及同住家人都有較大的感染風險。
- 產婦若感染猴痘病毒，可經胎盤垂直傳染給胎兒，或於產程中因接觸而傳染。
- 儘管密切接觸已知是傳染危險因子，目前尚未確定猴痘是否透過性接觸傳染。近期歐洲疫情為首次MSM持續傳播案例(與西非或中非無已知流行病學連結)，評估病毒通過密切接觸人傳人之風險為高，但無密切接觸個體間傳播風險很低。

• 潛伏期

猴痘的潛伏期約為5-21天，通常為6-13天。

Kaler J, Hussain A, Flores G, et al. Cureus 2022 July 03; 14(7): e26531.
台灣疾病管制局網站 www.cdc.gov.tw



猴痘的臨床表現

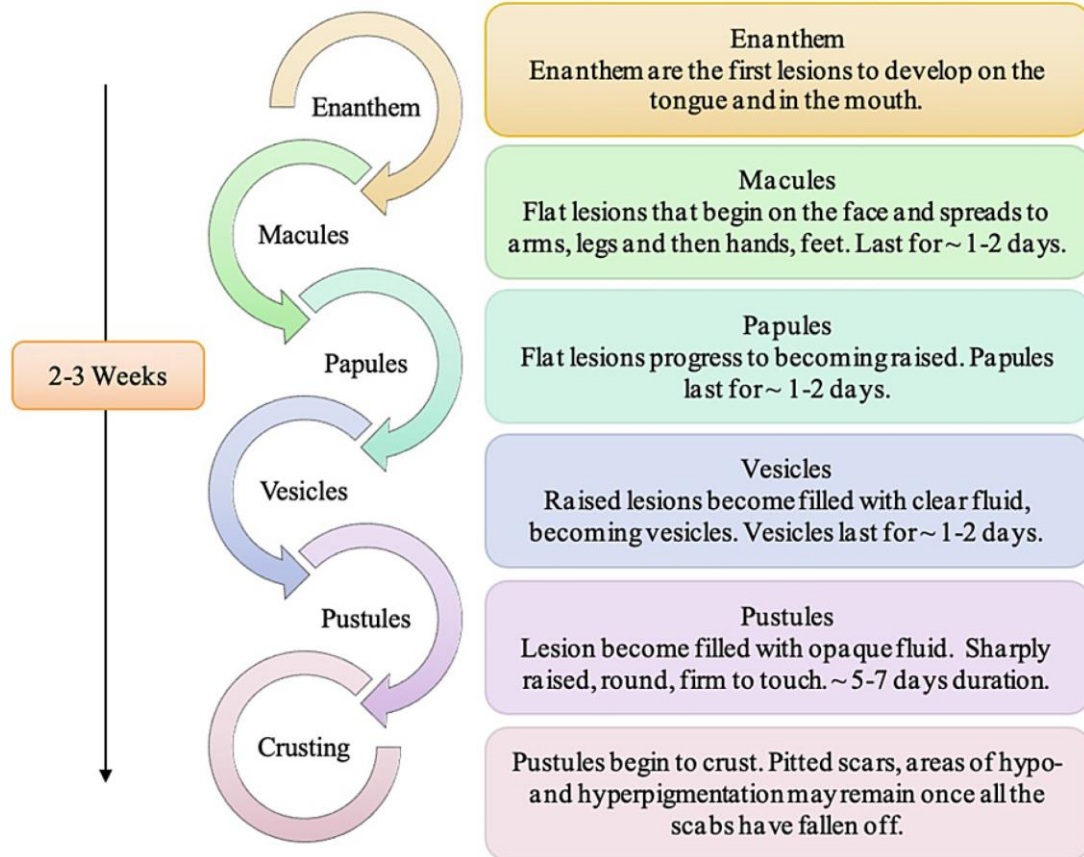
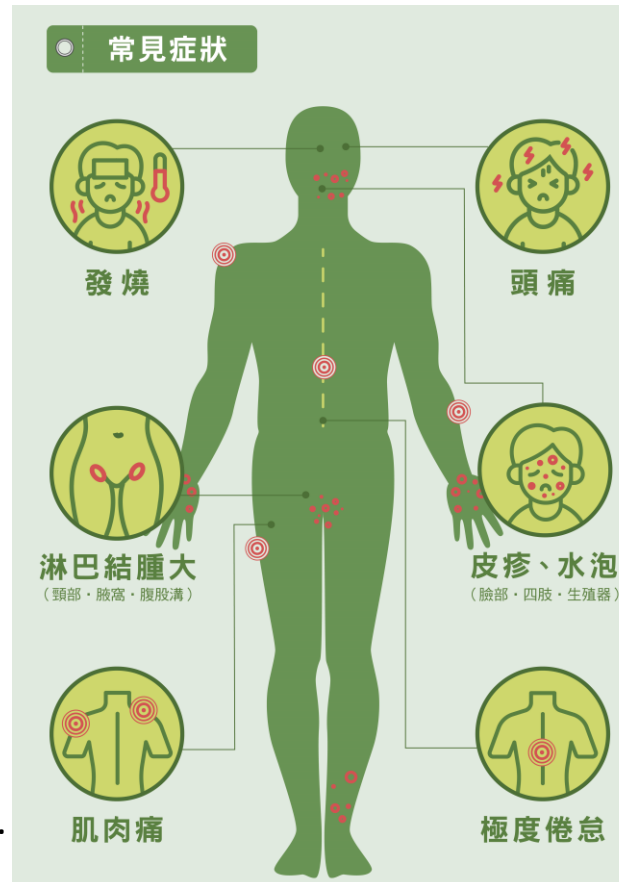
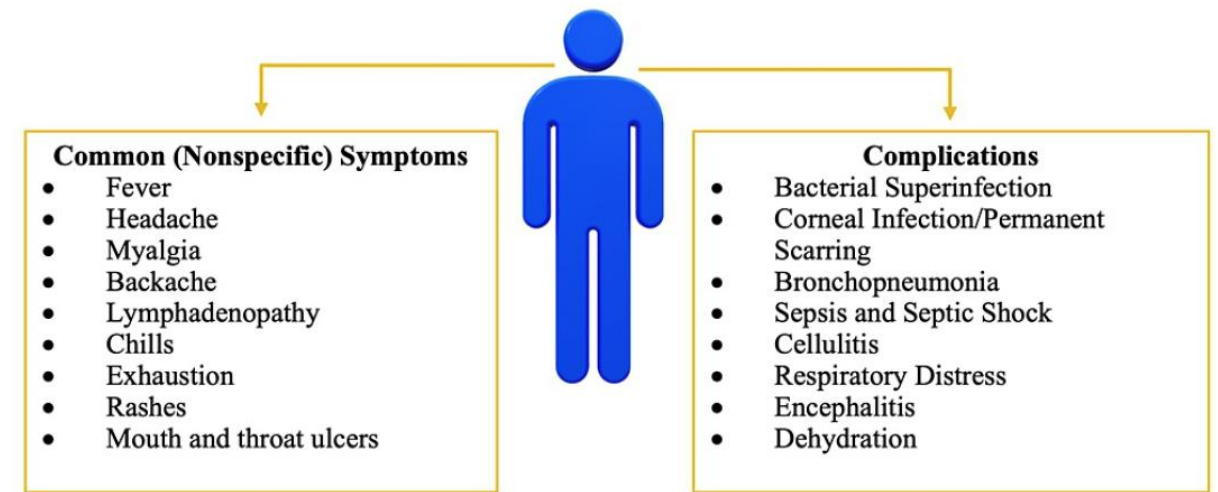


FIGURE 7: Stages of the Vesiculo-pustular Rash in Monkeypox Patients

Kaler J, Hussain A, Flores G, et al. Cureus 2022 July 03; 14(7): e26531.

