

Encapsulated Bacteria Session 5: Genome upload and annotation

Genomics and Clinical Microbiology 2025

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Scenario recap: fine typing results

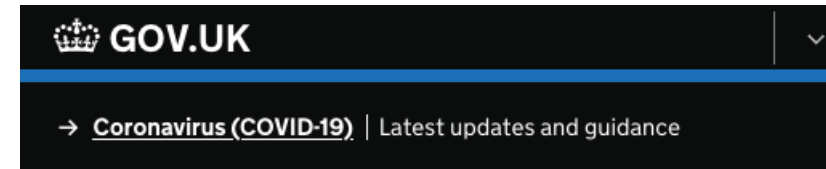
[illegible]

Meningococcal disease: still with us

Peltola, H. (1983). *Rev Infect Dis* 5, 71-91.



Vieusseux, G. (1806). Mémoire sur la maladie qui a régné a Genève au printemps de 1805. *J Med Chir Pharm* **11**, 163-182.



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News story

Recent increase in group B meningococcal disease among teenagers and young adults

Teenagers and young adults are urged to look out for symptoms and check that they have received all routine vaccinations.

From: [UK Health Security Agency](#)

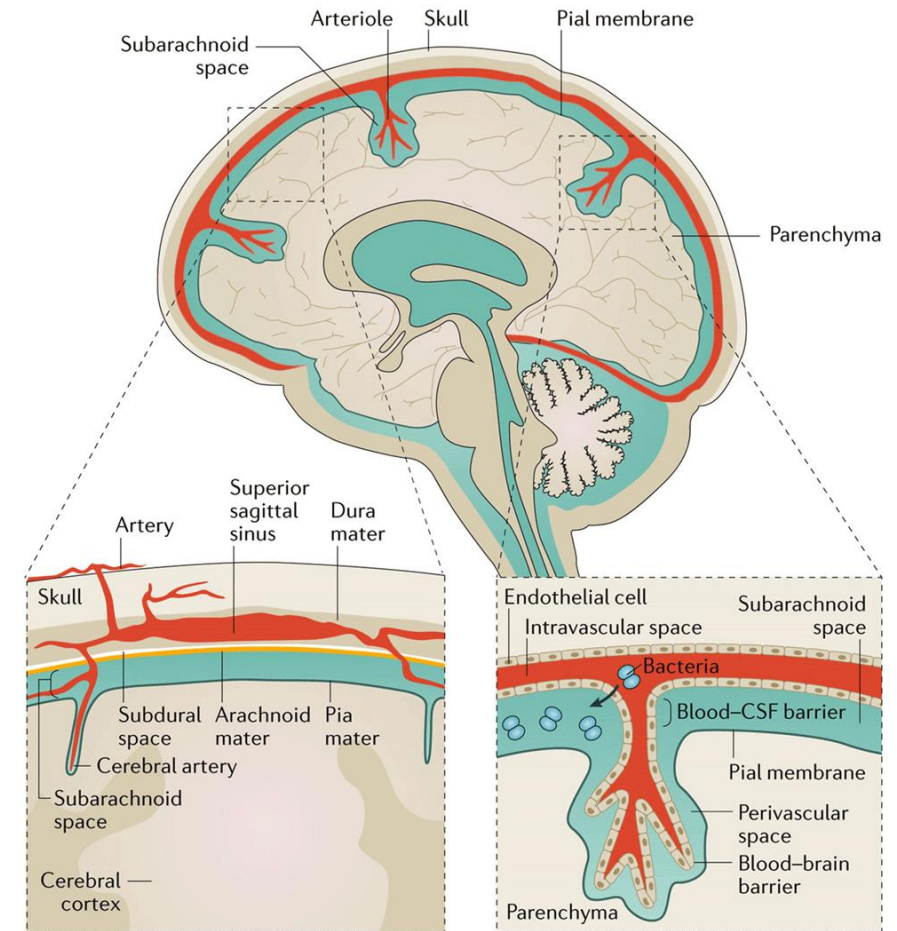
Published 19 January 2022

<https://www.gov.uk/government/news/recent-increase-in-group-b-meningococcal-disease-among-teenagers-and-young-adults>

Accessed 26th January 2022.

