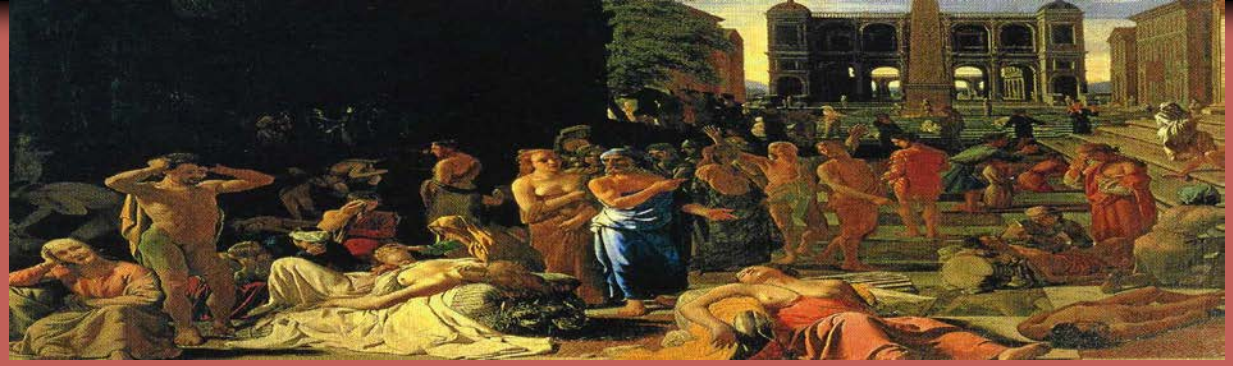
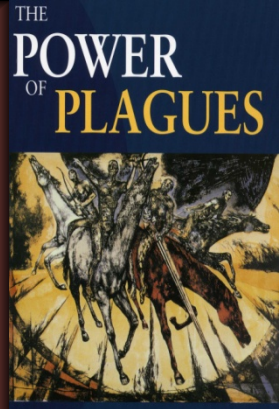
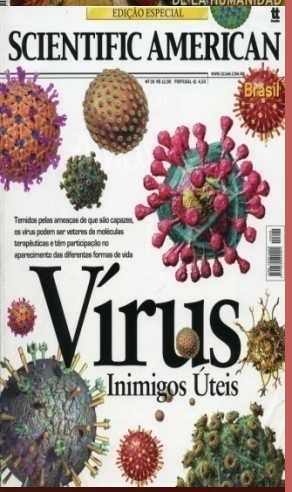
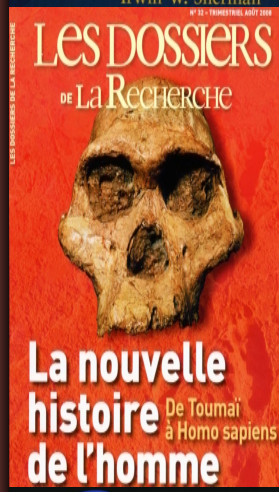




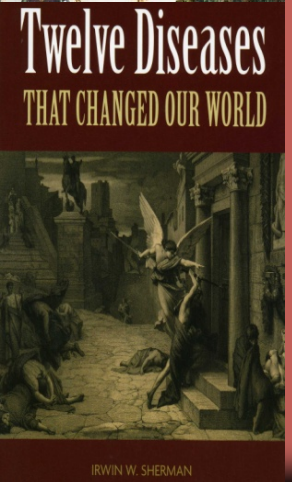
"Breve Resenha Histórica sobre a Evolução da Microbiologia e das Doenças Infecciosas desde a Antiguidade"

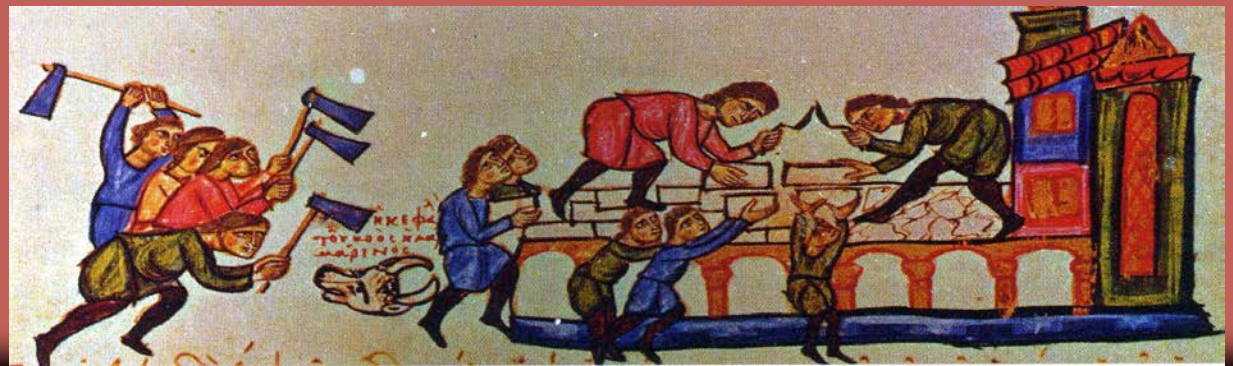


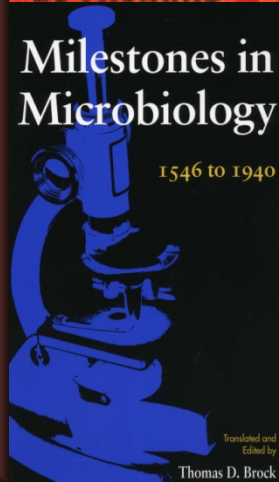


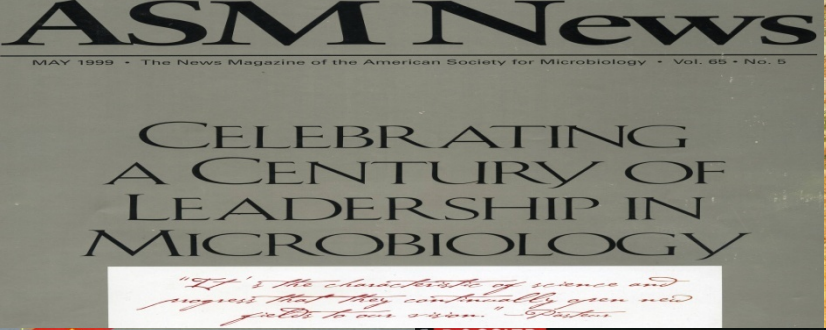
José Poças

Serviço de Doenças Infecciosas
CHS – HSB Setúbal





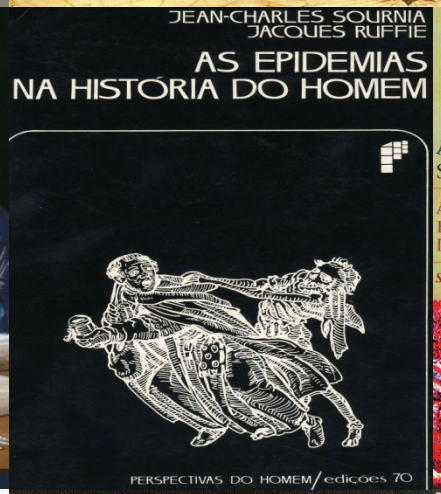


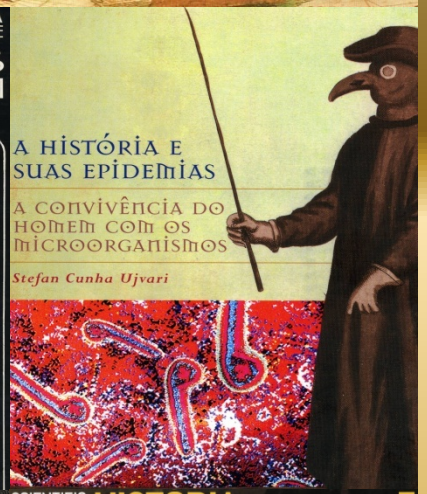

ASM News
MAY 1999 • The News Magazine of the American Society for Microbiology • Vol. 65 • No. 5
CELEBRATING A CENTURY OF LEADERSHIP IN MICROBIOLOGY

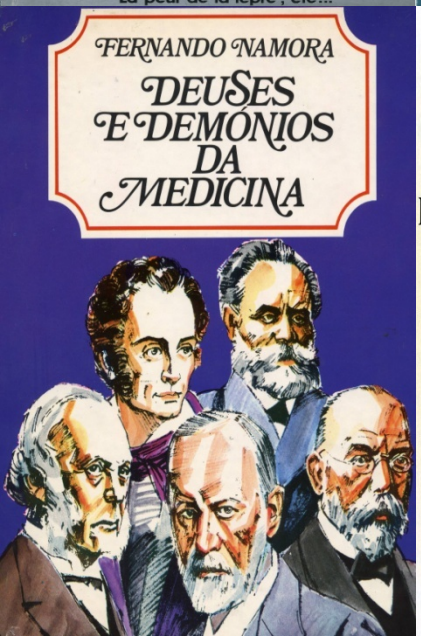
a Medicina nos Descobrimentos

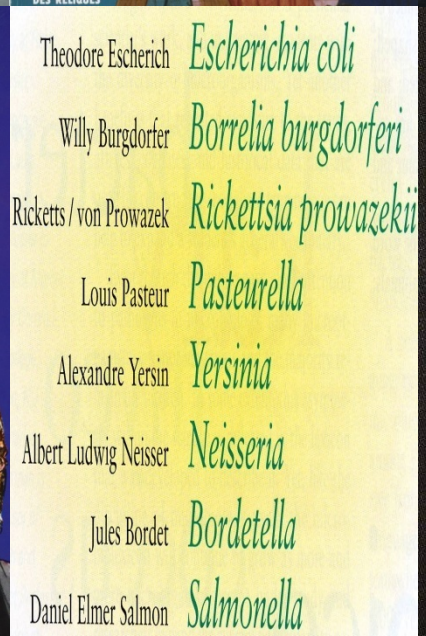
NUMERO SPECIAL
L'histoire
n° 74-29F
Les maladies ont une histoire
Les maladies des rois de France
Les hôpitaux au Moyen Age . Histoire du cance
La peur de la lèpre , etc...

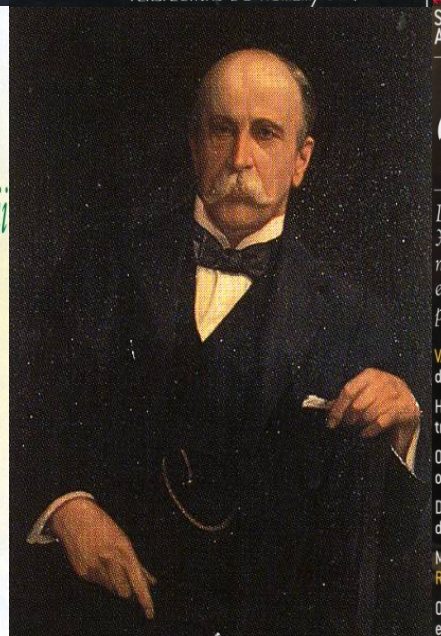
DOSSIER POUR LA SCIENCE
pourlascience.com
Les maux de nos ancêtres
L'ORIGINE DES ÉPIDÉMIES
LES INFECTIONS MORTELLES
LA GRANDE PESTE
LA GRIPPE ESPAGNOLE
MORT VIOLENTE ET POISON
MÉDECINE ET EMBAUMEMENT
IDENTIFICATION DES CORPS
AUTHENTIFICATION DES RELIQUES


JEAN-CHARLES SOURNIA
JACQUES RUFFIE
AS EPIDEMIAS NA HISTÓRIA DO HOMEM
PERSPECTIVAS DO HOMEM/edições 70


A HISTÓRIA E SUAS EPIDEMIAS
A CONVIVÊNCIA DO HOMEM COM OS MICROORGANISMOS
Stefan Cunha Ujvari


FERNANDO NAMORA
DEUSES E DEMÓNIOS DA MEDICINA


Theodore Escherich Escherichia coli
Willy Burgdorfer Borrelia burgdorferi
Ricketts / von Prowazek Rickettsia prowazekii
Louis Pasteur Pasteurella
Alexandre Yersin Yersinia
Albert Ludwig Neisser Neisseria
Jules Bordet Bordetella
Daniel Elmer Salmon Salmonella

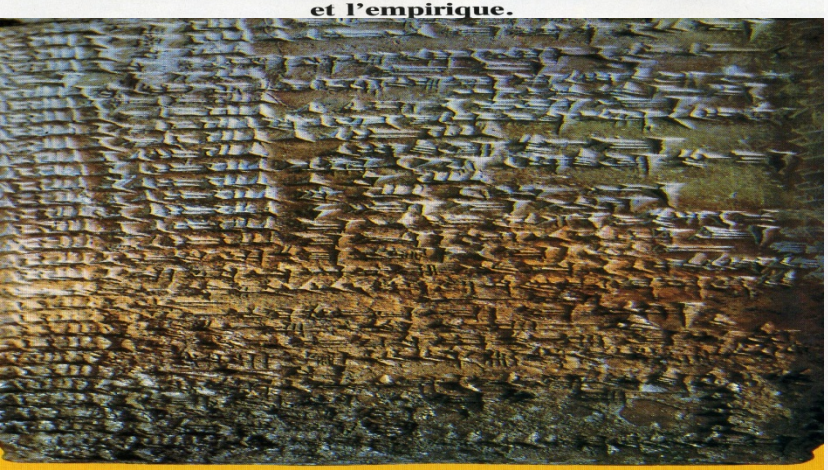


SCIENTIFIC AMERICAN HISTORIA
nº 5
O NASCIMENTO DA Medicina Moderna
Descobertas feitas no século XIX revolucionaram a maneira de encarar as doenças e lançaram as bases da pesquisa médica científica
VACINAS e a ditadura da saúde
Humanização do tratamento da LOUCURA
O avanço da CIRURGIA com o surgimento da ANESTESIA
Das EPIDEMIAS ao sistema de SAÚDE PÚBLICA
Microscópios, germes e a REVOLUÇÃO de PASTEUR
O impacto da PENICILINA e dos antibióticos

La magie et la médecine règnent à Babylone

par Jean Bottéro

Grâce à d'exceptionnels documents remontant au IIIe millénaire, Jean Bottéro nous révèle ici comment les Babyloniens luttaient contre le mal physique à l'aide de deux médecines : la « magique » et l'empirique.