台灣疾病管制局網站 www.cdc.gov.tw



- 症狀與天花相似，但病情較輕微。症狀包括發燒、畏寒/寒顫、出汗、頭痛、肌肉痛、淋巴腺腫大(如耳週、腋窩、頸部或腹股溝等處)、極度倦怠。
- 發燒一至三天後出現皮膚病灶，通常自臉部蔓延致身體其他部位，四肢比軀幹更常見。
- 皮膚病灶出現後會依斑疹(macules)、丘疹(papules)、水泡(vesicles)、膿疱(pustules)階段變化，最終結痂(crust)脫落，嚴重病患疹子數目可達數千。
- 症狀持續14至21天，致死率低於10%，大多數個案可於幾週內康復。
- 兒童及免疫功能低下者尤其容易重症，併發症包括繼發性細菌感染、肺炎、敗血症等。

Monkeypox rash

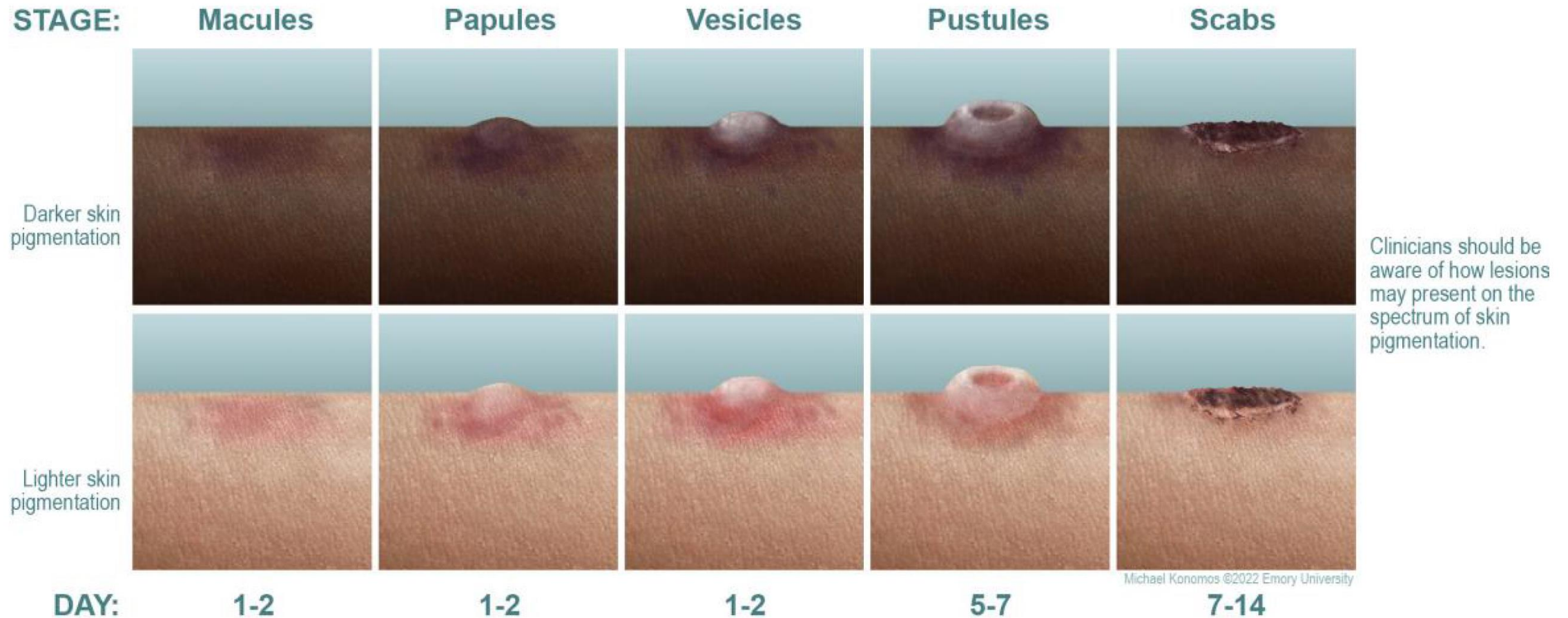


Figure 3. Stages of skin presentation and progression of monkeypox rash.

Titanji BK. Open Forum Infect Dis . 2022 Jun 23;9(7):ofac310.

Monkeypox 2022: Clinical manifestations

- Reported 528 infections diagnosed between April 27 and June 24, 2022 in 16 countries.
- Overall, 98% of the persons with infection were gay or bisexual men, 75% were White, and 41% had human immunodeficiency virus infection;
- Median age was 38 years.
- Transmission was suspected to have occurred through sexual activity in 95% of the persons with infection.
- 95% of the persons presented with a rash (with 64% having ≤ 10 lesions),
- 73% had anogenital lesions, and 41% had mucosal lesions (with 54 a single genital lesion).
- Common systemic features preceding the rash included fever (62%), lethargy (41%), myalgia (31%), and headache (27%); lymphadenopathy was also common (reported in 56%).
- Concomitant sexually transmitted infections were reported in 109 of 377 persons (29%) who were tested.
- Among the 23 persons with a clear exposure history, the median incubation period was 7 days (range, 3 to 20).

猴痘的臨床表現

Characteristic	All Persons (N = 528)
Median age (range) — yr	38 (18–68)
Sex or gender — no. (%)	
Male	527 (>99)
Female	0
Trans or nonbinary	1 (<1)
Sexual orientation — no. (%) [†]	
Heterosexual	9 (2)
Homosexual	509 (96)
Bisexual	10 (2)
Race or ethnic group — no. (%) [‡]	
White	398 (75)
Black	25 (5)
Mixed race	19 (4)
Latinx	66 (12)
Other or unknown	20 (4)
HIV positive — no. (%)	218 (41)
HIV negative or status unknown — no. (%)	310 (59)
Use of preexposure prophylaxis against HIV — no./total no. (%)	176/310 (57)
Foreign travel in month before diagnosis — no. (%) [‡]	147 (28)
Continent of travel — no./total no. (%)	
Europe	132/147 (90)
North America	9/147 (6)
Australasia	0/147
Africa and Middle East	2/147 (1)
Central and South America	2/147 (1)
Not stated	2/147 (1)