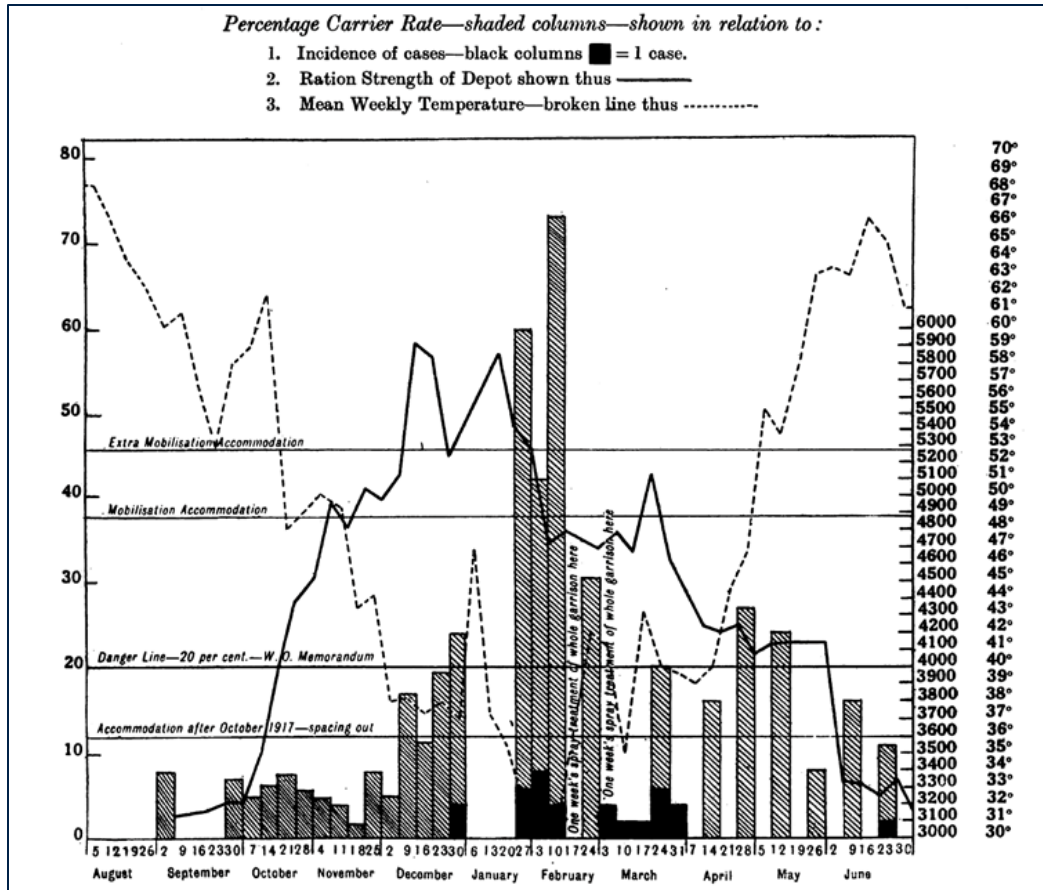
Meningitis and Invasive Meningococcal Disease

- Meningitis:
 - Inflammation of the meninges (tissues around the brain).
- Invasive Meningococcal Disease (IMD):
 - Invasion by the bacterium *Neisseria meningitidis* (the meningococcus);
 - Can be meningitis or septicaemia (blood poisoning).
- Severe and frequently fatal:
 - Survivors frequently suffer sequelae,
 - Digit or limb loss
 - Brain damage, deafness.