Un exemplaire, presque entièrement conservé, de la IXe tablette du *Traité de diagnostics et de pronostics*. Seul l'avers du document figure ici, avec les trente-six premières lignes de l'examen analytique de toutes les situations médicalement significatives présentées par *« le visage du malade »*, et dont le détail, en quarante-trois autres lignes, se poursuit au verso. La copie est de la première moitié du Ier millénaire avant notre ère (Paris, musée du Louvre ; cl. H. Josse).

Plaquette de bronze, apparemment destinée à servir d'amulette protectrice contre les maladies, mais dont l'interprétation détaillée reste obscure. Le registre du milieu représenterait un malade couché, peut-être en proie aux *« sept démons morbifiques »* alignés au-dessus de lui en corps d'hommes à tête léonine. Il implore le secours des dieux, en levant les bras au Ciel. Dans sa chambre à coucher (suggérée par la lampe, à l'extrême gauche), il est assisté, au pied et à la tête de son lit, par deux personnages, qui peut-être un seul représenté deux fois, pour suggérer qu'il s'évertue autour de la couche. L'habit qu'il(s) porte(nt) et qui le(s) déguise en poisson(s) suggère, dans la mythologie locale, qu'il s'agirait d'un(de) représentants d'Ea, patron de l'Exorcisme, affairé(s), en son nom, à traiter et à guérir le malade (Paris, musée du Louvre ; cl. H. Josse).

ELSEVIER SAUNDERS

INFECTIOUS DISEASE CLINICS OF NORTH AMERICA

Infect Dis Clin N Am 18 (2004) 17–27

Infectious diseases in ancient Egypt

Bob Brier, PhD

Department of Philosophy, Long Island University, C.W. Post Campus, 720 Northern Boulevard, Brookville, NY 11548, USA

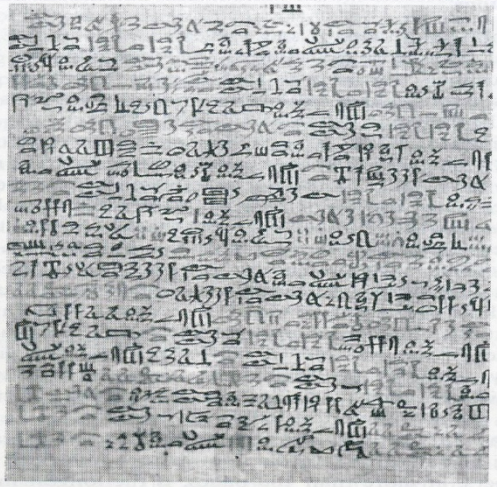


Fig. 1. Papyrus Ebers contains clinical and magical treatments for infectious diseases. Case headings are in red ink.

B. Brier / Infect Dis Clin N Am 18 (2004) 17–27

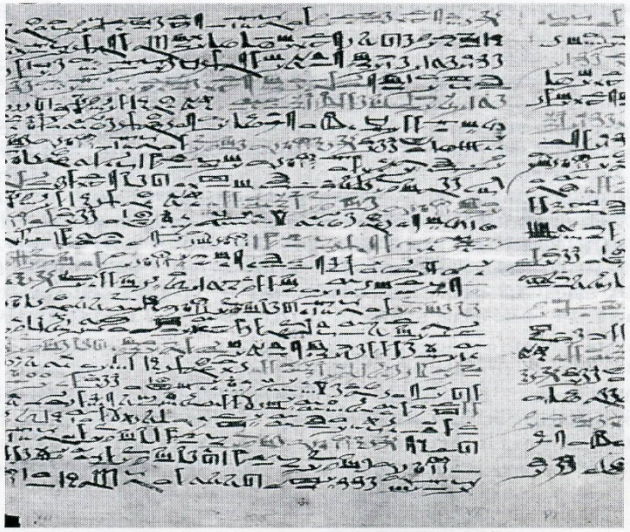


Fig. 2. The Edwin Smith Surgical Papyrus discusses an annual epidemic.

Homem pré-histórico já fazia a trepanação, orifício no crânio provavelmente para expulsar maus espíritos
De 10000 a 8000 a.C.

Construção das pirâmides de Gizé
De 2575 a 2474

3500
Placa de argila encontrada na Suméria mostra uma carroça equipada com rodas. É o primeiro registro da invenção, que deve ter surgido milhares de anos antes

770
Surgem os primeiros santuários ao deus grego da medicina: Esculápio

Cerca de 580
Nasce Pitágoras

Nascimento de Hipócrates de Cós, pai da medicina
460

Por volta de 440
Hipócrates de Chios vai a Atenas e inicia seus estudos sobre a quadratura do círculo

Nasce o filósofo grego Platão
Cerca de 428

384
Nasce o filósofo e cientista Aristóteles

Por volta de 300
Euclides prospera em Alexandria e escreve seus *Elementos*

Arquimedes (de 290/280 a 212/211) atua como um dos principais cientistas da Grécia Antiga
Ao longo do séc. III

260
Nasce Apolônio de Perga, autor das famosas *Cônicas*

Astrônomo egípcio Ptolomeu prospera em Alexandria e escreve o *Almagesto*
Século II d.C.

Por volta de 150
O médico Galeno começa seus estudos sobre anatomia humana

Fim da Antigüidade, com a queda do Império Romano do Ocidente
476

Início convencional da Idade Média
500

Em Saint-Gall é desenhado o projeto de um mosteiro beneditino com jardim de plantas medicinais, moinhos e uma escola
Por volta de 820

O *Domesday Book* aponta em seu recenseamento 5.624 moinhos hidráulicos na Inglaterra
1086

Na Espanha ocupada pelos muçulmanos, escritos gregos e árabes são traduzidos para o latim
Por volta de 1140

Construção das catedrais francesas
1140-1240

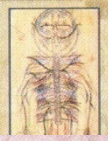
Alberto, o Grande é convocado pela Universidade de Paris, onde comenta, entre outros, os escritos de Aristóteles
1242

Construído o primeiro observatório estelar, em Nurembergue
1460

Fim convencional da Idade Média
1500

529
Fundação do monastério beneditino de Monte Cassino, fechamento das últimas academias antigas

Primeiros registros de moinhos para a produção têxtil
962



Por volta de 1010
Avicena escreve seu *Cânone*, que se tornaria obra de referência médica das universidades européias

1100
Fundação da Escola de Direito de Bolonha

1202
Leonardo de Pisa utiliza os algarismos árabes

1215
Fundação da Universidade de Paris

Por volta de 1300
A análise da urina (uroscopia) se impõe como método de diagnóstico

1377
Nicolau de Oresme publica a primeira obra científica em língua vulgar, sobre o movimento da Terra

1454
Gutenberg comercializa as Bíblias impressas na prensa a tipo inventada por ele

1492
Descoberta da América por Cristóvão Colombo

Tomada de Constantinopla
1453

Formação humanista de Erasmo de Roterdã
1509

Proclamação da visão de mundo heliocêntrica por Copérnico
1543

Della Porta escreve seu *Magia naturalis*
1558

Tycho Brahe constrói o seu Observatório do Castelo de Uraniborg
1574

De Magnete, de Gilbert
1600

Bacon publica seu *Novum organum*
1620

Torricelli inventa o termômetro de mercúrio
1643

Fundação da Royal Society
1660

Na Inglaterra, o ato de Habeas-Corpus garante os direitos inalienáveis do indivíduo
1679

RENASCENÇA (SÉCULOS XIV-XVI)

1492
Colombo descobre a América

1517
Lutero fixa suas teses em Wittenbergue

1551
Gesner publica seu *Historia anumalium*

1562
Eclosão das guerras religiosas na França

1590
Teoria do movimento de Galileu

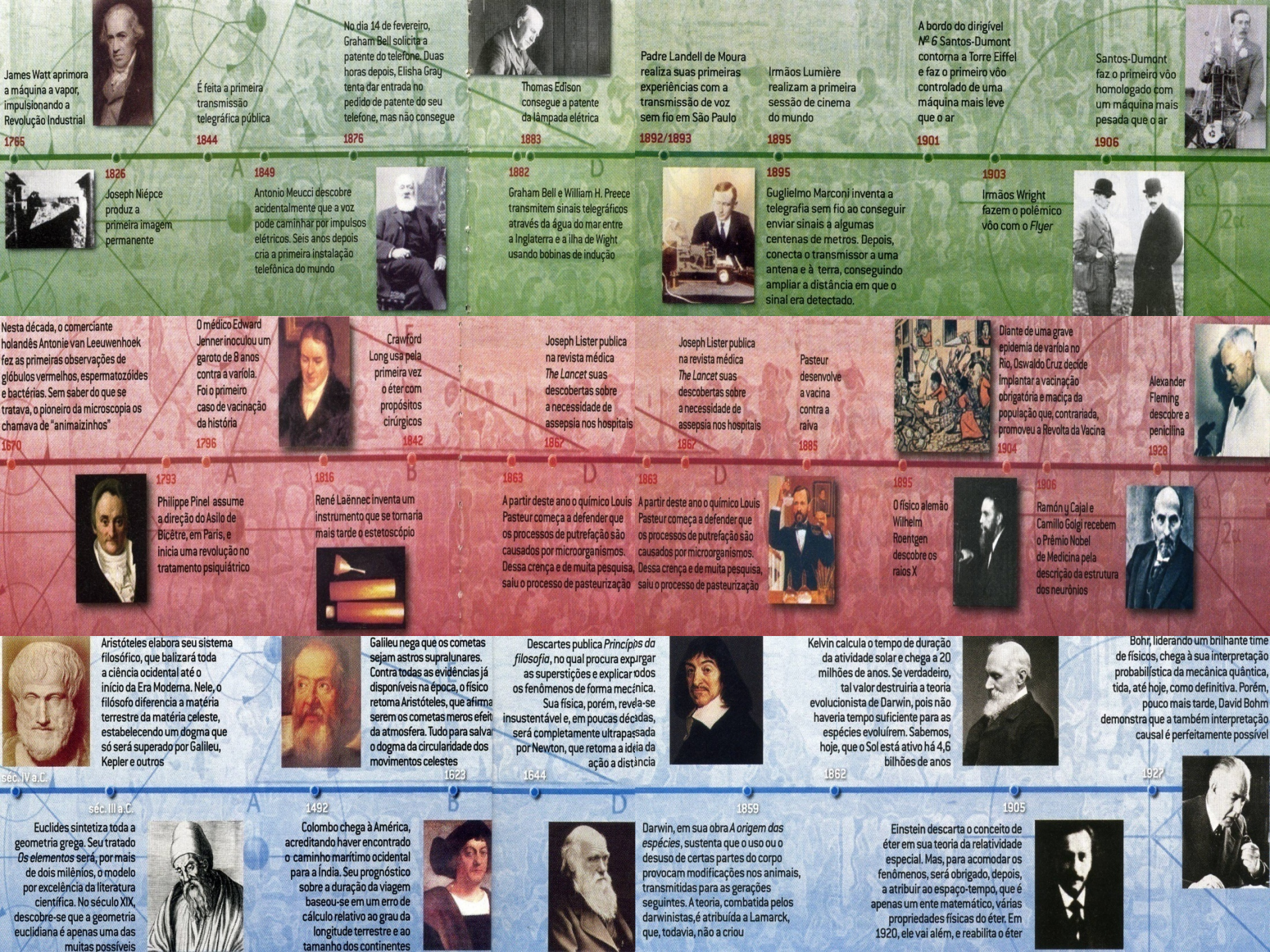
1610
Galileu descobre as luas de Júpiter