Characteristic	All Persons (N = 528)
Known to have undergone STI screening — no. (%)	377 (71)
Microbiologically confirmed concomitant STI present — no./total no. screened (%)	109/377 (29)
Gonorrhea	32/377 (8)
Chlamydia	20/377 (5)
Syphilis	33/377 (9)
Herpes simplex virus infection	3/377 (1)
Lymphogranuloma venereum	2/377 (1)
Chlamydia and gonorrhea	5/377 (1)
Other or not stated	14/377 (4)
HIV test taken — no./total no. with previously unknown or negative HIV status (%)	122/310 (39)
New HIV infection diagnosis — no./total no. (%)	3/122 (2)
Sexual history not known — no./total no. (%)	122/528 (23)
Median no. of sex partners in previous 3 months (IQR)	5 (3–15)
“Chemsex” reported in the previous month — no. (%)	106 (20)
Reported attendance at a sex-on-site event in the previous month — no. (%)	169 (32)

猴痘的臨床表現

Table 3. Diagnosis and Clinical Characteristics of Monkeypox in the Case Series.*

Characteristic	All Persons (N = 528)
Suspected route of transmission — no. (%)	
Sexual close contact	504 (95)
Nonsexual close contact	4 (1)
Other or unknown	17 (3)
Household contact	3 (1)
Contact with person known to have monkeypox — no. (%)	135 (26)
Reported clinical features — no. (%)	
Rash or skin lesions	500 (95)
Fever	330 (62)
Lymphadenopathy	295 (56)
Pharyngitis	113 (21)
Headache	145 (27)
Lethargy or exhaustion	216 (41)
Myalgia	165 (31)
Low mood	54 (10)
Proctitis or anorectal pain	75 (14)
Site of positive monkeypox viral PCR — no. (%)†	
Skin or anogenital lesion	512 (97)
Nose or throat swab	138 (26)
Blood	35 (7)
Urine	14 (3)
Semen	29 (5)
Site of skin lesions — no. (%)‡	

Table 3. Diagnosis and Clinical Characteristics of Monkeypox in the Case Series.*

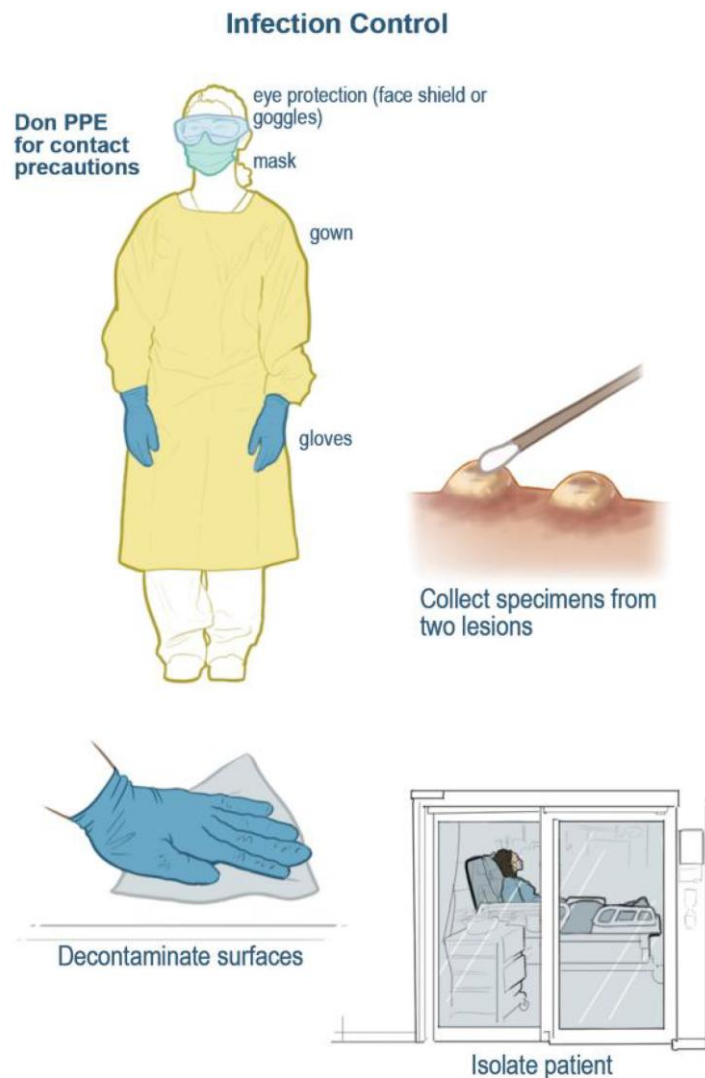
Characteristic	All Persons (N = 528)
Site of skin lesions — no. (%)‡	
Anogenital area	383 (73)
Face	134 (25)
Trunk or limbs	292 (55)
Palms or soles	51 (10)
Description of rash — no./total no. with rash reported (%)	
Vesiculopustular	291/500 (58)
Macular	19/500 (4)
Single ulcer	54/500 (11)
Multiple ulcers	95/500 (19)
Other	41/500 (8)

猴痘疫情

表一、2022 年之前和 2022 年猴痘疫情比較

	2022 年之前的猴痘	2022 年的猴痘
主要流行區域	中非、西非	歐洲、美洲
病毒株	Clade I, Clade II	Clade IIb 的變異株
主要感染族群	居住在熱帶雨林或附近的人	18–50 歲的男男性行為者和雙性戀者
傳染途徑	動物傳人，少數人傳人	人傳人
死亡率	0–11%	< 0.1%
臨床症狀	- 前驅期（1–3 天）：非特異性症狀，如發燒、淋巴結腫大、肌肉痠痛等。 - 皮疹期（2–4 周）：主要在臉部和四肢，通常同步演變（斑疹→丘疹→水疱→膿疱→結痂）。	- 前驅期：可能無症狀或非常輕微。 - 皮疹期（2–4 周）：可能在前驅症狀出現之前就有皮疹，數量較少，出現在生殖器或肛門周圍，同一時間會出現不同時期的皮疹。

猴痘的感染管制措施



醫院照護疑似或確定病例時：

- 標準防護措施
- 接觸傳染防護措施
- 飛沫傳染防護措施。

採檢/醫療照護人員建議：

- 穿戴手套、隔離衣、醫用口罩、護目裝備(護目鏡或全面罩)。
- 隔離病人
- 消毒環境

醫療機構感染管制建議

項目	說明
整體性建議	醫療機構人員照護疑似或確診猴痘病人，建議依循： • 標準防護措施。 • 飛沫傳染防護措施。 • 接觸傳染防護措施。
病人分流機制	• 第一線工作人員應先口頭詢問相關主訴及TOCC等資料。 • 詢問時應配戴醫用/外科口罩。 • 若發現符合通報定義之疑似個案，立即分流至預先規劃好之單獨診療室等候評估，使用時應維持房門關閉；並依相關規定通報。