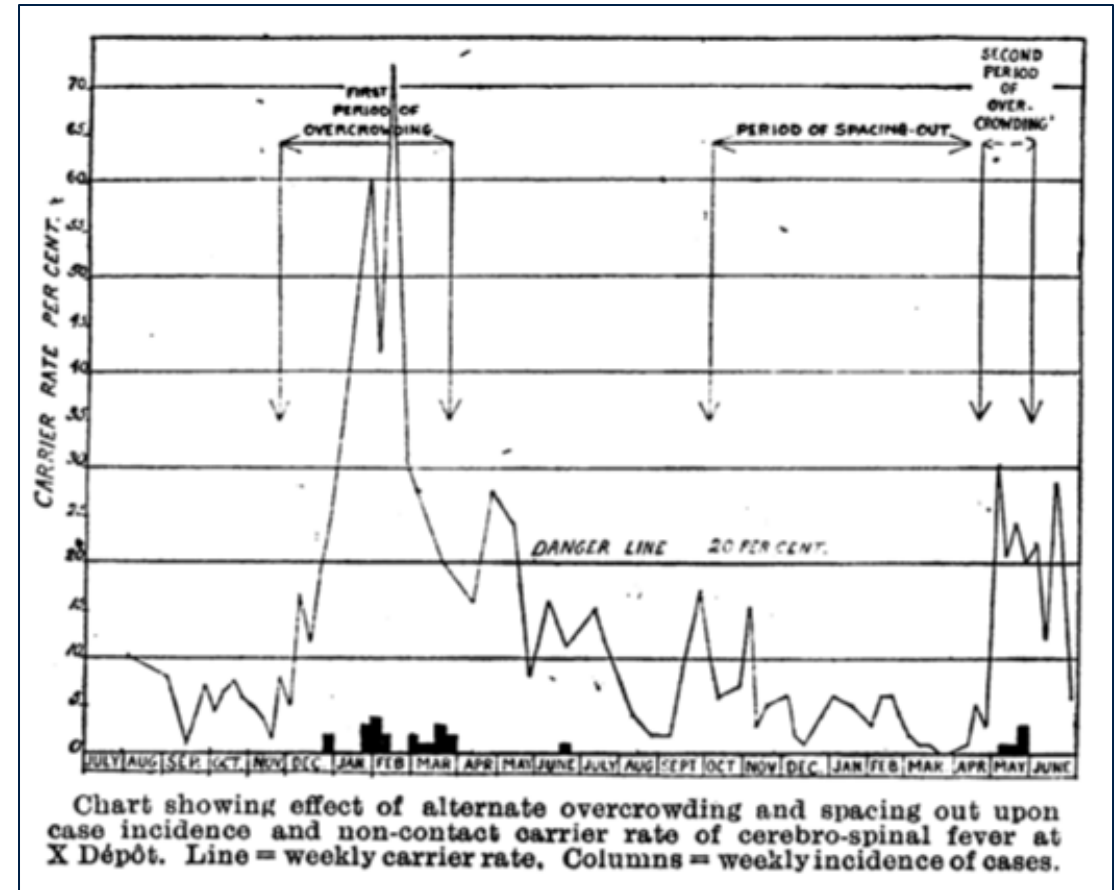


Rodrigues, C. M. C. & Maiden, M. C. J. (2018). A world without bacterial meningitis: how genomic epidemiology can inform vaccination strategy. *F1000Res* **7**, 401.

Carriage, disease, and social distancing, 1917



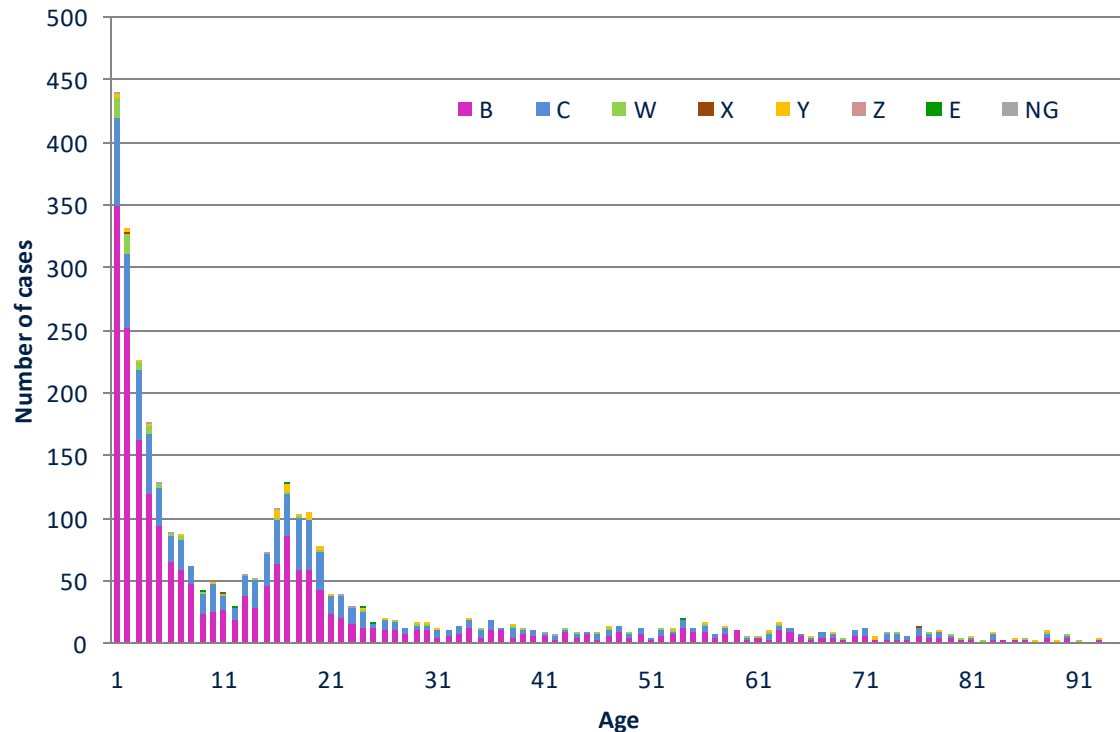
Glover, J. A. (1918). The Cerebro-Spinal Fever Epidemic of 1917 at X Depot. *J Hyg (Lond)* **17**, 350-365.



Glover, J. A. (1918). "Spacing out" in the Prevention of Military Epidemics of Cerebro-Spinal Fever. *Br Med J.* **2**, 509-512.