1629
Harvey descreve a circulação sangüínea

1648
Termina a Guerra dos Trinta Anos com a Paz da Vestfália

1672
Estudo das cores por Newton

1687
Newton publica seus *Principia*


James Watt aprimora a máquina a vapor, impulsionando a Revolução Industrial
1765
É feita a primeira transmissão telegráfica pública
1844
No dia 14 de fevereiro, Graham Bell solicita a patente do telefone. Duas horas depois, Elisha Gray tenta dar entrada no pedido de patente do seu telefone, mas não consegue
1876
Thomas Edison consegue a patente da lâmpada elétrica
1883
Padre Landell de Moura realiza suas primeiras experiências com a transmissão de voz sem fio em São Paulo
1892/1893
Irmãos Lumière realizam a primeira sessão de cinema do mundo
1895
A bordo do dirigível Nº 6 Santos-Dumont contorna a Torre Eiffel e faz o primeiro vôo controlado de uma máquina mais leve que o ar
1901
Santos-Dumont faz o primeiro vôo homologado com um máquina mais pesada que o ar
1906
1826
Joseph Niépce produz a primeira imagem permanente
1849
Antonio Meucci descobre acidentalmente que a voz pode caminhar por impulsos elétricos. Seis anos depois cria a primeira instalação telefônica do mundo
1882
Graham Bell e William H. Preece transmitem sinais telegráficos através da água do mar entre a Inglaterra e a ilha de Wight usando bobinas de indução
1895
Guglielmo Marconi inventa a telegrafia sem fio ao conseguir enviar sinais a algumas centenas de metros. Depois, conecta o transmissor a uma antena e à terra, conseguindo ampliar a distância em que o sinal era detectado.
1903
Irmãos Wright fazem o polêmico vôo com o Flyer
Nesta década, o comerciante holandês Antonie van Leeuwenhoek fez as primeiras observações de glóbulos vermelhos, espermatozóides e bactérias. Sem saber do que se tratava, o pioneiro da microscopia os chamava de "animaizinhos"
1670
O médico Edward Jenner inoculou um garoto de 8 anos contra a varíola. Foi o primeiro caso de vacinação da história
1796
Crawford Long usa pela primeira vez o éter com propósitos cirúrgicos
1842
Joseph Lister publica na revista médica The Lancet suas descobertas sobre a necessidade de assepsia nos hospitais
1867
Joseph Lister publica na revista médica The Lancet suas descobertas sobre a necessidade de assepsia nos hospitais
1867
Pasteur desenvolve a vacina contra a raiva
1885
Diante de uma grave epidemia de varíola no Rio, Oswaldo Cruz decide implantar a vacinação obrigatória e maciça da população que, contrariada, promoveu a Revolta da Vacina
1904
Alexander Fleming descobre a penicilina
1928
1793
Philippe Pinel assume a direção do Asilo de Bicêtre, em Paris, e inicia uma revolução no tratamento psiquiátrico
1816
René Laënnec inventa um instrumento que se tornaria mais tarde o estetoscópio
1863
A partir deste ano o químico Louis Pasteur começa a defender que os processos de putrefação são causados por microorganismos. Dessa crença e de muita pesquisa, saiu o processo de pasteurização
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1895
O físico alemão Wilhelm Roentgen descobre os raios X
1906
Ramón y Cajal e Camillo Golgi recebem o Prêmio Nobel de Medicina pela descrição da estrutura dos neurônios
Aristóteles elabora seu sistema filosófico, que balizará toda a ciência ocidental até o início da Era Moderna. Nele, o filósofo diferencia a matéria terrestre da matéria celeste, estabelecendo um dogma que só será superado por Galileu, Kepler e outros
séc. IV a.C.
Galileu nega que os cometas sejam astros supralunares. Contra todas as evidências já disponíveis na época, o físico retoma Aristóteles, que afirma serem os cometas meros efeitos da atmosfera. Tudo para salvar o dogma da circularidade dos movimentos celestes
1623
Descartes publica Princípios da filosofia, no qual procura expurgar as superstições e explicar todos os fenômenos de forma mecânica. Sua física, porém, revela-se insustentável e, em poucas décadas, será completamente ultrapassada por Newton, que retoma a ideia da ação a distância
1644
Kelvin calcula o tempo de duração da atividade solar e chega a 20 milhões de anos. Se verdadeiro, tal valor destruiria a teoria evolucionista de Darwin, pois não haveria tempo suficiente para as espécies evoluírem. Sabemos, hoje, que o Sol está ativo há 4,6 bilhões de anos
1862
Bohr, liderando um brilhante time de físicos, chega à sua interpretação probabilística da mecânica quântica, tida, até hoje, como definitiva. Porém, pouco mais tarde, David Bohm demonstra que a também interpretação causal é perfeitamente possível
1927
séc. III a.C.
Euclides sintetiza toda a geometria grega. Seu tratado Os elementos será, por mais de dois milênios, o modelo por excelência da literatura científica. No século XIX, descobre-se que a geometria euclidiana é apenas uma das muitas possíveis
1492
Colombo chega à América, acreditando haver encontrado o caminho marítimo ocidental para a Índia. Seu prognóstico sobre a duração da viagem baseou-se em um erro de cálculo relativo ao grau da longitude terrestre e ao tamanho dos continentes
1859
Darwin, em sua obra A origem das espécies, sustenta que o uso ou o desuso de certas partes do corpo provocam modificações nos animais, transmitidas para as gerações seguintes. A teoria, combatida pelos darwinistas, é atribuída a Lamarck, que, todavia, não a criou
1905
Einstein descarta o conceito de éter em sua teoria da relatividade especial. Mas, para acomodar os fenômenos, será obrigado, depois, a atribuir ao espaço-tempo, que é apenas um ente matemático, várias propriedades físicas do éter. Em 1920, ele vai além, e reabilita o éter

Bacillus

1875
Ferdinand J. Cohn contributes to the founding of the science of bacteriology. Cohn publishes an early classification of bacteria, using the genus name *Bacillus* for the first time. He also begins a journal *Beiträge zur Biologie der Pflanten*, in which Koch later publishes.

1876
Robert Koch publishes a paper on his work with anthrax, pointing explicitly to a bacterium as the cause of this disease. This validates the germ theory of disease. His work on anthrax was presented and his papers on the subject were published under the auspices of Ferdinand Cohn.

1878
Joseph Lister publishes his study of lactic fermentation of milk, demonstrating the specific cause of milk souring. His research is conducted using the first method developed for isolating a pure culture of a bacterium, which he names *Bacterium lactis*.

1880
Louis Pasteur develops a method of attenuating a virulent pathogen, the agent of chicken cholera, so it would immunize and not cause disease. This is the conceptual breakthrough for establishing protection against disease by the inoculation of a weakened strain of the causative agent. Pasteur uses the word "attenuated" to mean weakened. As Pasteur acknowledged, the concept came from Jenner's success at smallpox vaccination.

1881
Robert Koch struggles with the disadvantages of using liquid media for certain experiments. He seeks out alternatives, and first uses an aseptically cut slice of a potato as a solid culture medium. He also turns to gelatin, which is added to culture media; the resulting mixture is poured onto flat glass plates and allowed to gel. The plate technique is used to isolate pure cultures of bacteria from colonies growing on the surface of the plate.

1882
Ilya Ilich (Élie) Metchnikoff demonstrates that certain body cells move to damaged areas of the body, where they consume bacteria and other foreign particles. He calls the process phagocytosis. He proposes a theory of cellular immunity. With Ehrlich, Metchnikoff is awarded the Nobel Prize in Medicine or Physiology in 1908.

1884
Robert Koch publishes a *The Etiology of Tuberculosis*, in which he followed three steps: 1) the presence of the tubercule bacillus (as proved by staining) in tubercular lesions of various organs of humans and animals, 2) the cultivation of the organisms in pure culture on blood serum, and 3) the production of tuberculosis at will by its inoculation into guinea pigs. Koch was awarded the Nobel Prize in Physiology or Medicine in 1905.

1885
Louis Pasteur oversees injections of the child Joseph Meister with "aged" spinal cord infected with rabies virus. Pasteur uses the term "virus," meaning poison, but has no idea of the nature of the causative organism. Although the treatment is successful, the experiment itself is an ethical violation of research standards. Pasteur knew he was giving the child successively more dangerous portions.

1889
Martinus Beijerinck uses enrichment culture, minus nitrogenous compounds, to obtain a pure culture of the root nodule bacterium *Rhizobium*, demonstrating that enrichment culture creates the conditions for optimal growth of a desired bacterium.

1890
Emil von Behring and **Shibasaburo Kitasato** announce the discovery of diphtheria antitoxin serum. They inject a sublethal dose of diphtheria filtrate into animals and produce a serum that is specifically capable of neutralizing the toxin. They then inject the antitoxin serum into an uninfected animal to prevent a subsequent infection. Behring was awarded the Nobel Prize in Physiology or Medicine in 1901.

1890
Sergei Winogradsky succeeds in isolating nitrifying bacteria from soil. During the period 1890–91, Winogradsky performs the major definitive work on organisms responsible for the process of nitrification.

1891
Paul Ehrlich proposes that antibodies are responsible for immunity. He shows that antibodies form against the plant toxins ricin and abrin. With Metchnikoff, Ehrlich is jointly awarded the Nobel Prize in Physiology or Medicine in 1908.

1892
Dmitri Ivanowski publishes the first evidence of the filterability of a pathogenic agent, the virus of tobacco mosaic disease. He passes the agent through candle filters that retain bacteria, but can't be sure that the agent is a unique organism.

1893
Theobald Smith and **F.L. Kilbourne** establish that ticks carry *Babesia microti*, which causes babesiosis in animals and humans. This is the first account of a zoonotic disease and also the foundation of all later work on the animal host and the arthropod vector.

1899
Martinus Beijerinck recognizes soluble living microbes, a term he applies to the discovery of tobacco mosaic virus. A filtrate free of bacteria retains ability to cause disease in plants even after repeated dilutions. He calls the agent "contagium vivum fluidium"—contagious living fluid.

1899
The organizing meeting of the **Society of American Bacteriologists** is held at Yale, 27–29 December 1899. The Society is the first independent organization devoted to the promotion and service of bacteriology in the United States. It later becomes the American Society for Microbiology.

1900
Based on work of **Walter Reed**, it is demonstrated that yellow fever is caused by a filterable virus transmitted by mosquitoes. This is the first report of a viral agent known to cause human disease. Based on the findings of the Yellow Fever Commission, mosquito eradication programs were begun.

1911
Francis Peyton Rous discovers a virus that can cause cancer in chickens by injecting a cell-free filtrate of tumors. In 1909 a farmer brought Rous a hen that had a breast tumor. Rous performed an autopsy, extracted tumor cells, and injected them into other hens, where sarcoma developed. This is the first experimental proof of an infectious etiologic agent of cancer. Rous is awarded the Nobel Prize in Physiology or Medicine in 1966.

1912
Paul Ehrlich announces the discovery of an effective cure (Salvarsan) for syphilis, the first specific chemotherapeutic agent for a bacterial disease. Ehrlich was a researcher in Koch's lab, where he worked on immunology. He sought an arsenic derivative. The 606th compound worked. He brought news of the treatment to London, where Fleming became one of the few physicians to administer it.

1915/1917
The first discovery of bacteriophage, by **Frederick Twort**. Twort's discovery was something of an accident. He had spent several years growing viruses and noticed that the bacterial colonies became transparent, which indicated that they had lysed. **Felix d'Herrelle** independently describes bacteriophage and coins the name "bacteriophage."

1926
Albert Jan Kluyver and **Hendrick Jean Louis Donker** propose a universal model for metabolic events in cells based on a transfer of hydrogen atoms. The model applies to aerobic and anaerobic organisms.

1928
Frederick Griffith discovers transformation in bacteria and establishes the foundation of molecular genetics. He shows that injecting mice with a mixture of live, avirulent, rough *Streptococcus pneumoniae* type I and heat-killed, virulent smooth *S. pneumoniae* type II leads to the death of the mice. Live, virulent, smooth *S. pneumoniae* type II are isolated from the dead mice. Not until 1944 did Avery, Macleod, and McCarty take up Griffith's work and try to explain the results.