醫療機構感染管制建議

項目	說明
病人收治	• 需要住院的病人應優先安排入住具獨立衛浴之單人病室，房門應維持關閉。 • 在顧及病人隱私的情形下，於病室門口標示病人需要採取飛沫及接觸隔離防護措施。 • 病室內避免執行會引起環境中灰塵或病灶脫落結痂揚起的活動，例如使用會擾動空氣氣流的電風扇、掃地、使用吸塵器等。 • 感染管制措施應執行至患者病灶結痂脫落且形成新的皮膚層為止，重症患者或免疫力低下者其病毒殘存時間可能延長，可視臨床醫師判斷延後。
轉運病人至其他部門/機構	• 儘量避免轉送病人到其他部門/醫療機構。 • 若轉送是必須的，應提前告知轉入部門/機構所需採取之感染管制措施及適當個人防護裝備。 • 轉運過程中，若病人狀況允許，應戴上密合度良好的醫用口罩，且依病灶範圍以布單或隔離衣等適當覆蓋。

醫療機構感染管制建議

項目	說明
工作人員健康監測	• 曾在無適當防護下接觸確診病人之皮膚、黏膜、呼吸道分泌物、體液或污染物品的醫療照護工作人員。 • 每日進行症狀監測（包含發燒、頭痛、肌肉疼痛、淋巴結腫大、疲倦或出現皮疹等症狀）。 • 監測期至最後暴露日起21天為止，並應避免照顧免疫力低下之患者。 • 如出現相關症狀，應立即依機構內流程主動通報單位主管、感染管制人員或職業安全人員。
環境清潔消毒	• 每日最少應進行1次環境清潔工作。 • 消毒劑應依照廠商建議之稀釋方法、接觸時間與處理方式；或使用當天泡製的1：50（1000ppm）漂白水稀釋液。 • 建議採取濕式清潔消毒方式，避免使用會重新揚起灰塵之清潔方式（如掃地、吸塵器等）。

醫療機構感染管制建議

項目	說明
織品/布單與被服處理	- 處理使用過的被服及布單織品應盡量避免抖動，以防止污染空氣、環境表面和人，並儘速送洗。 - 在病室內將使用過的布單與被服裝入袋中，不可以在未經包裝的情形下直接帶出病室。 - 使用過的布單與被服應依處理具傳染性織品的流程裝袋，並視為具高感染風險進行清潔消毒。 ✓ 清洗方式 1. 高溫清洗：水溫$\geq 71^{\circ}\text{C}$至少清洗 25 分鐘； 2. 低溫清洗：水溫$\leq 70^{\circ}\text{C}$併用適當的洗劑於合適的濃度下清洗。 ✓ 添加濃度 50-150ppm 漂白水，或以烘乾整燙過程的高溫等方式，都有助於增加被服及布單織品的清洗消毒效益。
屍體處理	- 工作人員接觸確診猴痘患者之屍體，應穿戴適當個人防護裝備，包括N95口罩、防水隔離衣、手套及護目裝備等。 - 應使用完全密封且非滲透性的屍袋，慎防體液滲漏。屍袋表面以1：10的稀釋漂白水(5,000ppm)抹拭，保持屍袋外側清潔，並儘速送至太平間。 - 太平間的工作人員和禮儀師必須被告知有生物危害風險。

醫療機構感染管制建議

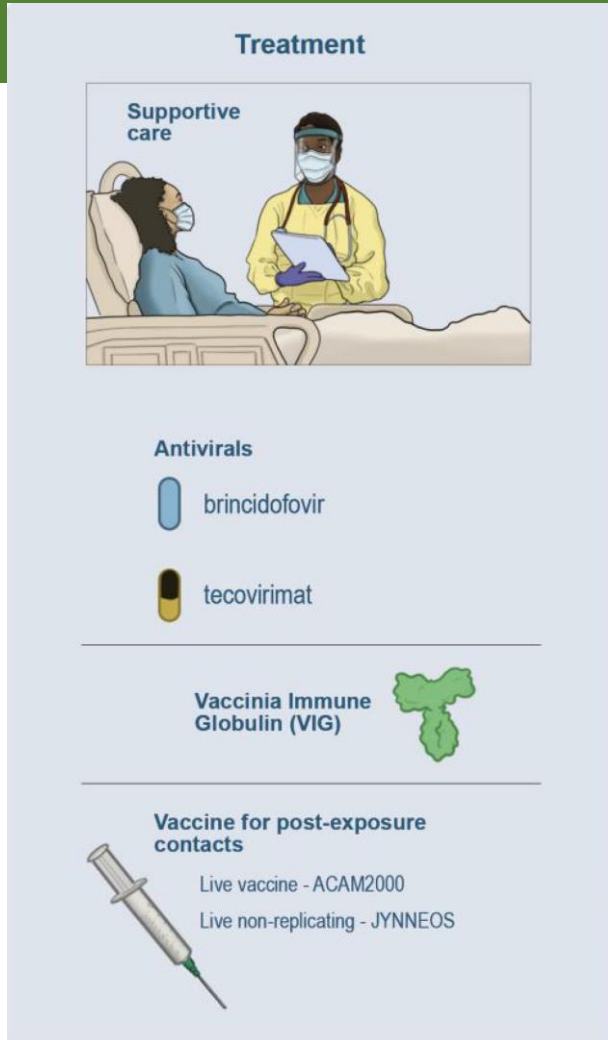
■ 個人防護裝備建議

場所	處置項目	呼吸防護		手套	隔離衣		護目裝備 (全面罩)	髮帽
		醫用/ 外科口 罩	N95或相 當等級(含) 以上口罩		一般 隔離衣	防水 隔離衣		
公共區域	入口服務人員、掛號、 批價、傳送等	V						
	詢問相關主訴及TOCC	V						
病人轉送	病室到院內其他單位		V	V	V			
分流看診區 或收治病室 (獨立檢查室 或單人病室)	一般性接觸病人之醫療 照護行為(如量體溫、血 壓、照X光)		V	V	V ^{註1}			
	執行發藥、更換輸液等 未直接接觸病人之醫療 照護行為		V	V	V ^{註1}			
	接觸病人血液、體液、 排泄物等風險之醫療照 護行為		V	V		V	V	
	呼吸道檢體(如咽喉拭 子)、傷口採檢		V	V		V	V	V
	執行可能產生飛沫微粒 (aerosol)的醫療處置		V	V		V	V	V
	環境清潔消毒 ^{註2}		V	V		V	V	V

註1：診治重症個案除依上表之建議外，可視病人狀況及所需執行之醫療處置等情形，調整個人防護裝備。

註2：清潔人員應著可清洗之防水鞋具，避免使用拋棄式鞋套。

猴痘的處置：支持性療法



Symptom/Complication	Supportive Treatment
Respiratory distress/Bronchopneumonia	Oral/intravenous antibiotics for prophylaxis, nebulizer treatments, non-invasive ventilation (ex. CPAP)
Sepsis	Oral/intravenous antibiotics, supplemental oxygen, corticosteroids, insulin
Gastrointestinal/mouth and throat ulcers	Oral/intravenous antiemetic and antidiarrheal medications, oral/intravenous rehydration
Fever	Antipyretic medications, external cooling
Superinfection skin	Oral/intravenous antibiotics, incision, and drainage, advanced wound management (ex. negative pressure wound therapy)
Inflammation/Lymphadenopathy	Oral/intravenous anti-inflammatory/analgesic medications
Corneal infection	Ophthalmic antibiotics/antivirals and corticosteroids
Skin scarring/Cellulitis/Skin lesions	Application of moist occlusive dressings to promote re-epithelization

