History

- Dimitri Ivanovsky Saint Petersburg 1892 TMV
- Martinus Berjerinck 1892

They used porcelain filters:

. Retaining bacteria

. Not the “filterable viruses”

Viruses not seen before the electron microscopy in the 1930ths

FACILITATING FACTORS IN DISEASE EMERGENCE

Demography: urban population concentration

Loss or lack of hygiene culture, Lack of water

World exchanges, travels

Atmospheric and food pollution facilitating oxidative stress and immunodeficiency

Ageing of immunodeficient populations

Global warming leading new ecological niches to vectors (insects)

The various strategies of viruses

Multiply and be transmitted

- Acute fulminant infection: Ebola, Marburg
- Zoonotic reservoir
- Paralyze the host's defence
  - . CMV, HIV
  - . Influenza inhibits action of interferon
- Being two ways: to multiply and become latent
  - . Retroviruses
  - . Herpes

The Human Genome

Genes (+ introns +promoters)		3%
Retroelements: retroviruses		8%
retrotransposons		13%
LTR		23%
Total		47%
Repeats		50%
LINE	22%	
SINE	13%	
Unknown		?

Our defence against viruses:

Innate

- Macrophages NK cells
- Cytokines: Interferons

Acquired:

- Antibodies
- Cell mediated cytotoxycity: CTL

Human made:

- specific chemical inhibitors

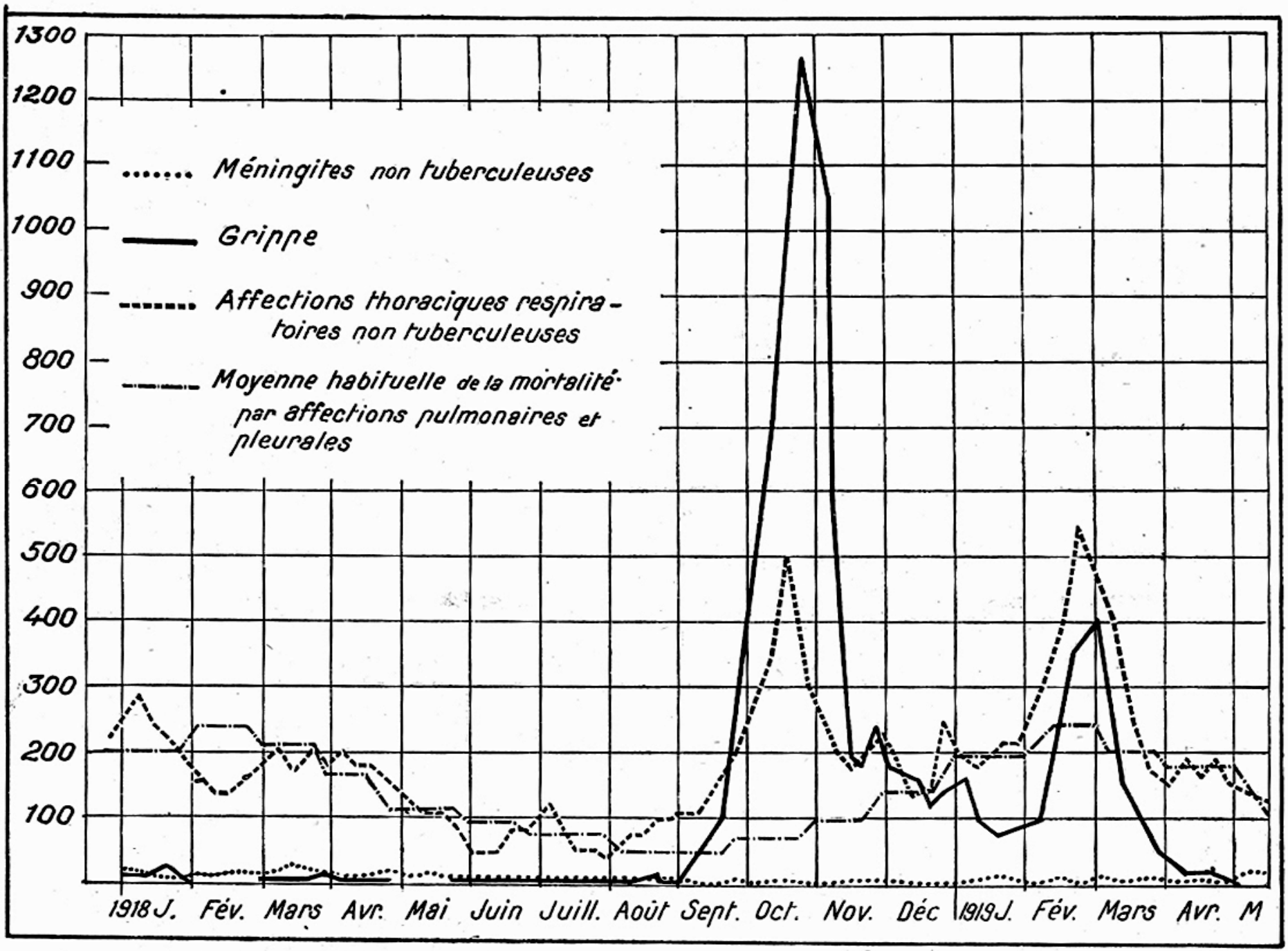


Fig. 3. — Marche des épidémies en 1918 et 1919.

Mortalidad producida por la gripe española en todo el mundo

Diferentes estimaciones

Autor	Año estimación	Número de muertos	Tasa por 1.000 habitantes (‰)
Jordan	1927	21.542.283	12 ‰
Webster; Lavel	1975	20.000.000 – 50.000.000	11- 27,6 ‰
Schild	1977	15.000.000 – 50.000.000	8,3 – 27,6 ‰
Beveridge	1978	15.000.000 – 25.000.000	8,3 – 13,8 ‰
Burnet	1979	50.000.000 – 100.000.000	27,6 – 55,2 ‰
Patterson; Pyle	1991	24.700.000 – 39.300.000	13,6 – 21,7 ‰
Johnson; Mueller	2002	48.798.038 50.000.000 – 100.000.000	2,5 – 5,5 ‰ (?)
Phillips; Killingray	2003	30.000.000 (6 months)	

Virulence factors of Influenza virus strains

	Sites of interaction
HA (Haemagglutinin) →	Multiple cleavage sites receptors
PB2 (Replication Complex) →	Lysine 627
NS1 (Non Structural Protein) →	Interferon antagonist, TLRs Ligand PDZ
PB1-F2 (New ORF) →	Mitochondria

Virulence factors of Influenza virus strains

	HA	PB2	NS1	PB1-F2	Transmissibility
« Spanish flu »	+	+	+	+	++
H5 N1	+	+	+	+	±
H1 N1	-	-	-	-	++

The worse scenario:

- An air-borne virus,

✓ Highly virulent, inflammatory

✓ Highly transmissible

✓ Paralysis of exchanges, travels

(cf the islandic volcano)

✓ No more meetings

✓ Only e-exchanges !

The immediate reaction:

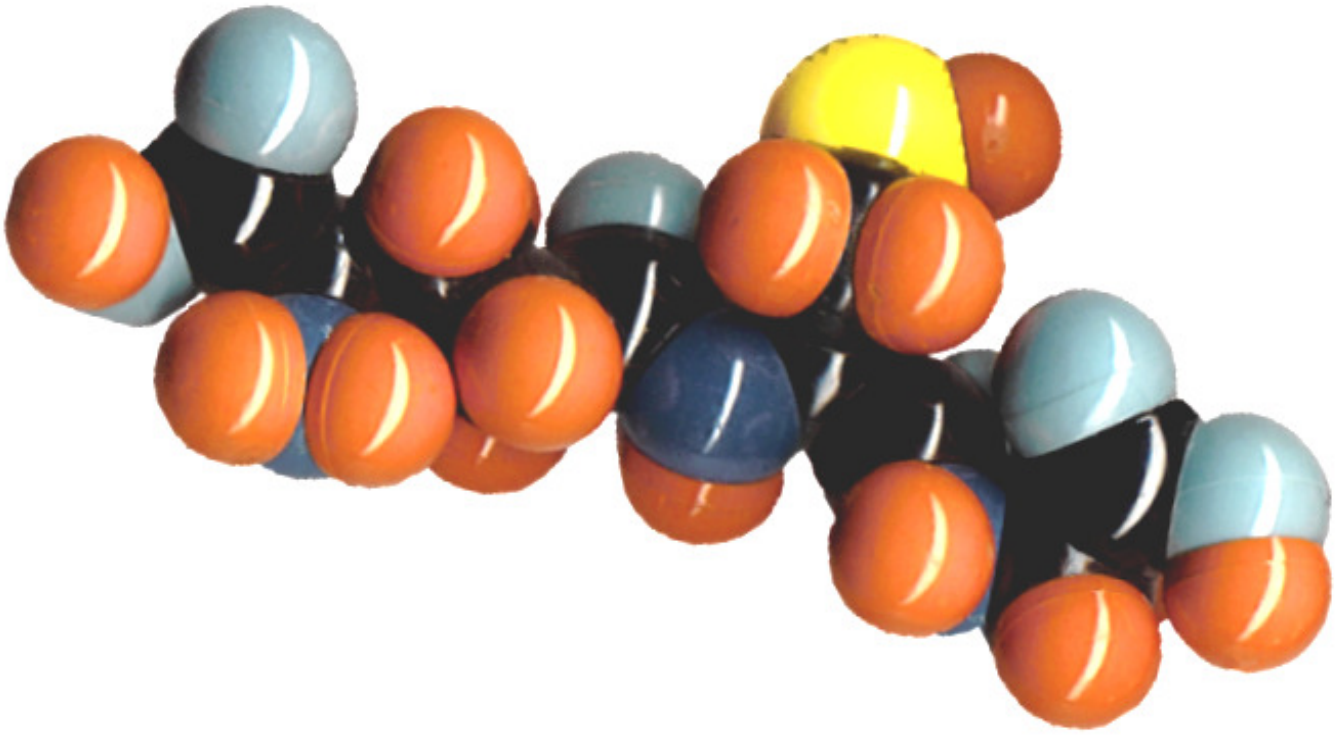
- Before the agent is diagnosed,
- Before we have a vaccine
-Or specific inhibitors

Boost the immune defence:

. Interferon
. Antioxidants
. Immunostimulants

Be quick in identification (PCR, sequencing)

Glutathione



ThyoGen Pharmaceuticals, Inc.

Remaining signs of HIV persistence after antiretroviral therapy

- ✓ Infectious particles in the blood
- ✓ Expression of Fas-l on monocytes
- ✓ Partial restoration of the immune system
- ✓ Viral reservoir

Nature of the reservoir : DNA ?

A newly discovered property of DNA :

Resonance emission of low frequency electromagnetic waves by high water dilutions of DNA.

FACTS

Detection of Ultra Low Frequencies Waves (ULF 500-2000 hertz) in certain dilutions of filtrates (100nM, 20nM, 15nM) from cultures of micro-organisms (virus, bacteria) or from the plasma of humans infected with the same agents.

This HIV DNA may reflect a shift to a DNA-DNA replication mechanism, and represent at least part of the HIV reservoir remaining under ART.

Interpretation :

ART pushes the virus towards an alternate way of replication

Productive cycle :

RT

RNA → DNA → RNA → proteins

Reservoir :

DNA polymerase

DNA ⇌ DNA

Conclusion

1)HIV DNA can be regularly detected in the plasma of patients treated by antiretroviral therapy.

2) This detection is obtained:

a) by EMS emission from aqueous dilutions of the plasma.

b) by EMS emission of DNA extracted from the plasma and the erythrocyte fraction

c) by nested PCR using primers corresponding to some HIV sequences (LTR) in the same fractions.