1929
Alexander Fleming publishes the first paper describing penicillin and its effect on gram-positive microorganisms. This finding is unique since it is a rare example of bacterial lysis and not just microbial antagonism brought on by the mold *Penicillium*. When penicillin is finally produced in major quantities in the 1940s, its power and availability effectively launch the "Antibiotics Era." With Florey and Chain, Fleming is awarded the Nobel Prize in Physiology or Medicine in 1945.

1931
C. B. Van Niel shows that photosynthetic bacteria use reduced compounds as electron donors without producing oxygen. Sulfur bacteria use H_2S as a source of electrons for the fixation of carbon dioxide. He posits that plants use water as a source and release oxygen.

1935
Gerhard J. Domagk uses a chemically synthesized antimetabolite, Prontosil, to kill streptococci in mice. It is later shown that Prontosil is hydrolyzed in vivo to an active compound, sulfanilamide. One of the first patients to be treated with Prontosil was Domagk's daughter, who had a streptococcal infection that was unresponsive to other treatments. Domagk is awarded the Nobel Prize in Physiology or Medicine in 1939.

1935
Wendell Stanley crystallizes tobacco mosaic virus and shows it remains infectious. However, he does not recognize that the infectious material is nucleic acid and not protein. Together with Northrop and Sumner, Stanley is awarded the Nobel Prize in Chemistry in 1946.

1941
George Beadle and **Edward Tatum** jointly publish a paper on their experiments using the fungus *Neurospora crassa* to establish that particular genes are expressed through the action of correspondingly specific enzymes. The first gene to be identified controlled the synthesis of an enzyme in a series that led to generation of niacin. This report is the genesis of the "one gene-one enzyme" concept. With Lederberg, Beadle and Tatum are awarded the Nobel Prize in Physiology or Medicine in 1958.

1943
Max Delbrück and **Salvador Luria** provide a statistical demonstration that inheritance in bacteria follows Darwinian principles. Particular mutants, such as viral resistance, occur randomly in bacterial populations, even in the absence of the virus. More importantly, they occur in small numbers in some populations and in large numbers in other cultures. With Delbrück and Hershey, Luria is awarded the Nobel Prize in Physiology or Medicine in 1969.

1944
Oswald Avery, Colin MacLeod, and **Maclyn McCarty** show that transformation of *Streptococcus pneumoniae* from an avirulent phenotype to a virulent phenotype is the result of the transfer of DNA from dead smooth organisms to live rough ones. They also show that the transforming principle is destroyed by pancreatic deoxyribonuclease, which hydrolyzes DNA but is not affected by pancreatic ribonuclease or proteolytic enzymes.

1944
Albert Schatz, E. Bugie, and **Selman Waksman** discover streptomycin, soon to be used against tuberculosis. Streptomycin has the same specific antibiotic effect against gram-negative microorganisms as penicillin does on gram positives. Waksman is awarded the Nobel Prize in Physiology or Medicine in 1952.

1946
Joshua Lederberg and **Edward L. Tatum** publish the first paper on conjugation in bacteria. The process is based on the generation of daughter cells able to grow in media that cannot support growth of either of the parent cells. Their experiments showed that this type of gene exchange requires direct contact between bacteria. From the work of Beadle and Tatum, Lederberg knew that fungi reproduced sexually, and he suspected that bacteria did as well.

1949
Microbiologist **John Franklin Enders**, virologist **Thomas H. Weller,** and physician **Frederick Chapman Robbins** together develop a technique to grow poliovirus in test tube cultures of human tissues. This approach gave virologists a practical tool for the isolation and study of viruses. Enders, Weller, and Robbins were awarded the Nobel Prize in Medicine in 1954.

1952
Joshua Lederberg and **Norton Zinder** report on transduction, or transfer of genetic information by viruses. They show that a phage of *Salmonella typhimurium* can carry DNA from one bacterium to another.

1952
Alfred Hershey and **Martha Chase** suggest that only DNA is needed for viral replication. They use radioactive isotopes ^{35}S to track protein and ^{32}P to track DNA and show that progeny T2 bacteriophage isolated from lysed bacterial cells have the labeled nucleic acid. Further, most of the labeled protein does not enter the cells but remains attached to the bacterial cell membrane.

1953
James Watson and **Francis Crick,** together with **Maurice Wilkins,** describe the double-helix structure of DNA. The chemical structure is based on X-ray crystallography of DNA done by Rosalind Franklin. Crick, Wilkins, and Watson are awarded the Nobel Prize in Physiology or Medicine in 1962.

1959
Peter Mitchell proposes the chemiosmotic theory, in which a molecular process is coupled to the transport of protons across a biological membrane. He argues that this principle explains ATP synthesis, solute accumulations or expulsions, and cell movement (flagellar rotation). Mitchell is awarded the Nobel Prize in Chemistry in 1978.

1960
Francois Jacob, David Perrin, Carmen Sanchez, and **Jacques Monod** propose the operon concept for control of bacteria gene action. Jacob and Monod later propose that a protein repressor blocks RNA synthesis of a specific set of genes, the *lac* operon, unless an inducer, lactose, binds to the repressor. With Lwoff, Jacob and Monod are awarded the Nobel Prize in Physiology or Medicine in 1965.

1961
Marshall Nirenberg and **J. H. Matthaei** observe that a synthetic polynucleotide, poly U, directs the synthesis of a polypeptide composed only of phenylalanine. They conclude that the triplet UUU code for phenylalanine. This is the start of successful efforts to decipher the genetic code. With Robert Holley and Har Gobind Khorana, Nirenberg is awarded the Nobel Prize in Physiology or Medicine in 1968.

1961
Sydney Brenner, Francois Jacob, and **Matthew Meselson** use phage-infected bacteria to show that ribosomes are the site of protein synthesis and confirm the existence of a messenger RNA. They demonstrate that infection of *Escherichia coli* by phage T4 stops cell synthesis of host RNA and leads to T4 specific synthesis. The T4 RNA attaches to cellular ribosomes and directs protein synthesis.

1964
Charles Yanofsky and coworkers define the relationship between the order of mutatable sites in the gene coding for *Escherichia coli* tryptophan synthetase and the corresponding amino acid replacements in the enzyme. Tryptophan synthetase has two subunits, one of which could be mutated. The missense mutants in the alpha subunit could be mapped and related to the genetic fine structure of the gene. The property of correlating a mutation with an amino acid replacement is called colinearity.

1970
Howard Temin and **David Baltimore** independently discover reverse transcriptase in RNA viruses, which uses single-stranded RNA as a template to synthesize a single-stranded DNA complement. This process establishes a pathway for genetic information flow from RNA to DNA. With Dulbecco, Baltimore and Temin are awarded the Nobel Prize in Physiology or Medicine in 1975.

1973
Stanley Cohen, Annie Chang, Robert Helling, and **Herbert Boyer** show that if DNA is broken into fragments and combined with plasmid DNA, such recombinant DNA molecules will reproduce if inserted into bacterial cells. They show that plasmids act as vectors for maintaining cloned genes. The discovery is a major breakthrough for genetic engineering, allowing for such advances as gene cloning and the modification of genes.

1975
Georg Kohler and **Cesar Milstein** physically fuse mouse lymphocytes with neoplastic mouse plasma cells to yield hybridomas that also produce specific antibodies and can survive indefinitely in tissue culture. Monoclonal antibodies permit the generation of diagnostic tests that are highly specific and also function as probes to study cell function. With Jerne, Kohler and Milstein are awarded the Nobel Prize in Physiology or Medicine in 1984.

1977
Walter Gilbert and **Frederick Sanger** independently develop methods to determine the exact sequence of DNA. Gilbert uses the technique to determine the sequence of all 5,375 nucleotides of the bacteriophage ΦX174, the first complete determination of the genome of an organism. With Berg, Gilbert and Sanger are awarded the Nobel Prize in Chemistry in 1980.

1977
Carl Woese uses ribosomal RNA analysis to identify a third form of life, the *Archaea*, whose genetic makeup is distinct from but related to both *Bacteria* and *Eucarya*.

1979
Smallpox is declared officially eliminated; last natural case seen in Somalia in 1977. Small quantities of the causative virus, variola virus, remain held under tightly controlled conditions in the U.S. and former U.S.S.R. The only microbial disease ever deliberately eradicated.

1982
Stanley Prusiner finds evidence that a class of infections he calls prions cause scrapie, a fatal neurodegenerative disease of sheep. Prusiner is awarded the Nobel Prize in Physiology or Medicine in 1997.

1983
Luc Montaigner and **Robert Gallo** announce their discovery of the human immunodeficiency virus (HIV) believed to cause AIDS.

1986
Kary Mullis uses a heat-stable enzyme from *Thermus aquaticus* to establish polymerase chain reaction technology. The DNA polymerase replicates the DNA of interest plus oligonucleotide primers on either side. The primers are allowed to anneal and the reaction repeated to amplify the target DNA by many-fold. Mullis is awarded the Nobel Prize in Chemistry in 1993.

1995
Craig Venter, Hamilton Smith, Claire Fraser, and **colleagues at TIGR** elucidate the first complete genome sequence of a microorganism—*Haemophilus influenzae* Rd.

1822 — Louis Pasteur naît à Dôle (Jura).

1824 — Décès de Louis XVIII. Début du règne de Charles X.

1830 — Après la révolution de juillet, Louis-Philippe monte sur le trône. Monarchie parlementaire. Colonisation de l'Algérie.

1832 — Épidémie de choléra à Paris.

1835 — *Le rouge et le noir* de Stendhal. Controverse entre Cuvier (1769-1832) et Geoffroy Saint-Hilaire (1772-1844) sur l'organisation des animaux.

1839 — Schleiden et Schwann fondent la théorie cellulaire, selon laquelle la cellule est l'unité élémentaire universelle des êtres vivants.

1843 — Louis Pasteur entre à l'École normale supérieure de Paris.

1844 — *Les trois mousquetaires* d'Alexandre Dumas.

1847 — Il soutient sa thèse en chimie et physique.

1848 — Révolution. Proclamation de la IIe République, dont Louis-Napoléon Bonaparte est élu président.

1849 — Nouvelle épidémie de choléra à Paris. *La petite Fadette* de George Sand.

1852 — Pasteur est nommé professeur de chimie à l'Université de Strasbourg. Il épouse Marie Laurent, fille du recteur. De ce mariage naîtront un fils et quatre filles, dont trois mourront dans l'enfance.

1853 — Pasteur reçoit un prix pour ses études sur l'acide racémique.

1855 — Pasteur est nommé directeur scientifique et administrateur de l'École normale supérieure de Paris, où il installe son laboratoire.

1857 — Début de ses travaux sur la fermentation alcoolique.

1859 — Champollion (1790-1832) déchiffre les hiéroglyphes. Darwin (1809-1882) publie *De l'origine des espèces*. *Faust* de Gounod.

1862 — Pasteur est élu à l'Académie des sciences.

1863 — Début de ses études sur le vin. Controverses avec Pouchet.

1865 — Mendel (1822-1884) découvre les lois de l'hérédité. Claude Bernard (1813-1878) publie son *Introduction à l'étude de la médecine expérimentale*, où il définit les principes de la recherche fondamentale. Abolition de l'esclavage aux États-Unis. À la demande du gouvernement, il étudie la maladie du ver à soie.

1867 — Pasteur reçoit un prix pour sa méthode de conservation du vin et obtient la chaire de chimie à la Sorbonne. Exposition universelle à Paris.

1868 — *Les misérables* de Victor Hugo. *Déjeuner sur l'herbe* de Manet. Une attaque cérébrale le laisse en partie paralysé.

1870 — *Les Canotiers* de Renoir. Pasteur commence des recherches sur la bière. Guerre franco-allemande. Défaite française et chute de l'Empire. Début de la IIIe République.

1871 — *Le bateau ivre* de Rimbaud. La Commune Paris.

1872 — *Impression soleil levant* de Monet. Mac Mahon président de la République. *Romances sans paroles* de Verlaine.

1873 — Pasteur est élu à l'Académie de médecine. Il étudie les contagions microbiennes.

1876 — Invention du téléphone.

1877 — Pasteur étudie le charbon et le vibrion responsable de la septicémie ; il établit les règles de l'asepsie.

1878 — Edison fait breveter une lampe à incandescence.

1879 — Pasteur découvre l'immunisation par inoculation de cultures atténuées du microbe du choléra des poules. Démission de Mac Mahon. Jules Grévy est élu président.

1881 — Koch découvre le bacille de la tuberculose et, deux ans plus tard, l'agent du choléra. Lois de Jules Ferry pour une école laïque, gratuite et obligatoire (1881-1882). Première expérience réussie de vaccination préventive contre le charbon, sur 60 brebis à Pouilly-le-Fort.

1883 — Mission en Égypte de E. Roux et L. Thuillier, collaborateurs de Pasteur. Controverse avec Koch.

1884 — Loi sur la liberté syndicale.