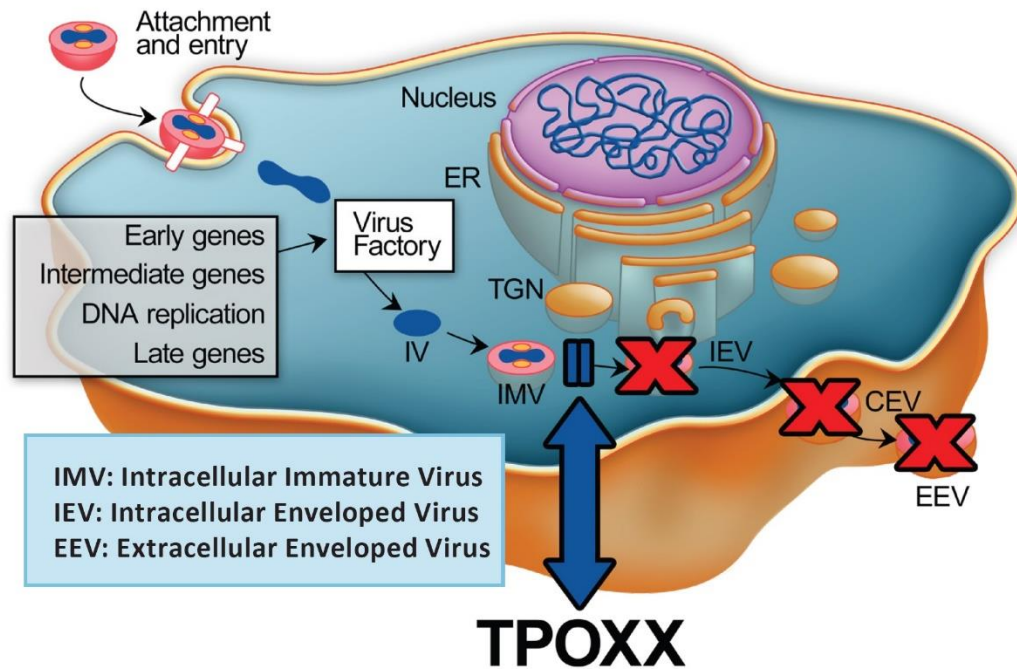
TABLE 1: Symptoms/Complications and Potential Supportive Treatment

Kaler J, Hussain A, Flores G, et al. Cureus 2022 July; 14(7): e26531. 台灣疾病管制局網站 www.cdc.gov.tw

Titanji BK. Open Forum Infect Dis . 2022 Jun23;9(7):ofac310.

大多數猴痘病患的病程為自限性(self-limiting)，因此以輸液治療與維持營養等支持性療法為主，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。

猴痘口服抗病毒藥物: Tecovirimat (TPOXX)



TPOXX: Inhibits the viral envelope formation and spread of the virus

Hruby D.E., Byrd C.M. 2006. Less is More: Poxvirus Proteolysis. Microbe. 1(2):70-5.

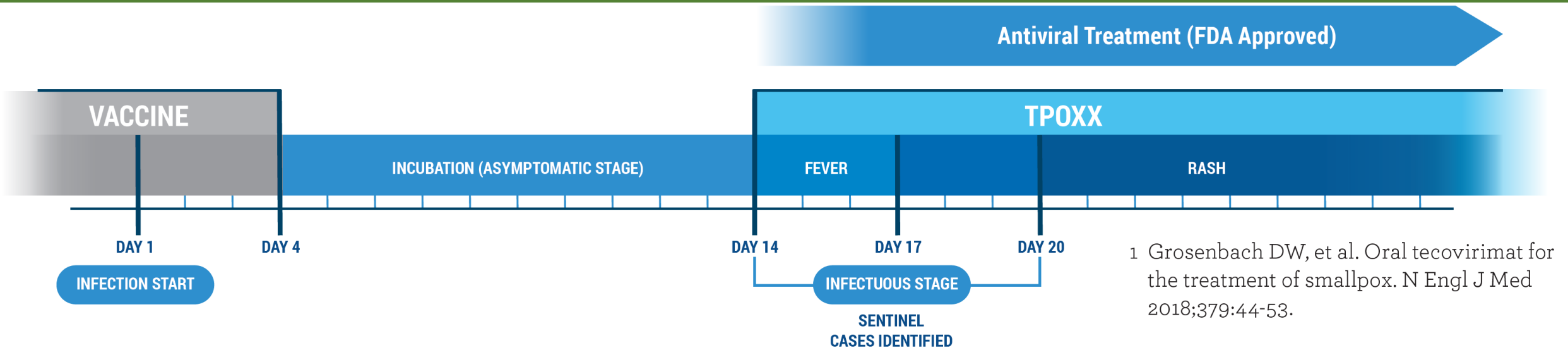
- Tecovirimat inhibits systemic spread of variola virus (the virus that causes smallpox) by **preventing the formation of a secondary viral envelope.**
- In the absence of this envelope, viral particles remain inside the cell in which they are produced and cannot spread to and infect other cells

作用機制為干擾正痘病毒屬表面蛋白質(VP37)，以抑制病毒正常繁殖、減慢感染傳播，有口服膠囊與靜脈注射兩種劑型，適用於成人及體重至少13公斤以上的孩童，成人劑量為600mg每12小時一次，共使用14天。

<https://www.siga.com/wp-content/themes/sigahba/TPOXX-Fact-Sheet.pdf>

Grosenbach DW, et al. Oral tecovirimat for the treatment of smallpox. N Engl J Med 2018;379:44-53.

Tecovirimat (TPOXX): Efficacy and Safety studies



1 Grosenbach DW, et al. Oral tecovirimat for the treatment of smallpox. N Engl J Med 2018;379:44-53.

- A placebo-controlled human pharmacokinetic and safety study was performed in 449 adult volunteers, of which 359 received TPOXX.
- Human dosing at 600 mg twice daily for 14 days was selected for testing, and provided exposures in excess of animal exposures.
- No concerning adverse events was observed, 6 subjects (2%) had their treatment discontinued due to adverse reactions.
- A dedicated drug-drug interaction study determined that drug interactions exist for co-administration of repaglinide and midazolam.
- Results of the animal studies and the pivotal human safety study were published in The New England Journal of Medicine in July 2018

<https://www.siga.com/wp-content/themes/sigahba/TPOXX-Fact-Sheet.pdf>

Grosenbach DW, et al. Oral tecovirimat for the treatment of smallpox. N Engl J Med 2018;379:44-53.