Meningococcal Disease and carriage

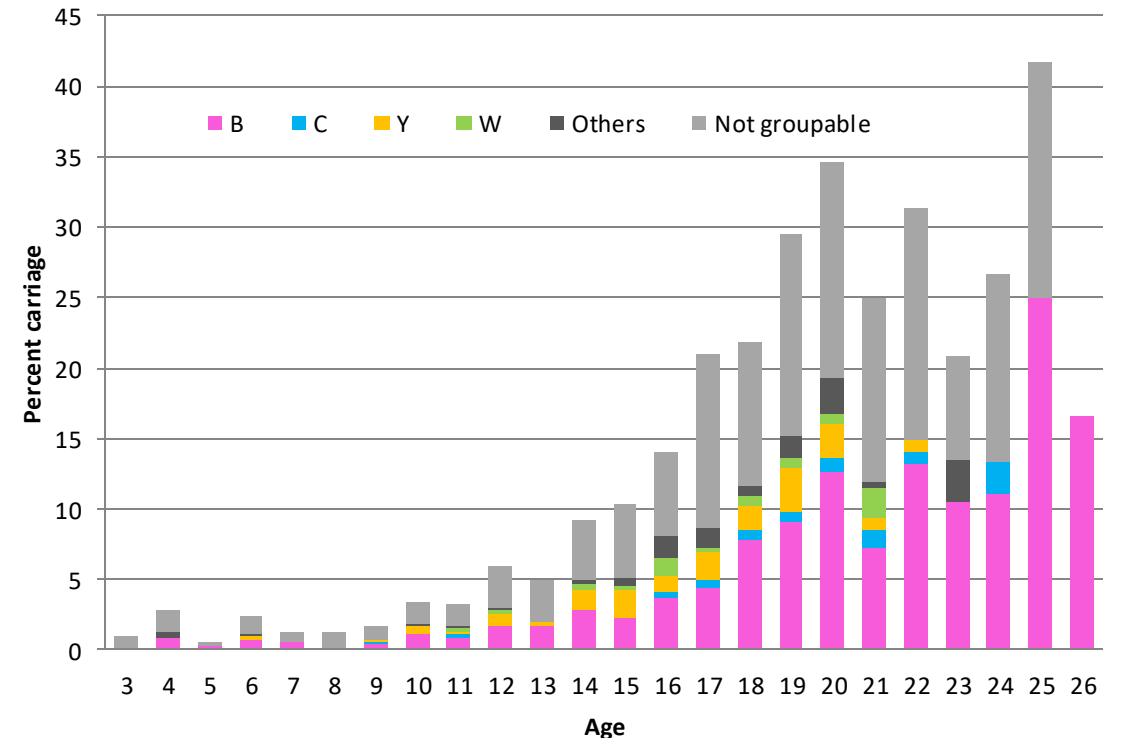
IMD Europe 2000-2002



Frosch, M. & Maiden, M. C. (2007). The European networking for combating meningococcal disease. *FEMS Microbiol Rev* **31**, 1-2.

Brehony, C., Jolley, K. A. & Maiden, M. C. (2007). Multilocus sequence typing for global surveillance of meningococcal disease. *FEMS Microbiol Rev* **31**, 15-26.

Carriage Germany 1999-2001



Claus, H., Maiden, M. C., Wilson, D. J., McCarthy, N. D., Jolley, K. A., Urwin, R., Hessler, F., Frosch, M. & Vogel, U. (2005). Genetic analysis of meningococci carried by children and young adults. *J Infect Dis* **191**, 1263-1271.

Carriage Studies



UK Meningococcal Carriage Study

Today's Date / / Name of School

**** This information is completely confidential. It will not be seen by school staff or other students. ****

Q1 What is your current age in years? 15 ☐ 16 ☐ 17 ☐ 18 ☐ 19 ☐

Q2 I am: male ☐ female ☐

Q3 What is your home postcode?

Q4 Which school year are you in? S5 ☐ S6 ☐

Q5 Do you currently have a cold or sore throat? NO ☐ YES ☐

Q6 Are you currently taking or have you recently stopped taking antibiotics?
not taken in the past month ☐ stopped in the last month ☐ stopped in the last week ☐ yes, currently taking ☐

Q7 How many cigarettes do you smoke in a typical day?
0 ☐ 1-5 ☐ 6-10 ☐ 11-20 ☐ more than 20 ☐

Q8 How many times have you smoked an e-cigarette in the last week?
0 ☐ 1-2 ☐ 3-4 ☐ 7 or more ☐

Q9 How many times have you smoked a waterpipe (shisha, hookah, hubbly bubbly) in the last month?
0 ☐ 1 ☐ 2 ☐ 3-4 ☐ 5 or more ☐