1885 — Pasteur vaccine Joseph Meister contre la rage. La Chine reconnaît le protectorat français sur le Vietnam. *Germinal* de Zola.

1887 — Pasteur est nommé Secrétaire perpétuel de l'Académie des sciences. Affaire Boulanger. Démission de Grévy. Sadi Carnot est élu président. *Le Horla* de Maupassant.

1888 — Inauguration de l'Institut Pasteur à Paris. *Gymnopédies* de Satie.

1889 — Exposition universelle à Paris. Inauguration de la Tour Eiffel.

1890 — Première manifestation du 1er mai. *Cinq poèmes de Baudelaire* de Debussy.

1892 — Jubilé de Pasteur à la Sorbonne pour ses 70 ans.

1894 — Assassinat du président Sadi Carnot. Jean Casimir-Périer lui succède. Début de l'affaire Dreyfus.

1895 — Pasteur meurt le 28 septembre. Démission de Casimir-Périer. Félix Faure président de la République. Premières projections cinématographiques des frères Lumière.

1822 — Johann Mendel naît le 20 (ou le 22) juillet à Heinzendorf, en Silésie autrichienne (aujourd'hui Hynčice, République tchèque).

1826 — La *Symphonie inachevée*, de Franz Schubert.

1831 — Le botaniste français Augustin Sageret (1753-1852) étudie l'hybridation des melons.

1834 — Le *Zollverein*, union douanière des États allemands, exclut l'Autriche, préparant l'élimination des Habsbourg des affaires allemandes.

1835 — Fondation à Prague de la *Matice ceska*, maison d'édition diffusant des ouvrages littéraires ou scientifiques en langue tchèque.

1836 — *Mai*, poème de Karel Hinek Mácha.

1840 — Ferdinand Ier succède à son père François II à la tête de l'Empire autrichien. Le pouvoir est aux mains d'un conseil de régence présidé par Metternich.

1843 — Mendel obtient son diplôme du *Gymnasium* de Troppau, puis fréquente l'Institut philosophique d'Olmütz, en Moravie.

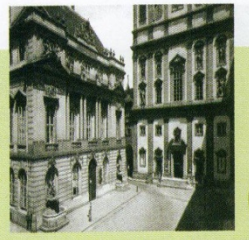
Novice au monastère de Saint-Thomas à Brünn, Mendel prend le nom de Gregor.

1848 — Mendel signe une pétition revendiquant des droits civiques pour les moines.

Révolutions de Prague et Vienne pour une renaissance culturelle et nationale tchèque. Metternich est chassé. La famille impériale se réfugie à Olmütz. Ferdinand Ier abdique en faveur de son neveu François-Joseph.

1849 — Victoire autrichienne dans le Piémont (Italie). François-Joseph rétablit la domination autrichienne sur la Lombardie et réprime la rébellion hongroise avec l'aide du tsar Nicolas Ier.

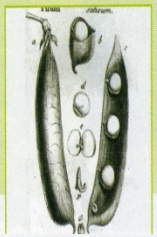
1851 — Mendel est auditeur en sciences naturelles à l'Université de Vienne.



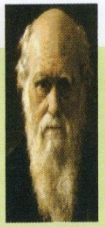
1853 — De retour à Brünn, Mendel est nommé professeur remplaçant dans un institut supérieur d'orientation technique.

1854 — Il publie une communication sur les dommages provoqués par la bruche du pois sur les cultures.

1856 — Il entame des croisements sur les plantes du pois.



1859 — Charles Darwin (1809-1882) présente sa théorie de l'évolution dans *De l'origine des espèces*.

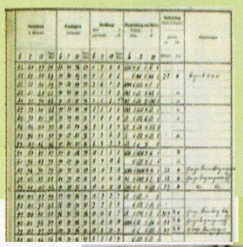


1861 — Entrée du Parti national tchèque au Parlement.

Défaite autrichienne à Magenta et Solferino contre l'alliance franco-sarde : les Autrichiens sont chassés de Lombardie.

1862 — Fondation du *Sokol*, mouvement sportif nationaliste tchèque.

Mendel présente ses premières observations météorologiques.



1865 — Mendel expose ses résultats sur l'hérédité des caractères. Le botaniste français Charles Naudin (1815-1899) établit indépendamment une partie de ces résultats à partir de croisements sur le datura, la linaire et le tabac.

1866 — Mendel publie ses conférences dans les actes de la Société des sciences naturelles. Karl Wilhelm von Nägeli entame avec lui une correspondance scientifique soutenue.

Défaite autrichienne contre la Prusse à Sadowa. L'Autriche est exclue de la nouvelle confédération germanique et la Vénétie est rendue aux Italiens.

La fiancée vendue, opéra de Bedřich Smetana.

1867 — Création de la monarchie austro-hongroise : un roi, deux gouvernements, deux parlements.

1868 — Mendel est élu membre du Comité central de la Société d'agriculture de Silésie et Moravie, dont il deviendra président deux ans plus tard.

1870 — L'abbé Napp décède. Mendel est élu nouvel abbé du monastère de Saint-Thomas. et doit interrompre une partie de ses recherches.

1871 — Naissance du peintre abstrait Francišek Kupka.

1877 — *Contes de Mala Strana*, recueil satirique de Jan Neruda.

1878 — Il est élu vice-président de la Société d'apiculture de la Moravie.

Le traité de Berlin confie à l'Autriche-Hongrie l'administration de la Bosnie-Herzégovine ottomane, qui s'est soulevée en 1875.

1884 — Mendel décède à Brünn le 6 janvier. Le nouvel abbé fait détruire ses documents personnels et notes scientifiques.

Danses slaves, d'Antonin Dvořák.

1900 — Hugo de Vries, Carl Correns et Erich von Tschermak redécouvrent les articles de génétique de Mendel.

1902 — Walther Flemming observe pour la première fois les chromosomes, que Walter Sutton identifie comme la structure porteuse des gènes. William Bateson et Lucien Cuénot démontrent la validité des lois de Mendel chez l'animal.

1905 — Bateson crée le terme « génétique ».

1911 — Wilhelm Johannsen distingue le *génotype* du *phénotype*.

1915 — Thomas Morgan présente sa théorie chromosomique de l'hérédité dans *Mechanism of mendelian heredity*.

1940 — George Beadle et Edward Tatum montrent qu'il existe une relation précise entre les gènes et les protéines.

1944 — Oswald Avery démontre que les gènes sont constitués d'ADN.

1953 — James Watson et Francis Crick découvrent la structure à double hélice de l'ADN.

1961 — André Lwoff, François Jacob et Jacques Monod montrent que l'expression des gènes est contrôlée par des protéines.

INTRODUÇÃO

A Peste de Ashdod, de Nicolas Poussin, 1631. Desde a Antigüidade e por muitos séculos acreditou-se que as grandes epidemias fossem causadas por impurezas atmosféricas e que as doenças pudessem ser transmitidas pelo mau cheiro de cadáveres e enfermos

21 PROJETS FOUS pour le XXIe siècle

L'accélérateur du savoir
Science & Vie
Mensuel n° 1000 - janvier 2001

1913-2001
Un siècle de science et de vie

spécial numéro 1000

Axel Kahn

Généticien, institut Cochin de génétique moléculaire

Le premier antibiotique

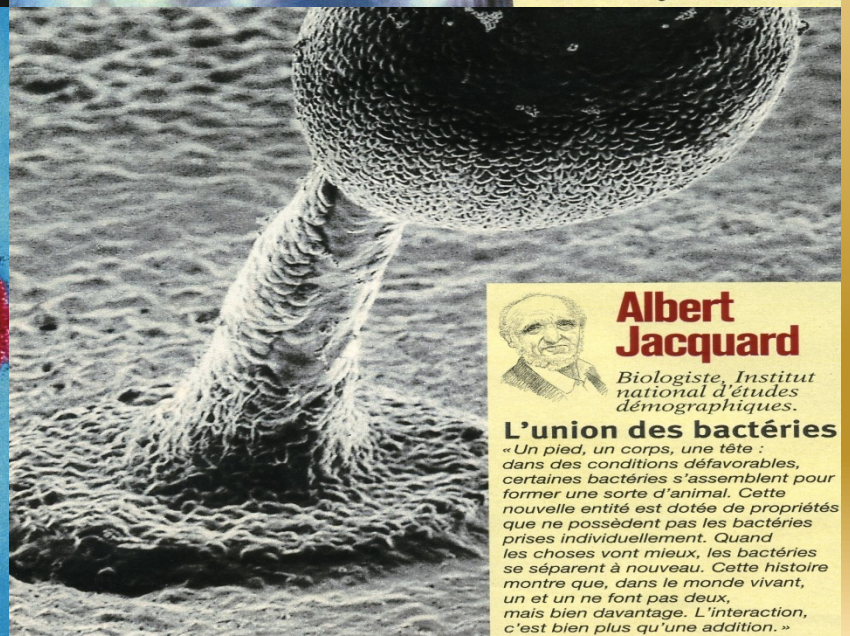
« En 1928, quand Alexander Fleming prit cette photo d'une culture de staphylocoques détruite par le champignon penicillium, il ne savait pas encore qu'il avait sous les yeux l'un des médicaments les plus importants du siècle : le premier antibiotique. Cette découverte est l'héritière de trois grands bouleversements scientifiques du XIXe siècle : la théorie de l'évolution de Charles Darwin, la découverte de la génétique par Gregor Mendel, et celle des micro-organismes par Louis Pasteur. Elle me paraît emblématique du rôle majeur que jouent désormais les biotechnologies en médecine. »

Luc Montagnier

Médecin, Institut Pasteur.

Le virus du sida

« Quand j'ai vu cette image pour la première fois, j'ai été frappé de constater que ce virus ne ressemblait à rien de connu chez l'homme. Nous avons alors pensé qu'il pouvait être responsable de cette nouvelle maladie. Ce fut déterminant pour l'orientation de nos recherches. »



Albert Jacquard

Biologiste, Institut national d'études démographiques.

L'union des bactéries

« Un pied, un corps, une tête : dans des conditions défavorables, certaines bactéries s'assemblent pour former une sorte d'animal. Cette nouvelle entité est dotée de propriétés que ne possèdent pas les bactéries prises individuellement. Quand les choses vont mieux, les bactéries se séparent à nouveau. Cette histoire montre que, dans le monde vivant, un et un ne font pas deux, mais bien davantage. L'interaction, c'est bien plus qu'une addition. »

LES GRANDES ÉPIDÉMIES DE L'HISTOIRE DE L'HUMANITÉ

Table 2
Suspected and potential typhus outbreaks, based on historical, clinical, and epidemiologic descriptions

Outbreak	Period	Likelihood	Other possible diseases
Athenian plague	Fifth century BC	Possible	Smallpox
Antonine plague (Western Europe)	Second century AD	Unlikely	Smallpox
Justinian plague (Western Europe)	Sixth century	Unlikely	Plague
Crusades (Europe)	Thirteenth century	Possible	Plague, dysentery
Conquest of Granada	Fifteenth century	Likely	
Mexico	Sixteenth century	Likely	Smallpox
Hungarian disease	Sixteenth century	Likely	
30 Years' War (Europe)	Seventeenth century	Likely	
Napoleonic Wars (Eastern Europe)	1812	Likely	Other louse-borne diseases
World War I (Russia, Europe)	1914–1918	Proven	Trench fever
Bolchevik Revolution (Russia)	1917–1925	Proven	Other louse-borne diseases
World War II (Europe, North Africa)	1940–1945	Proven	
Burundi civil war (Africa)	1997–present	Proven	Trench fever

Data from Refs. [1,2,28].