猴痘口服抗病毒藥物TPOXX® (tecovirimat) 使用方案

(111年9月7日版)

使用對象：符合疾病管制署公布猴痘確定病例定義且具下列情形之一，並經醫師評估及病患或代理人同意使用者。

- (一) 猴痘**重症患者**，臨床表現包括出血性疾病、融合型皮膚病灶、敗血症、腦炎等。
- (二) 其他經疾病管制署同意使用之特殊情形。

藥物說明

- **歐洲藥品管理局(EMA)**已核准使用於治療正痘病毒屬之天花、猴痘及牛痘，同時也可用於治療因接種天花疫苗而產生的併發症；
- **國食品藥物管理局(FDA)**核准使用於治療天花
- **國疾病管制與預防中心(CDC)**因應猴痘疫情，專案核可使用於猴痘治療重症或有重症危險因子之高風險患者已降低死亡率。
- **台灣：**目前尚未取得我國藥物許可證，以專案進口方式採購儲備(111.07.13.)。
- 適用對象為成人或體重13公斤以上之兒童；
- 本藥物無特殊禁忌症，惟與repaglinide共同使用可能導致低血糖，

Tecovirimat dose

表 1：成人與體重至少 40 公斤之兒童病人建議劑量

體重	劑量	膠囊數量
40 公斤至未滿 120 公斤	每日兩次 600 mg	每日兩次 3 顆膠囊
120 公斤以上	每日三次 600 mg	每日三次 3 顆膠囊

表 2：兒童與成人建議劑量和備藥說明

體重	劑量	膠囊數量	藥物-食物準備
13 公斤至未滿 25 公斤	每日兩次 200 mg	每日兩次 1 顆膠囊之內容物	將 1 顆 TPOXX 膠囊內容物與 30 mL 液體或軟質食物混合。 服用完所有混合物。
25 公斤至未滿 40 公斤	每日兩次 400 mg	每日兩次 2 顆膠囊之內容物	將 2 顆 TPOXX 膠囊內容物與 30 mL 液體或軟質食物混合。 服用完所有混合物。
40 公斤至未滿 120 公斤	每日兩次 600 mg	每日兩次 3 顆膠囊之內容物	將 3 顆 TPOXX 膠囊內容物與 30 mL 液體或軟質食物混合。 服用完所有混合物。
120 公斤以上	每日三次 600 mg	每日三次 3 顆膠囊之內容物	將 3 顆 TPOXX 膠囊內容物與 30 mL 液體或軟質食物混合。 服用完所有混合物。

小心地打開下POXX膠囊,將所有內容物與30mL液體(例如:牛奶、巧克力牛奶)或軟質食物(例如:蘋果醬、優才各)混合,並應於混合後30分鐘內服用完所有混合物。



Tecovirimat 藥物不良反應

造成Tecovirimat停藥之不良反應

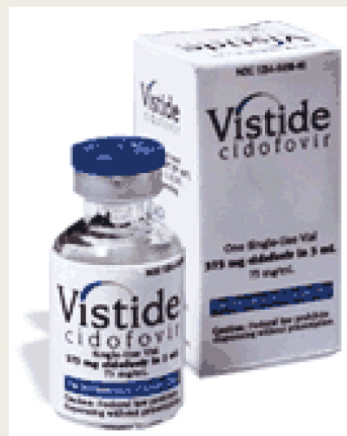
- 有6名受試者(2%)因不良反應而停止治療。每位受試者的不良反應(與嚴重程度)詳列如下：
- 腦電圖變化, 不正常。
- 輕微冒部不適、口乾、注意力降低與煩躁不安。
- 輕微噁心和發燒、中度腹瀉、嚴重頭痛。
- 輕微可觸摸到的紫斑
- 輕微噁心、發燒和發冷。
- 輕微臉部發紅、臉部腫脹和搔癢

不良反應	Tecovirimat 600mg (N=359)(%)	Placebo (N=90)(%)
頭痛	12	8
噁心	5	4
腹痛	2	1
嘔吐	2	0

2.Cidofovir與Brincidofovir

均為干擾病毒核酸合成之抗病毒藥物。

- 國外核准之適應症為CMV病毒感染。雖無臨床資料，但體外試驗與動物實驗資料顯示對正痘病毒屬有療效。



From:

1. Gilead Sciences. Available at: <https://web.stanford.edu/group/virus/orthomyxo/2000/ortho/cidofovir.html#>
2. Drrugs.com. Available at: <https://www.drugs.com/tembexa.html>

3. Vaccinia Immune Globulin Intravenous (VIGIV)

是針對天花病毒的靜脈注射免疫球蛋白。

- 美國FDA核准其用於治療接種天花疫苗後之併發症，亦可在緊急狀況下以「試驗用新藥(investigational new drug, IND)」模式用於治療正痘病毒屬病毒感染病患。



From: US ARMY MEDICAL MATERIEL AGENCY. Available at: <https://www.amlc.army.mil/USAMMA/Logistics/Distribution-Operations-Center-Vaccine/Vaccine-Information/Smallpox-Vaccine/>

Prevention and Treatment of Human Poxvirus

Table 1

Candidate of vaccines and antiviral drugs for prevention and treatment of human poxvirus.

Categories	Names	Features	Anti-poxvirus	Reference
Vaccines	ACAM 2000	Second-generation vaccine	Smallpox virus, MPXV	Brown and Leggat (2016)
	IMVAMUNE	Third-generation vaccine	Smallpox virus, MPXV	Petersen et al. (2019a)
Antiviral drugs	Tecovirimat (ST-246)	Small molecule virus inhibitor	Smallpox virus, MPXV, and cowpox virus.	Yang et al. (2005) , Thakur et al. (2022)
	Cidofovir	Viral DNA polymerase inhibitors	MPXV	Magee et al. (2008)
	Brincidofovir 289 derivative (CMX001)			Magee et al. (2005) Delaune and Iseni (2020)
	Nioch-14			Delaune and Iseni (2020)
	Ribavirin, Tiazofurin	Inosine monophosphate dehydrogenase inhibitors	All of poxviruses	Baker et al. (2003)
	C-CA3-ADO, C3-NPC A	S-adenosylhomocysteine hydrolase inhibitors	All of poxviruses	Baker et al. (2003)
	HPMA, Adenosine N1 oxide (ANO)	DNA polymerase inhibitors	All of poxviruses	Baker et al. (2003)

猴痘疫苗適應症

■WHO建議給予疫苗接種族群：

- 高風險醫護人員、處理正痘病毒之實驗室人員或第一線公衛人員等高風險族群。(Pre-exposure prophylaxis, PrEP)
- 曾有高風險接觸之密切接觸者在最後一次接觸4天內，給予暴露後預防接種 (Post-exposure prophylaxis, PEP)
- 由於歐美此波疫情在特定高風險族群快速傳播，WHO與英美在內多國陸續建議給予男男性行為族群、多重性伴侶者與在性產業場所工作者暴露前預防接種。(PrEP)

■WHO針對2022年猴痘疫情控制，仍建議以公衛措施為主要手段，包括監測、接觸者追蹤、病患隔離與治療照護，現階段仍不建議大規模接種猴痘疫苗。

WHO recommendations for Monkeypox vaccine

Table 1: Use of vaccines for primary preventive (pre-exposure) vaccination (PPV) for prevention of monkeypox: WHO interim recommendations (19 August 2022)