Q10 Does any other person at home smoke cigarettes? NO ☐ YES, outside the house ☐
YES, inside the house ☐

Q11 How many days in the last week have you been to a party, pub, bar or night club?
0 ☐ 1 ☐ 2-3 ☐ 4-5 ☐ 6 ☐

Q12 How many people have you kissed (kissing with tongues, not just lips or cheeks) in the last week?
0 ☐ 1 ☐ 2-3 ☐ 4 or more ☐

Q13a Do you have a regular girlfriend or boyfriend? NO ☐ YES ☐

Q13b If YES: do they smoke cigarettes? NO ☐ YES ☐
do they smoke shisha? NO ☐ YES ☐

Q14 What is your ethnic group?
White ☐ Asian/Asian British ☐ Black/African/Caribbean/Black British ☐
Mixed/multiple ethnic ☐ Other ethnic group ☐

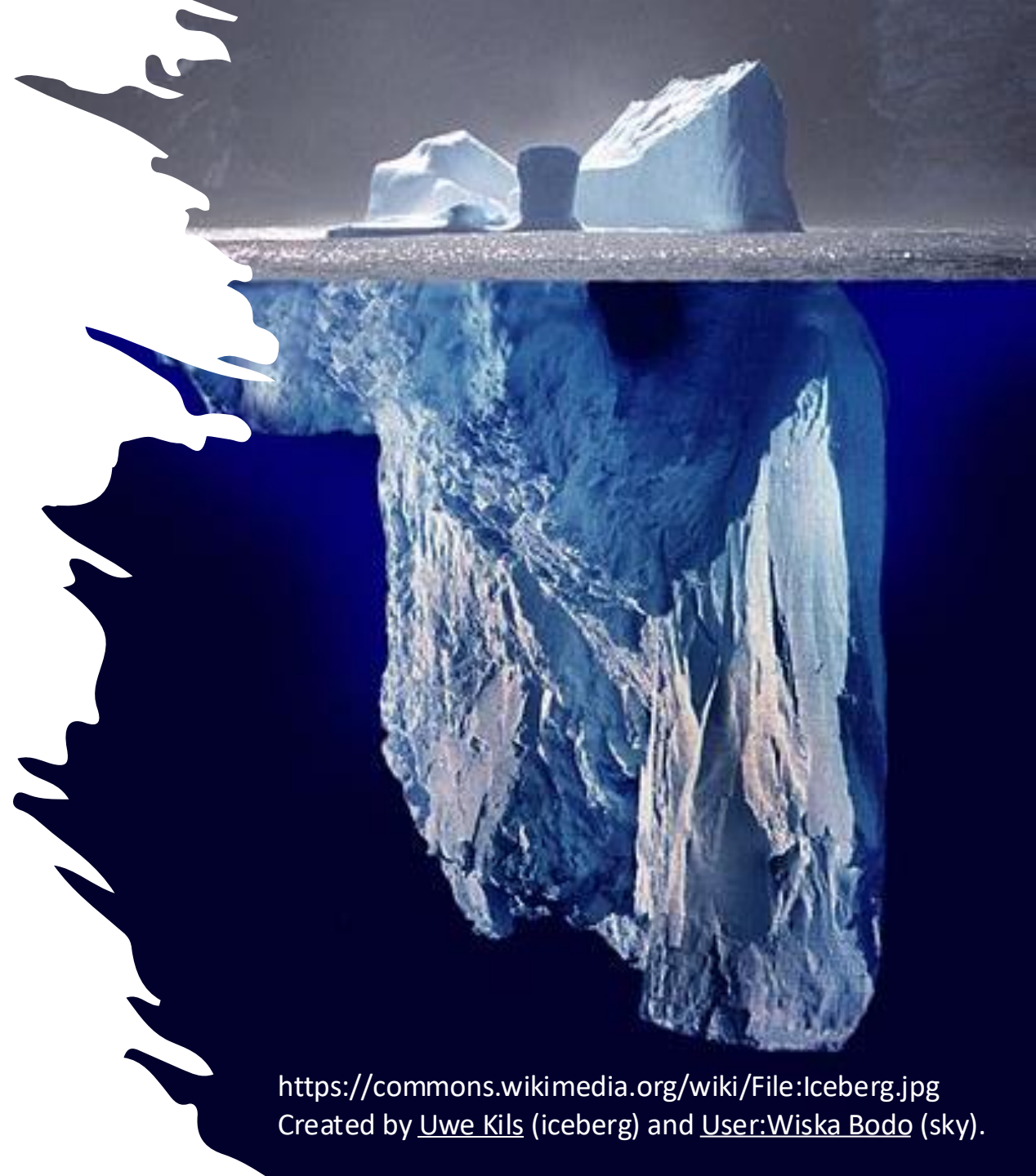
Thank you for completing this questionnaire