Table 1 (*continued*)

Year	Conflict	Sample afflicted group or location	Disease	Estimated mortality
1596–1602	Anglo-Spanish War (1587–1604)	Spain	Bubonic plague	0.5–0.6 million
1632–1633	Thirty Years' War (1618–1648)	Protestant population, Dresden	Bubonic plague	7714
1643	English Civil War (1640–1649)	Parliamentary Army at Reading	Typhus fever	? ("great mortality")
1650	Cromwell's Irish Campaign (1649–1650)	Garrison at Kilkenny	Bubonic plague	900 (cavalry and foot soldiers)
1689	Irish War (1689–1691)	Protestant Army (near Dundalk)	Typhus fever	6000
1709	Second Northern War (1700–1721)	Danzig	Bubonic plague	32,599
1717	Austro-Turkish War (1716–1718)	Austrian troops at Siege of Belgrade	Typhus and dysentery	4000
1738	Russo-Austrian War (1735–1739)	Russian troops	Bubonic plague	30,000
1761–1762	Seven Years' War (1756–1763)	British forces at Siege of Habana	Yellow fever	8000
1771–1772	Russo-Turkish War (1768–1772)	Moscow	Bubonic plague	52,300
1781	Comuneros' uprising in New Granada (1781)	Socorro	Smallpox	6000
1792–1795	War of the First Coalition (1792–1797)	Metz	Typhus fever	4870
1801–1803	Haitian-French War (1801–1803)	French Army in Haiti	Yellow fever	22,000
1808	Peninsular War (1808–1814)	Besieged military and civilian population, Saragossa	Typhus fever	72,000
1809	Walcheren expedition (1809–1810)	British Army on Walcheren Island	Malaria, typhus, typhoid, and dysentery	3960
1812–1813	Napoleon's Russian expedition (1812–1813)	French soldiers and civilians at Vilna	Typhus fever	55,000
1831	Polish insurrection (1830–1831)	Warsaw Province	Cholera	13,103
1854–1856	Crimean War (1853–1856)	British and French Armies, Black Sea	Cholera	circa 18,000
1866	Austro-Prussian War (1866)	Austrian Crownlands	Cholera	165,000
1870–1871	Franco-Prussian War (1870–1871)	France and Germany	Smallpox	circa 300,000
1898	Spanish-American War (1898)	US Volunteer Army, USA	Typhoid fever	circa 1500

Table 1
Sample epidemic events associated with war, 500 BC to AD 2000

Year	Conflict	Sample afflicted group or location	Disease	Estimated mortality
circa 480 BC	Persian invasion of Greece (480–479 BC)	Persian Army in Greece	Plague or dysentery (?)	> 300,000 (?)
430–425 BC	Great Peloponnesian War (431–404 BC)	Athens	Unknown	> 100,000 (?)
212 BC	Second Punic War (218–202 BC)	Russian Army at Siege of Syracuse	Influenza (?)	?
88 BC	Social War (91–88 BC)	Army of Octavius in Rome	?	17,000
AD 125	Roman colonial wars, Africa	Roman Army in Utica	?	up to 30,000
251–266	Roman-Gothic War (249–270)	Africa, Europe, and Near East	Measles or smallpox (?)	up to 5000/d (Rome)
425	Hun raids on Roman Empire (*c*.375–454)	Hun Army (advance on Constantinople)	?	? (epidemic forced retreat)
569 or 571	Elephant War (569 or 571)	Abyssinian Army at Siege of Mecca	Bubonic plague with smallpox (?)	60,000 (?)
638–639	Muslim conquest of Persia (634–651)	Syrian Army in Amwäs	?	25,000 (in 639)
1010 or 1011	Later Viking raids in England (899–1016)	Danes in Kent	*Dolor viscerum* (dysentery) (?)	?
1148	Second Crusade (1147–1149)	Army of Louis VII and civilians at Adalia	Typhoid, dysentery, or bubonic plague (?)	?
1218	Fifth Crusade (1217–1221)	Crusader Army at Damietta	Severe scurvy	? (15%–20% of army)
1270	Eighth Crusade (1270)	Crusader Army at Carthage	Dysentery	? ("many deaths")
1346	Siege of Kaffa	Tartar Army at Kaffa	Bubonic plague	? ("infinite' numbers")
1485	Wars of the Roses (1455–1485)	England	Sweating sickness	? ("most" students at Oxford)
1489–1490	War of Granada (1482–1492)	Spanish Army in Granada	Typhus fever	? (up to 17,000 before 1490)
1495 *ff.*	Italian Wars (1494–1495)	Continental Europe	Syphilis	?
1518–1520	Wars of Spanish Conquest (1519–1546)	Mexico	Smallpox	2–15 million
1552	5th War Against Charles V (1552–1559)	Army of Charles V at Metz	Typhus fever and dysentery	10,000

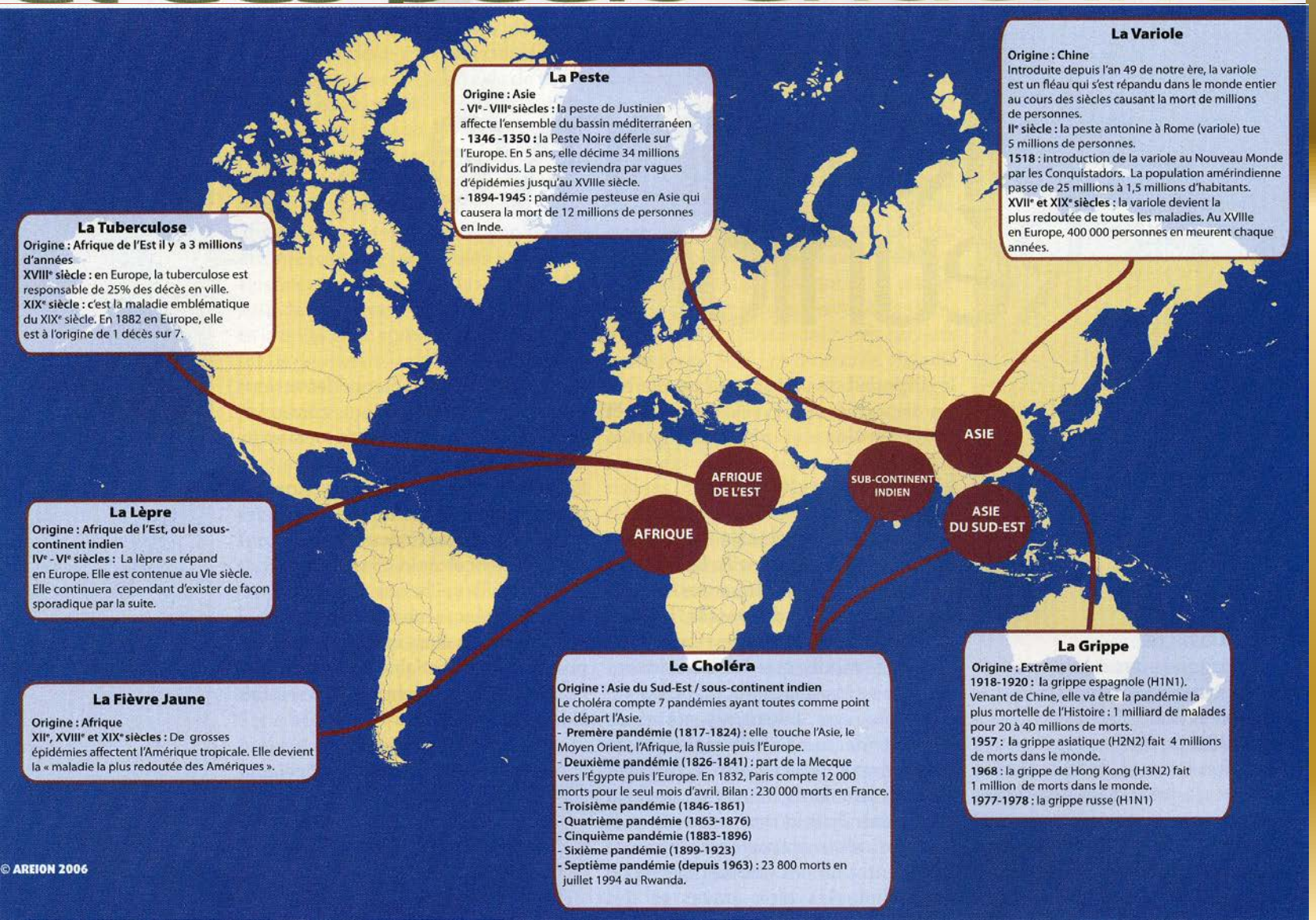
(*continued on next page*)

1902–1904	Philippine-American War (1899–1902)	Philippines	Cholera	circa 200,000
1914–1915	World War I (1914–1918)	Serbian Soldiers and Austrian prisoners of war, Serbia	Typhus and relapsing fevers	30,000
1917–1922	Russian Revolution and Civil War (1917–1921)	Russia	Typhus fever	2.5–3 million
1918–1919	World War I (1914–1918)	Global pandemic	Influenza	20–40 million
1942–1945	World War II (1939–1945)	Allied forces in Pacific and Southeast Asia	Scrub typhus	636
1942–1943	World War II (1939–1942)	Servicemen and civilians, Malta	Poliomyelitis	37
1965–1975	Vietnam War (1964–1973)	Vietnam	Human plague	838 (1966–1970)
1971	Pakistan Civil War (1971)	East Pakistan refugees in India	Cholera	circa 10,000
1984–1994	Sudanese Civil War (1956–)	Upper Nile, Southern Sudan	Visceral leishmaniasis	95,000–112,000
1995–1997	Burundian Civil War (1993–)	Internally displaced persons	Louse-borne typhus	?
1999	Angolan Civil War (1975–)	Luanda and other provinces	Poliomyelitis	circa 80
2002	Operation Enduring Freedom	British forces at Bagram, Afghanistan	Norwalk-like virus disease	0 (29 cases)

Data from Refs. [4,17,18].

M.R. Smallman-Raynor, A.D. Cliff / Infect Dis

Épidémies : histoire des menaces et des peurs anciennes



La Peste

Origine : Asie
- **VIe - VIIIe siècles :** la peste de Justinien affecte l'ensemble du bassin méditerranéen
- **1346 -1350 :** la Peste Noire déferle sur l'Europe. En 5 ans, elle décime 34 millions d'individus. La peste reviendra par vagues d'épidémies jusqu'au XVIIIe siècle.
- **1894-1945 :** pandémie pesteuse en Asie qui causera la mort de 12 millions de personnes en Inde.

La Variole

Origine : Chine
Introduite depuis l'an 49 de notre ère, la variole est un fléau qui s'est répandu dans le monde entier au cours des siècles causant la mort de millions de personnes.
IIe siècle : la peste antonine à Rome (variole) tue 5 millions de personnes.
1518 : introduction de la variole au Nouveau Monde par les Conquistadors. La population amérindienne passe de 25 millions à 1,5 millions d'habitants.
XVIIe et XIXe siècles : la variole devient la plus redoutée de toutes les maladies. Au XVIIIe en Europe, 400 000 personnes en meurent chaque années.

La Tuberculose

Origine : Afrique de l'Est il y a 3 millions d'années
XVIIIe siècle : en Europe, la tuberculose est responsable de 25% des décès en ville.
XIXe siècle : c'est la maladie emblématique du XIXe siècle. En 1882 en Europe, elle est à l'origine de 1 décès sur 7.

La Lèpre

Origine : Afrique de l'Est, ou le sous-continent indien
IVe - VIe siècles : La lèpre se répand en Europe. Elle est contenue au VIe siècle. Elle continuera cependant d'exister de façon sporadique par la suite.

La Fièvre Jaune

Origine : Afrique
XIIe, XVIIIe et XIXe siècles : De grosses épidémies affectent l'Amérique tropicale. Elle devient la « maladie la plus redoutée des Amériques ».

Le Choléra

Origine : Asie du Sud-Est / sous-continent indien
Le choléra compte 7 pandémies ayant toutes comme point de départ l'Asie.
- **Premère pandémie (1817-1824) :** elle touche l'Asie, le Moyen Orient, l'Afrique, la Russie puis l'Europe.
- **Deuxième pandémie (1826-1841) :** part de la Mecque vers l'Égypte puis l'Europe. En 1832, Paris compte 12 000 morts pour le seul mois d'avril. Bilan : 230 000 morts en France.
- **Troisième pandémie (1846-1861)**
- **Quatrième pandémie (1863-1876)**
- **Cinquième pandémie (1883-1896)**
- **Sixième pandémie (1899-1923)**
- **Septième pandémie (depuis 1963) :** 23 800 morts en juillet 1994 au Rwanda.

La Grippe

Origine : Extrême orient
1918-1920 : la grippe espagnole (H1N1). Venant de Chine, elle va être la pandémie la plus mortelle de l'Histoire : 1 milliard de malades pour 20 à 40 millions de morts.
1957 : la grippe asiatique (H2N2) fait 4 millions de morts dans le monde.
1968 : la grippe de Hong Kong (H3N2) fait 1 million de morts dans le monde.
1977-1978 : la grippe russe (H1N1)

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Impact of Plague on Human History

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[c]State University of New York School of Medicine, Stony Brook, NY, USA

Table 1
Clinical presentations of plague

Clinical features	Bubonic[a] plague	Pneumonic plague	Septicemic[a] plague
Symptoms			
Fever/chills	+++	+	+
Malaise/anorexia	+	+	+
Slurred speech/memory loss	++	–	–
Lethargy/delirium/stupor	+++	–	–
Weakness	++	–	–
Ataxia/vertigo	+	–	–
Insomnia	+++	–	–
Dry cough	–	–	
Shortness of breath	–	+	–
Nausea/vomiting/diarrhea	++	–	–
Abdominal pain	+++	–	+
Signs			
Cervical adenitis	+++	–	–
Suppurative lymphadenitis	+++	–	–
Hemorrhagic mediastinitis	–	+	–
Tracheobronchitis	–	++	–
Multilobar pneumonia	–	+++	
Pleural effusion	–	++	–
Cyanosis (late)	+	–	+
Splenomegaly	+	–	–
Petechiae	++	–	–

[a] Secondary plague pneumonia (hematogenous) may complicate bubonic or septicemia plague. Sepsis precedes secondary plague pneumonia by 1–2 days and is characterized by sudden onset of chest pain with hemoptysis and thick mucopurulent sputum.
Data from Refs. [1,10–13].