Population group	Interim recommendations for vaccination
General population	Not recommended
Individuals at high risk of exposure, importantly but not exclusively gay, bisexual and other men who have sex with men (MSM) or individuals with multiple sexual partners	Recommended <i>Vaccines to be used:</i> • ACAM2000 • LC16 • MVA-BN
Health workers at risk of exposure, research laboratory personnel,* clinical laboratory personnel performing diagnostic testing for <i>orthopoxviruses</i> ,** and designated response team members at risk for occupational exposure to monkeypox	Recommended <i>Vaccines to be used:</i> • ACAM2000 • LC16 • MVA-BN
Individuals for whom replicating vaccine is not recommended because of young age (children), pregnancy, immune deficiencies, immunosuppression therapies*** or atopic dermatitis****	Recommended <i>Vaccines to be used:</i> • LC16 • MVA-BN

Vaccines and immunization for monkeypox: Interim guidance, 24 August 2022

天花與猴痘疫苗比較

表二、天花與猴痘疫苗比較[20]

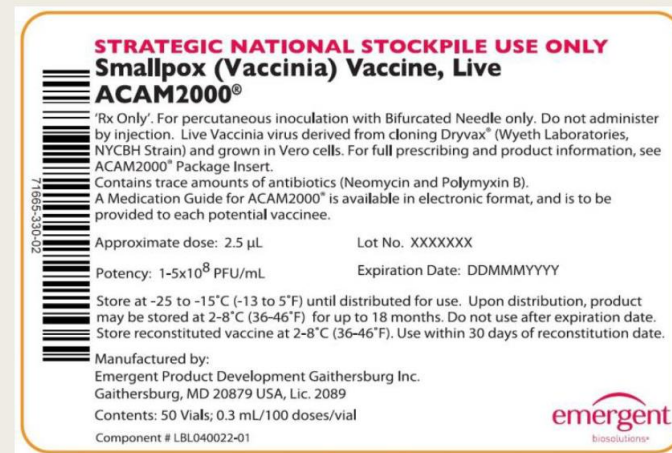
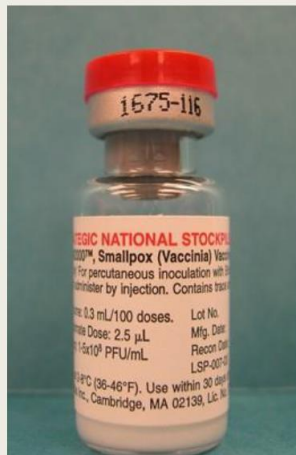
	第一代	第二代	第三代	
疫苗名稱	Dryvax 等	ACAM2000	LC16	MVA-BN (JYNNEOS)
製造商	許多國家自製	美國 Gaithersburg	日本 KM	丹麥 Bavarian Nordic
病毒株	Lister 等多種 天花病毒株	ACAM1000	繼代減弱之 Lister 株	Modified Vaccinia Ankara-BN (MVA-BN)
病毒是否可 複製	活性可複製 (Live replicating)	活性可複製	活性可複製	活性不可複製 (Live, non-replicating)
基礎劑接種 方式與時程	皮下接種一劑	皮下接種一劑	皮內接種一劑	皮下接種兩劑，間隔 28 天
核准適應症	無	預防 18 至 64 歲具 感染風險者之天花 感染（美國）	預防兒童與成人之 天花感染（日本）	預防 18 歲以上具感染 風險者之天花或猴痘 感染（美國）

猴痘疫苗: ACAM2000

■ACAM2000

為含有活病毒的天花疫苗。

- 目前被美國FDA核准用於感染天花高風險者(如實驗室操作天花病毒之人員)。
- 由於副作用較大，在此波疫情中並非優先考慮使用。



From:

- 1.US ARMY MEDICAL MATERIEL AGENCY. Available at: <https://www.amlc.army.mil/USAMMA/Logistics/Distribution-Operations-Center-Vaccine/Vaccine-Information/Smallpox-Vaccine/>
- 2.Drrugs.com. Available at: <https://www.drugs.com/pro/acam2000.html>

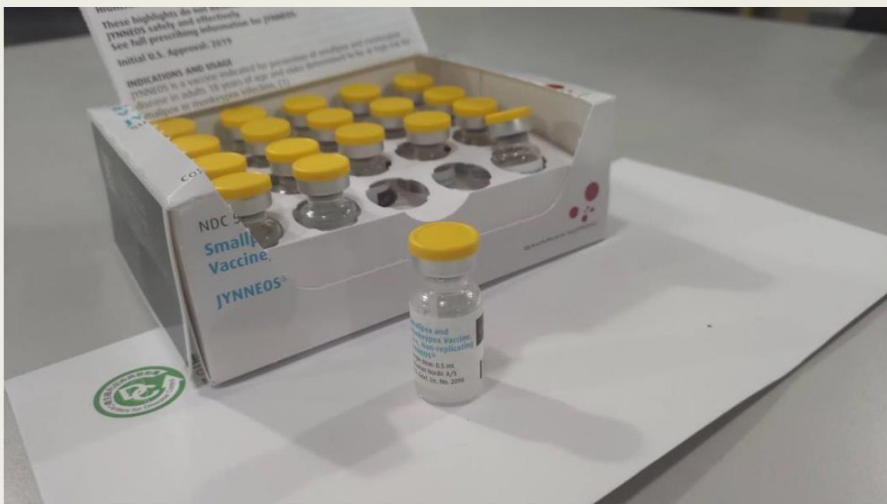
ACAM 2000: People Who Should Not Get Vaccinated

- You should not get the ACAM2000 vaccine if:
 - Weakened immune system from any cause, including HIV infection, due to the increased risk of severe side effects.
 - Pregnant or breastfeeding.
 - Heart condition, skin conditions like eczema, psoriasis, or dermatitis, or eye disease treated with topical steroids.
 - A history of a severe allergic reaction after a previous dose or component of ACAM2000 vaccine.
 - Cannot safely isolate from others who live in your home who have these same medical conditions.
- Infants under 12 months of age should not get the ACAM2000 vaccine.

猴痘疫苗 JYNNEOS

■MVA-BN(JYNNEOS/Imvamune/IMVANEX)

- 減毒活性非複製型疫苗(live-attenuated, non-replicating)，為第一個獲准用於預防猴痘的疫苗
- 相較於第一代天花疫苗，副作用較少，安全性較高(無因意外接觸所致疫苗株傳播之風險)，且施打便利
- 美國FDA於2019年核准MVA-BN(JYNNEOS)疫苗，可用來預防天花和猴痘感染，適用於18歲以上感染猴痘之高風險族群。



疫苗特性與成分：

- 我國儲備之猴痘疫苗 JYNNEOS®，為丹麥 Bavarian Nordic A/S 公司產製
- 為單劑型包裝，每劑 0.5mL 含有 0.5×10^8 IU 至 3.95×10^8 IU 非複製型經修飾之牛痘病毒 (non-replicating, live Modified Vaccinia Virus Ankara - Bavarian Nordic)

猴痘疫苗 JYNNEOS 建議使用對象

- 依據 111 年 8 月 8 日衛生福利部傳染病防治諮詢會預防接種組(ACIP)111 年第 6 次會議決議
- 用於 18 歲以上具猴痘感染風險之成人，預防猴痘感染
- 包括以下對象：
 - 一、 暴露前預防(PrEP)：正痘病毒屬之實驗室操作人員（病毒培養）。
 - 二、 暴露後預防(PEP)：「猴痘疫情調查及接觸者追蹤指引之接觸者匡列處置 原則」所列高暴露風險密切接觸者（如附件 1）。
 - 三、 其他特殊狀況報經疾管署同意者。