UKMENCAR4 Questionnaire v1.2 11/08/14 REC REF 14/SC/1163

Bratcher, H. B., Rodrigues, C. M. C., Finn, A., Wootton, M., Cameron, J. C., Smith, A., Heath, P., Ladhani, S., Snape, M. D., Pollard, A. J., Cunningham, R., Borrow, R., Trotter, C., Gray, S. J., Maiden, M. C. J. & MacLennan, J. M. (2019). UKMenCar4: A cross-sectional survey of asymptomatic meningococcal carriage amongst UK adolescents at a period of low invasive meningococcal disease incidence. *Wellcome Open Res* 4, 118.

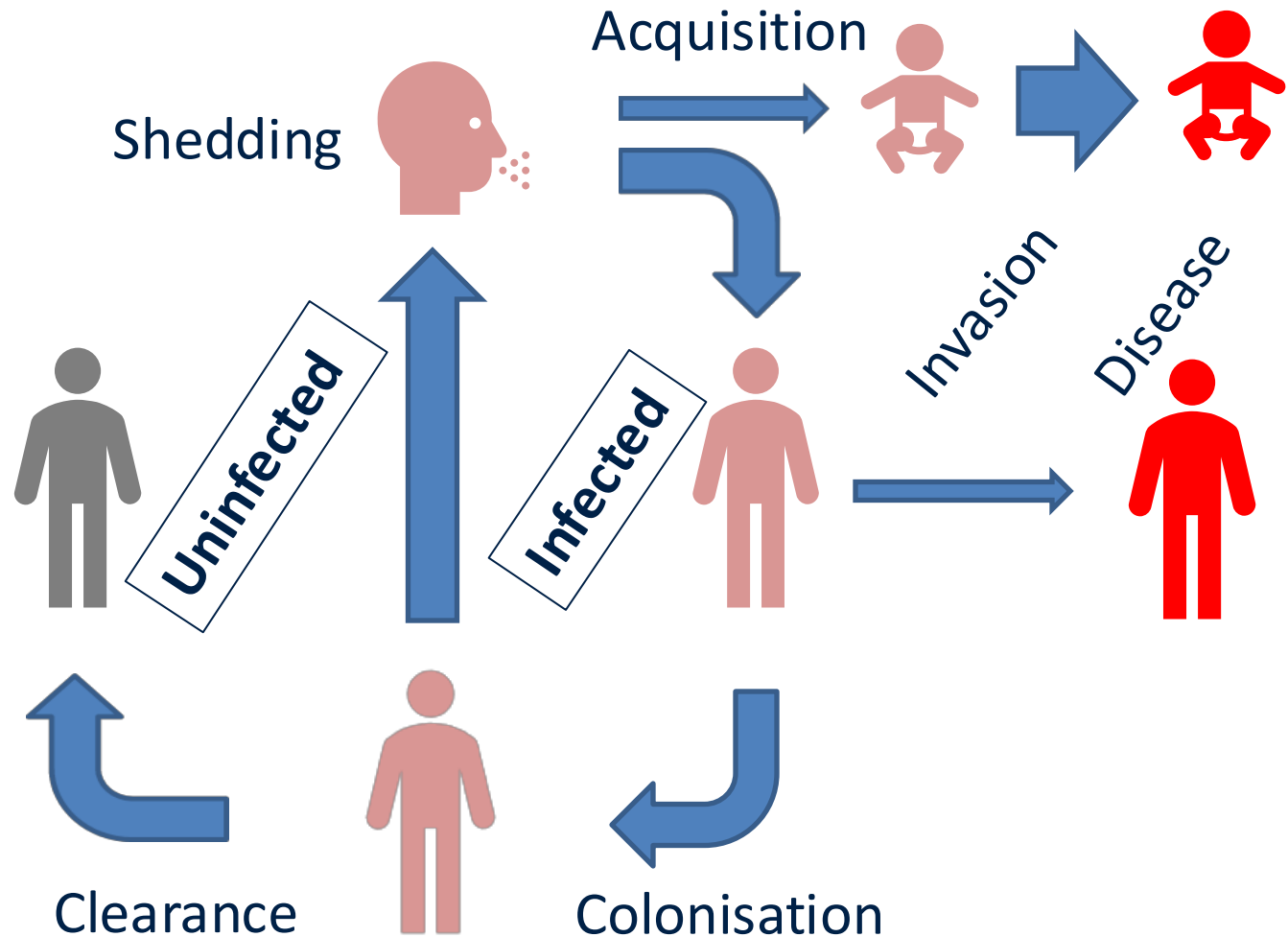
IMD: the 'tip of the iceberg'

- For the meningococcus the great majority infections are not observed:
 - an 'accidental' pathogen.
- Asymptomatic infections, carriage, are major drivers of transmission.
- Eliminating disease requires knowledge of transmission,
 - and in its absence disease control is difficult or impossible.



