BACTERIOPHAGES : SHARING PHARMACEUTICAL EXPERIENCE AROUND A CLINICAL CASE

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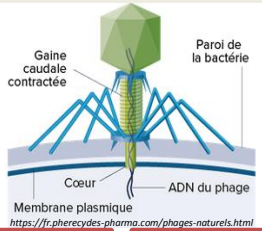
Background

Phage therapy, an ancient therapy forgotten in our Western countries, consists of the administration of bacteriophages for the treatment of **infected patients at the end of their therapeutic options**.
Bacteriophages are **virus that specifically infect a bacterial strain**, unable to infect a eukaryotic cell and therefore harmless to humans.
At the moment, phage therapy **does not have a regulatory framework** but is closely monitored by the National Drug Safety Agency (ANSM) *via* its temporary specialized scientific committee "phagotherapy", which met in 2016 and 2019.



https://fr.pherecydes-pharma.com/phages-naturels.html

Objective

Share our pharmaceutical experience of bacteriophages through the case of a patient:

- 65-year-old male
- With a severe **osteoarticular infection** with **multi-resistant** *Streptococcus dysgalactiae equisimilis* and *Staphylococcus aureus* on a calcaneal stump
- Amputated for diabetic foot ulcers.

Methods

- **Information of the ANSM** of the patient's pejorative clinical situation via a request for a nominative Temporary Use Authorization (ATU) of bacteriophages. This cannot be honored but allows the use of phages to be monitored.
- Request for **compassionate treatment** from the only industrial company involved in France: **Pherecydes Pharma**. This laboratory has a collection of phages whose effectiveness is tested by producing a **phagogram** based on a recent bacteriological sample. Two strains of anti-*staphylococcus aureus* phages were active in our patient's case.
- **Pharmaceutical compounding:**

Under medical and pharmaceutical responsibilities due to the absence of quality and industrial production standards.

In ISO 5 Controlled Atmosphere Zone under laminar flow Microbiological Safety Cabinet.

Dilution of the entire contents of each 1 mL vial of phage in an empty sterile bag with NaCl. Total volume depending on the surface to be treated (here 30 ml).

Storage for 2 hours at room temperature. A file tracking the decrease in the concentration provides information on the last concentration known by the manufacturer.

Bio-decontamination of the biological safety cabinet before and after preparation; waste disposal via Waste from Infectious Risk Care Activities (DASRI).

- **Administration**: First cycle J1 J3 then 2nd cycle 7 days later J1 J3 J6 **applied locally** and in **osteo-articular injection**.

Results

The results were satisfactory in association with detersive gestures and antibiotic therapy, with **harmonious wound budding after 5 administrations**. The evolution was secondarily unfavourable following the discontinuation of tazocillin 3 days after the last phage administration. This led to a **transtibial amputation** 16 days after the last phage administration.

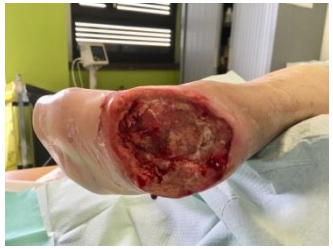


Figure 1 – wound two months before phage administration

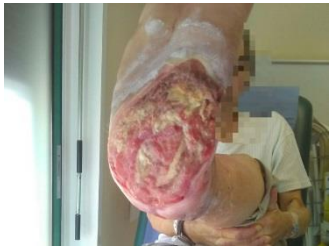


Figure 2 – wound ten days after the last administration of phages

Conclusion

As a promising therapy, supported by the ANSM, phage therapy requires the definition of its **precise indications** and **administration methods** (rhythm, route, dose), after the completion of clinical trials (*phagoburn* completed, others to come). For the time being, a manufacturing laboratory in France is making available compassionate strains of **anti-S. aureus** and **anti-P. aeruginosa**, not industrially manufactured but of a quality compatible with clinical use. Its ability to produce phages using a qualified process that will allow the granting of ATUs is expected by the end of 2019.

References

Minutes of the meeting of the temporary specialized scientific committee on Phage therapy - feedback and perspectives, 21 March 2019, ANSM
Documentation Pherecydes Pharma