Table 2
Differential diagnostic features of the Athenian plague

Clinical description by Thucydides	Time of occurrence	Bubonic plague	Typhoid fever	Smallpox	Measles	Epidemic typhus
Rapid onset	Early	+	–	+	+	+
Fever	Early	+	+	+	+	
Red eyes	Early	–	–	+	+	+
Runny nose and sneezing	Early	+	–	–	+	+
Red throat and hoarseness	Early	–	–	–	+	+
Foul breath	Early	–	–	–	+	+
Retching and convulsions	Middle	–	–	–	–	+
Livid red rash	Middle	–	–	+	+	+
Blisters and sores	Middle	+	–	+	–	+
Sensation of intense internal heat	Middle	–	–	+	+	+
Sleeplessness	Late	+	–	–	+	–
Diarrhea	Late	–	+	+	–	+
Gangrene of the body or extremities	Late	–	–	+	–	+
Loss of sight	Late	–	–	+	–	+
Loss of memory	Late	–	–	–	–	+
Death by exhaustion	Late	–	–	–	+	+

Data from Refs. [1,5,10,16,17].

Table 3
Differential diagnostic features of the Antonine plague

Clinical description by Galen	Time of occurrence	Bubonic plague	Typhoid fever	Measles	Epidemic typhus	Smallpox
Rapid onset	Early	+	–	+	+	+
Slight fever	Early	+	+	+	+	+
Foul breath	Middle	–	–	+	+	+
Livid red rash	Middle	–	–	+	+	+
Blisters and sores	Middle	–	–	–	+	+
Sensation of intense internal heat	Middle	–	–	+	+	+
Sleeplessness	Late	+	–	+	–	–
Diarrhea	Late	–	+	–	+	+
Ulcers of the trachea/larynx	Late	–	–	–	–	+
Red throat and hoarseness	Late	–	–	+	+	+
Death by hemorrhage	Late	–	–	–	–	+

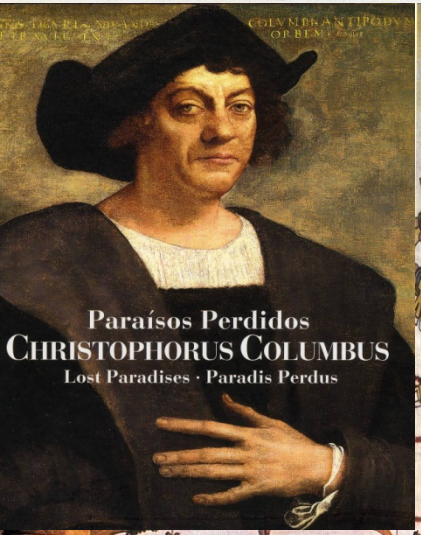
Data from Refs. [1,5,8–10,18,19].

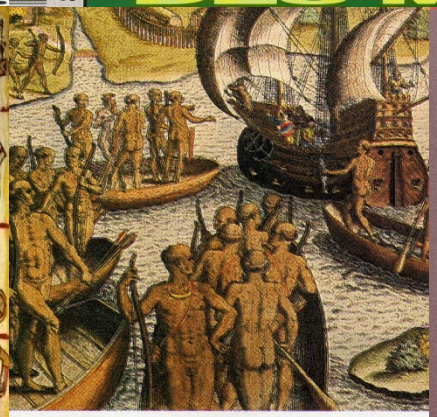
Table 4
Differential diagnostic features of the Justinian plague

Clinical description by Procopius	Time of appearance	Typhoid fever	Measles	Epidemic typhus	Smallpox	Bubonic plague
Rapid onset	Early	–	+	+	+	+
Slight fever	Early	+	+	+	+	+
Coma	Middle	–	–	–	–	+
Buboes	Middle	–	–	–	–	+
Delirium	Middle	–	–	+	–	–
Vomiting blood	Middle	–	–	–	–	+
Sleeplessness	Middle	–	+	–	–	+
Diarrhea	Middle	+	–	+	–	–
Red throat and hoarseness	Middle	–	+	+	+	+
Death by hemorrhage	Late	–	–	–	+	–
Disease leaves many survivors crippled	Late	–	–	–	–	+

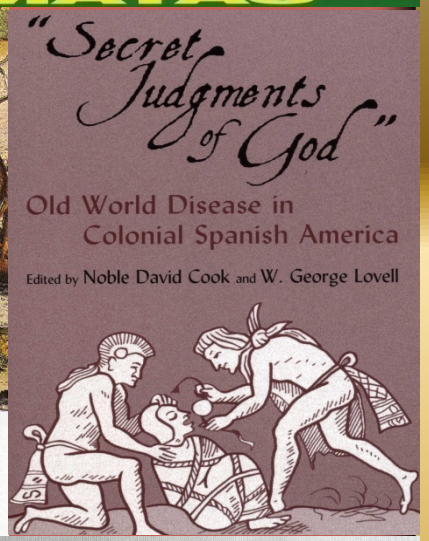
Data from Refs. [1,5,10,22–24].

Le choc microbien

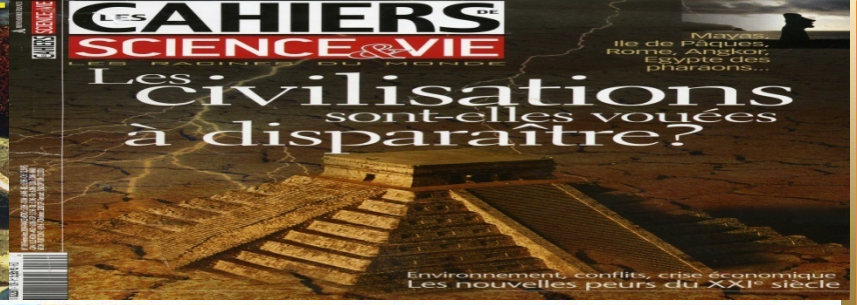


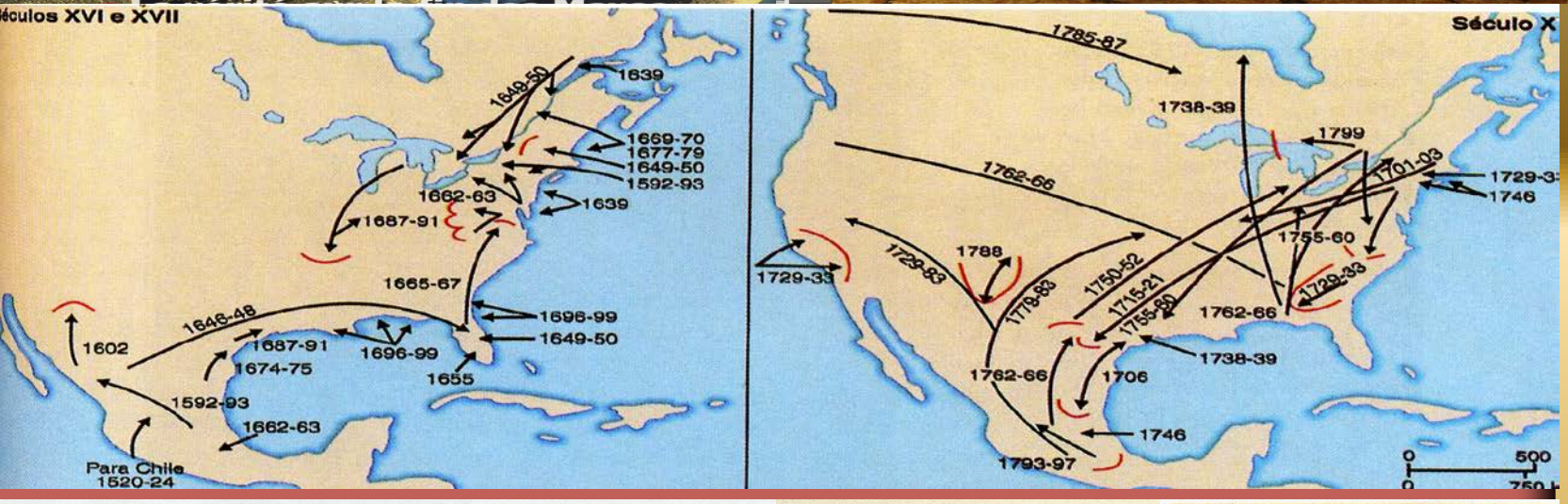


La découverte du Nouveau Monde entraîne des échanges microbiens meurtriers : syphilis dans un sens, grippe et tuberculose dans l'autre.



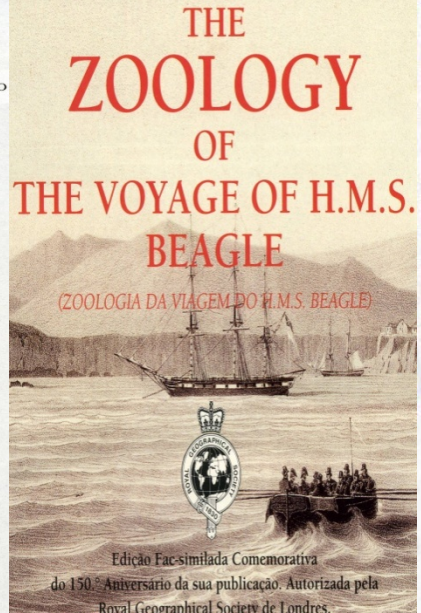
Public Health Service Physician Checking for Signs of Trachoma in Prospective Immigrants at Ellis Island.





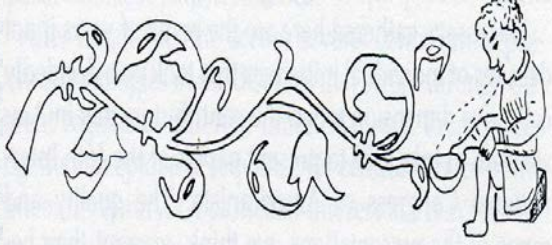
12
Mapa da disseminação da varíola entre os indígenas da América do Norte. A doença espalhou-se pela costa marítima nos séculos XVI e XVII, para depois invadir o interior do continente no século XVIII.

13
Desenho de índios astecas acometidos pela varíola no século XVI. Compilado de um compêndio pelo missionário católico do mesmo século, Frei Bernardino de Sahagún.



OS ALAKALUF, uma das etnias da Patagónia, entretanto exterminadas. Foto de 1890

A Bloody Flux (*Florentine Codex*)



Swelling of the Throat (*Florentine Codex*)

The Herb Seller (*Florentine Codex*)

Abscesses of the Neck (*Florentine Codex*)

Fever (*Florentine Codex*)

Coughing (*Florentine Codex*)

Pustules (*Florentine Codex*)

Table 1.2. Principal causes of disease-related death in central Mexico, 1521–1595

Year	Epidemic
1521	Smallpox
1531	Measles
1545	Typhus (?)
1550	Mumps
1563	Measles (?)
1576	Typhus (?)
1595	Measles

Table 3.1. Old World epidemics in Ecuador, 1524–1618

1524–27	Smallpox epidemic (Huayna Capac falls victim)
1531–33	Possibly plague and measles introduced from Central America
1531	Oroya fever and *verruga peruana* among Pizarro's troops on the coast
[1539]	Smallpox epidemic in Popayán, Colombia
1546	Pneumonic plague, or possibly typhus, in Peru and southern Columbia and hence probably in Ecuador
1558	Smallpox, measles, and possibly influenza
1562	Smallpox in Cuenca
[1566]	Smallpox epidemic in Almaguer, southern Colombia
1582	Epidemic in Cuenca, possibly smallpox
1585–91	Smallpox, measles, and possibly mumps spreading north from Cuzco; typhus moving south from Cartagena
[1589]	Influenza epidemic in Potosí
[1597]	Outbreak of measles and "pains in the side" in Lima
1604	Unidentified epidemic in Quito
1606	Diphtheria in Quito
1611	Measles and typhus in Quito
1612	Scarlet fever appears, with measles and typhus
1614	Typhus and diphtheria present in Quito
[1614]	Diphtheria present in Cuzco
1618	Epidemics of measles and *mal del valle* in the province of Quito

Sources: Evidence for each epidemic is given in the text. The epidemics in brackets occurred in neighboring regions but so far have not been identified in Ecuador.