<https://commons.wikimedia.org/wiki/File:Iceberg.jpg>
Created by [Uwe Kils](#) (iceberg) and [User:Wiska Bodo](#) (sky).

Meningococcal Transmission, Infection, and Invasion



The meningococcus is ordinarily a commensal, causing disease rarely.

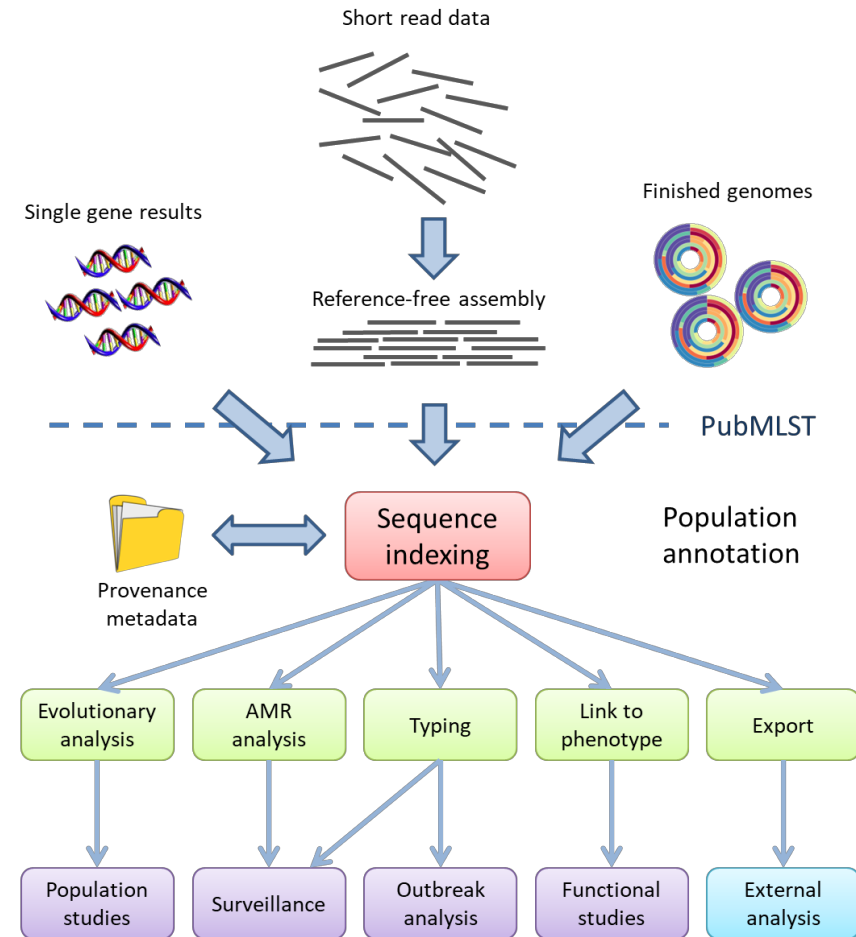
Invasion plays no role in transmission, so it can be thought of as an **accidental pathogen**.

Trotter, C. L. & Maiden, M. C. (2009). Meningococcal vaccines and herd immunity: lessons learned from serogroup C conjugate vaccination programs. *Expert Rev Vaccines* 8, 851-861.