接觸者匡列處置原則

接觸風險等級	情境描述	情境舉例	處置
高	無適當防護之長時間持續密切接觸，包括： ● 皮膚黏膜與確診病患皮膚黏膜接觸。 ● 皮膚黏膜與確診病患之分泌物或痂皮接觸。 ● 皮膚黏膜與被確診病患之分泌物或皮膚病灶、痂皮汙染之物品(如衣物或床單)接觸。 ● 吸入確診病患飛沫微粒(aerosol)或乾燥分泌物之揚塵。	● 同住家人。 ● 曾有任何形式性接觸之性伴侶。 ● 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，且位於同一房間或相距 2 公尺內之醫療相關人員。 ● 清掃被汙染的房間時無適當防護，可能吸入飛沫或揚塵者。 ● 實驗室操作過程中曾於無適當防護狀況下暴露於具活性的猴痘病毒，或可能含有病毒之檢體者。	● 針對高風險密切接觸者開立健康監測通知書，主動追蹤其健康狀況至最後一次與病例接觸後 21 天，並每日至「接觸者健康管理系統」進行回報。 ● 評估後給予暴露後預防接種。應於最後一次暴露後四天內接種。 ● 衛教接觸者若無症狀可正常工作生活，但建議避免近距離接觸免疫低下者、孕婦與孩童，以及在健康監測期間避免性行為、捐血。 ● 如於追蹤期間出現發燒或出疹，應協助其就醫。
中	不符合上述高風險接觸定義，但符合下列任一者： ● 曾提供確診病患醫療照護，且未配戴符合接觸情境之防護裝備。 ● 交通工具左右鄰座者。	● 曾與病患共處同一空間(相距 2 公尺內)，累計超過三小時，且未佩戴外科口罩以上等級防護裝備之醫療相關人員。 ● 醫療相關人員之衣物與病患皮疹、體液或受污染之床單或敷料曾有接觸，且未穿著隔離衣者。 ● 飛機左右鄰座者。	● 衛教接觸者應自我健康監測至最後一次與病例接觸後 21 天。 ● 若無症狀可正常工作生活，但建議避免近距離接觸免疫低下者、孕婦與孩童，以及在健康監測期間避免性行為、捐血。 ● 如於追蹤期間出現發燒或出疹，應協助其就醫。
低	不符合上述高、中風險情境，但符合下列任一者： ● 社區一般接觸，或戶外接觸。 ● 接觸時有持續配戴符合接觸情境之防護裝備。	● 短暫交談互動。 ● 曾與確診病患共處同一空間，但無前述高、中等級接觸者。	一般衛教。

猴痘疫苗 JYNNEOS 建議接種時機

接種時機：

1. 高風險接觸者應在最後一次暴露後 4 天內接種，以達最佳預防效果。
2. 若在暴露後 4 至 14 天內接種，則無法預防發病，僅可降低疾病嚴重程度
3. 若高風險接觸者為嚴重免疫不全、孕婦、孩童等易併發重症之對象，可經諮詢傳染病防治醫療網網區指揮官後，於最後一次暴露後 14 天內接種。
4. 如已出現猴痘症狀，則不建議接種。

猴痘疫苗

■我國已儲備猴痘疫苗（MVA-BN）

■我國猴痘疫苗接種對象

- 暴露前預防(PrEP)：
 - 操作正痘病毒屬之實驗室人員。
- 暴露後預防(PEP)：
 - 疾管署「猴痘疫情調查及接觸者追蹤指引之接觸者匡列處置原則」所列之高暴露風險密切接觸者：
 - 其他特殊情況經疾管署同意者。

■接種時機：於首次暴露後4天內，最遲應於14天內接種。

■接種劑量及間隔：建議接種兩劑(0.5ml/劑)，間隔四週。

Indications for Monkeypox vaccine

	Pre-exposure indications	Post-exposure indications*	Administration	Common side-effects	Serious adverse events	Contraindications
Replication-competent vaccinia virus, second-generation (ACAM2000)	Research laboratory personnel working with orthopoxviruses; clinical laboratory personnel doing diagnostic testing for orthopoxviruses; designated response team members; health care-personnel who administer ACAM2000 or care for patients infected with orthopoxviruses; and not recommended for the general population as of June, 2022	Unprotected direct contact with an active orthopoxvirus lesion or fluid or a contaminated item; being within 2 m of an individual with an active orthopoxvirus case for 3 h or more	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, fatigue, and bacterial infection at the administration site	Myopericarditis and pericarditis, encephalitis, progressive vaccinia, erythema multiforme major, eczema, vaccinatum, generalised vaccinia, post-vaccinal encephalitis or encephalomyelitis, blindness due to autoinoculation, and fetal death in pregnant women	Atopic dermatitis†, active exfoliative skin condition†, immunosuppression†, pregnancy†, age <1 year†, breastfeeding, serious vaccine component allergy, underlying heart disease, and ≥3 major cardiac risk factors
Attenuated, minimally replication-competent vaccinia virus, third-generation (LC16m18, available in Japan)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis; not recommended for the general population as of June, 2022	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women if modified vaccinia virus Ankara-Bavarian Nordic not available; licensed in Japan for use in children	Single percutaneous dose with bifurcated needle	Pruritus, lymphadenopathy, administration site soreness, fever, headache, myalgia, rash, and fatigue	None noted in clinical trials	Serious vaccine component allergy
Replication-deficient modified vaccinia Ankara, third-generation (JYNNEOS)	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, immunosuppression, or atopic dermatitis	Same as above; preferred for those with contraindications for replicating vaccines, immune deficiencies, or atopic dermatitis; preferred for pregnant women	Two subcutaneous doses, 28 days apart	Injection site reactions, myalgia, headache, fatigue, nausea, and chills	None	Serious vaccine component allergy
*Post-exposure vaccination is ideally provided within 4 days of exposure to prevent infection; however, vaccination within 4–14 days of exposure can reduce disease severity if infection were to occur. †Including household contacts with the condition.						
Table 1: Indications, administration, side-effects, and contraindications for smallpox and monkeypox vaccination^{32–37}						

Conclusions

- 猴痘為繼COVID-19第二個新興病毒性傳染病，並且世界衛生組織宣布為public health emergency of international concern
- 猴痘臨床表多為30-40歲男性，經親密接觸性行為，常見症狀包括皮疹(85-98%)、發燒(48-84%)、淋巴結腫大(30-60%)。
- 2022猴痘臨床表現不典型包括皮疹最早出現於生殖器或會陰部，且不一定會擴散至身體其他部位、皮疹數目較少、發燒等前驅症狀較不明顯，臨床需要提高警覺
- 猴痘的感染管制措施依循標準防護措施、接觸及飛沫傳染防護措施。
- 猴痘的藥物治療包括Tecovirimat, Cidofovir, brincidofovir, vaccinia immune globulin
- 猴痘的預防-疫苗: PrEP, PEP, JYNNEOS