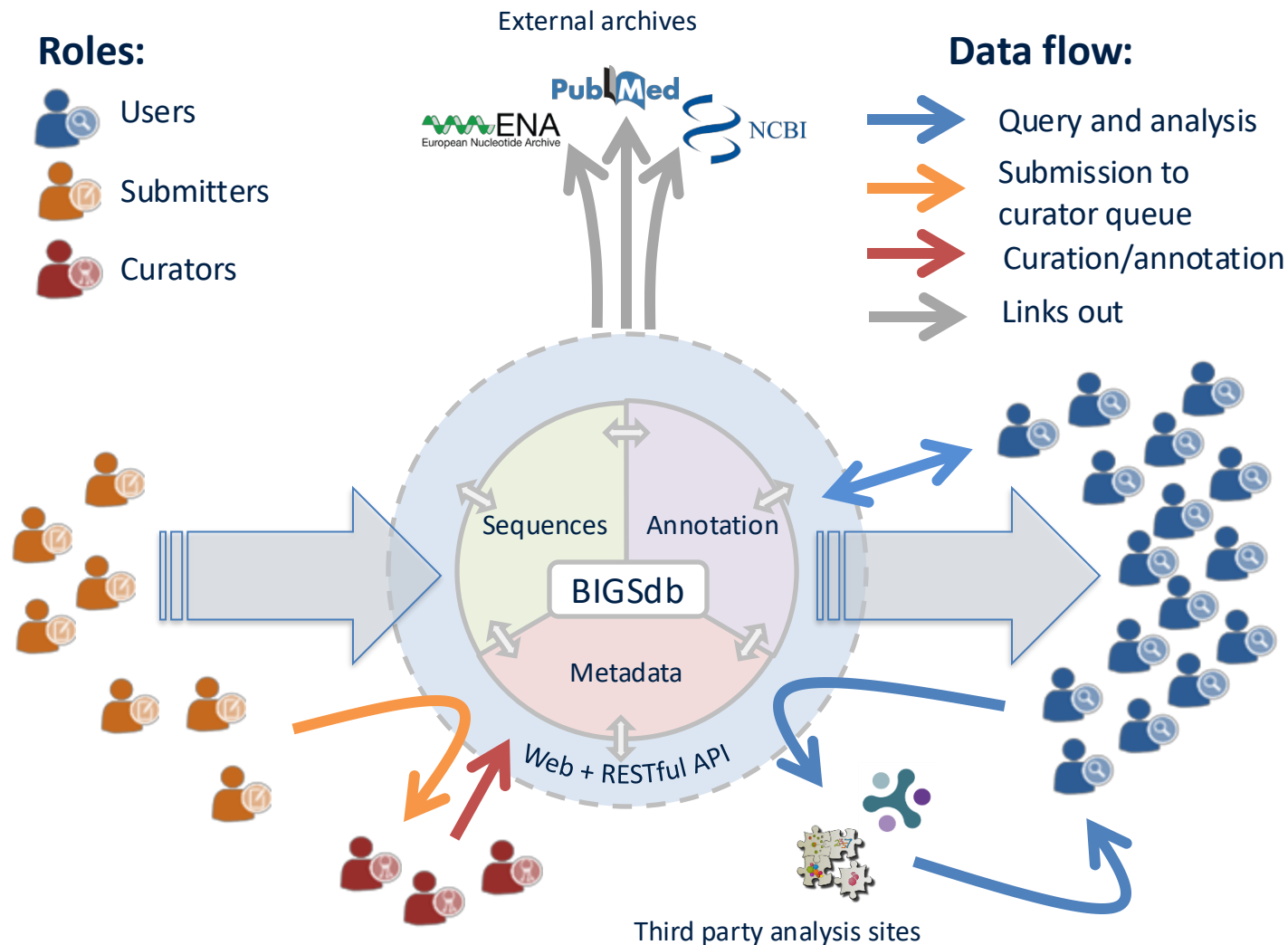
BIGSdb and Population genomics

- **Open source**
- **Web-based**
- **Links:**
 - Sequence data (all types);
 - Provenance information (what, where);
 - Phenotype information (how).
- **Contains:**
 - Sequence bins;
 - Allele/scheme databases;
 - Isolate records;
 - Links to literature.

Jolley, K. A. & Maiden, M. C. (2010). BIGSdb: Scalable analysis of bacterial genome variation at the population level. *BMC Bioinformatics* **11**, 595.



BIGSdb and the PubMLST platform



Jolley, K. A., Bray, J. E. & Maiden, M. C. J. (2018). Open-access bacterial population genomics: BIGSdb software, the PubMLST.org website and their applications. *Wellcome Open Res* **3**, 124.

The of the outbreak and its context

- Five months after the specimen 9 was submitted, a further specimen (specimen 10) from another case of meningococcal septicaemia was received.
- This was from a 6 month-old child, a relative of all the previous cases.
- Following this case, a carriage study (throat swabs) was carried out of the extended family (n=112) from which all the reported cases emanated.
 - 14 meningococci were cultured and one PCR positive was obtained (carriage rate 13.4%)
- Following subculture, DNA was extracted and sequenced for the chromosomal DNA obtained from eight B:P1.7-2,4:ST-6697(cc41/44) meningococci (carriage rate 7.14%) obtained in the carriage study. This was also done for the isolates from specimens 7 and 10.
 - These data have been assembled.

Exercise

- The PubMLST database contains:
 - the outbreak specimens (genome and other sequence data);
 - the 8 carried isolates from the outbreak strain obtained from the extended family;
 - reference and historical isolates;
 - a range of analysis tools.
- Upload your assembled genomes and annotate them for comparative analysis.
- Discussion Points:
 - What do these data tell you about the relationships between carried and disease-associated meningococci?
 - What additional information would be useful, in addition to the microbiological/genomic data?
 - What public health action, if any, is required?
 - What is your understanding of this outbreak now?