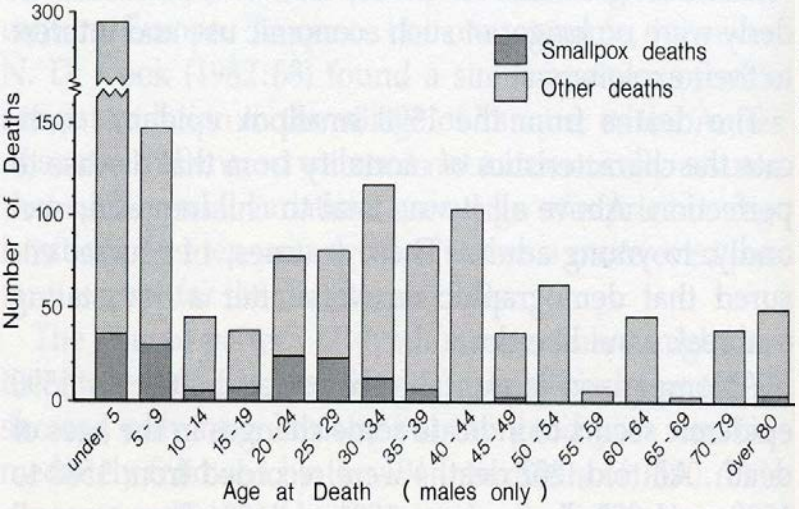


Figure 5.4. Ages of death in Aymaya

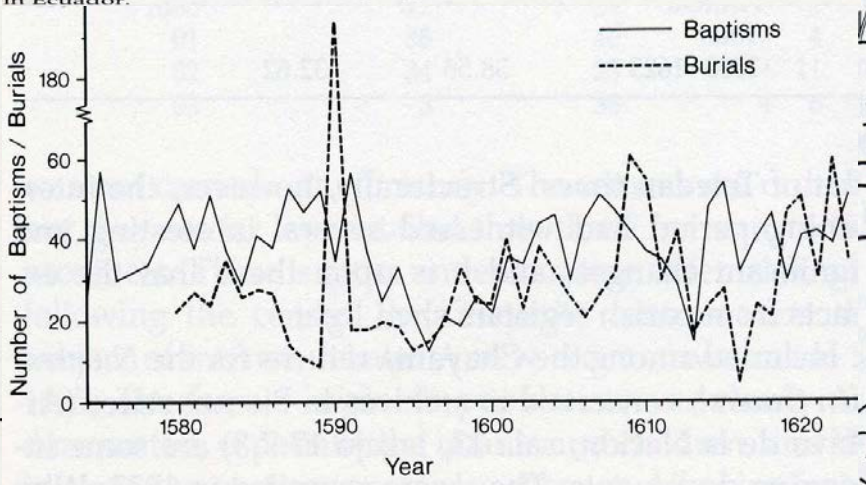
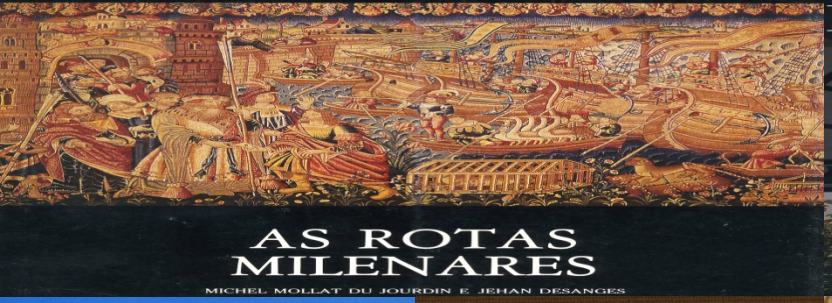
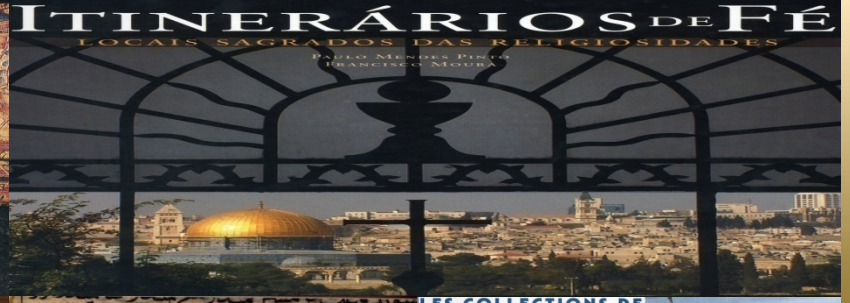
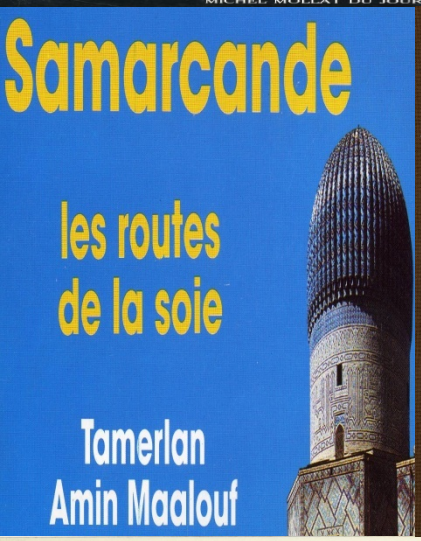
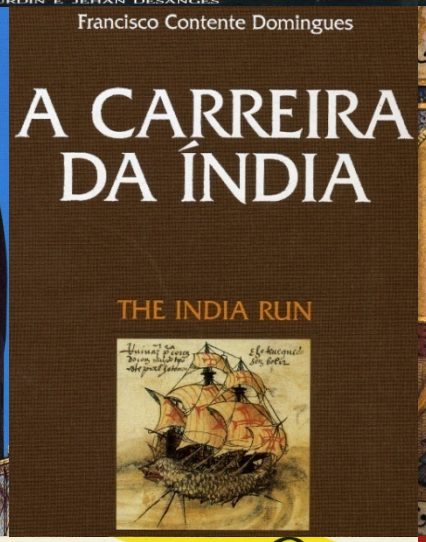


Figure 5.3. Baptisms and burials in Aymaya, 1574–1623


AS ROTAS
MILENARES
MICHEL MOLLAT DU JOURDIN E JEHAN DESANGES

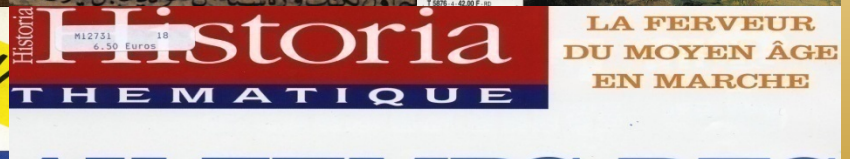

ITINERÁRIOS DE FÉ
LOCAIS SAGRADOS DAS RELIGIOSIDADES
PAULO MENDES PINTO
FRANCISCO MOURA


Samarcande
les routes
de la soie
Tamerlan
Amin Maalouf


Francisco Contente Domingues
A CARREIRA
DA ÍNDIA
THE INDIA RUN

LES COLLECTIONS DE
L'HISTOIRE
L'APPEL DU PAPE
La prise de Jérusalem
200 ANS DE GUERRE SAINTE
Vie et mort
des États croisés
LA RUPTURE AVEC L'ORIENT
La guerre
sainte de l'islam
Le temps des
croisades

L'HISTOIRE
SPECIAL


Historia
THEMATIQUE
LA FERVEUR
DU MOYEN ÂGE
EN MARCHE

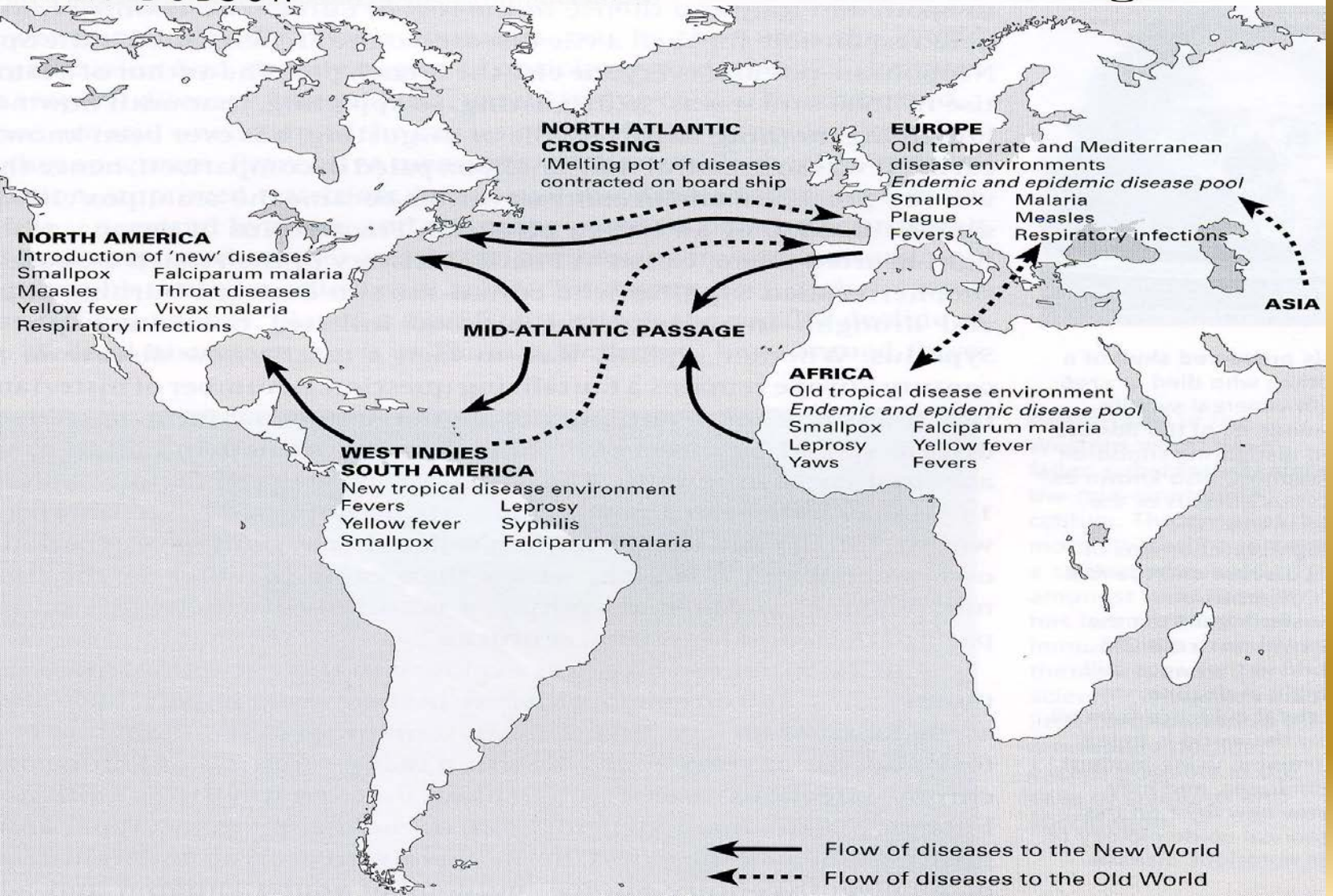
PAIX ET GUERRE
EN
MÉDITERRANÉE
de l'aventure grecque au réveil de l'islam

AU TEMPS DES
PÈLERINAGES

Epidemics and the Geography of Disease

MARY DOBSON

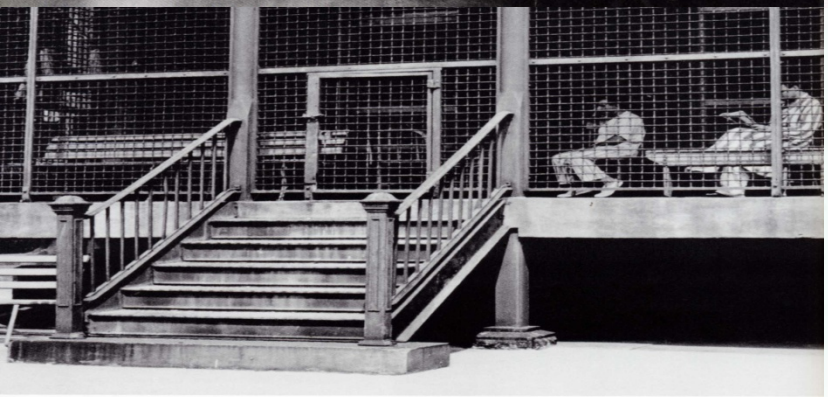
The opening-up of the Americas and the fusing of the Old and New Worlds gave rise to an explosion in the rate and scale of disease exchange. Europeans introduced many diseases to America with severe consequences for native populations. The transfer of slaves from Africa to America added a new element to the Columbian exchange.



Forgotten ELLIS ISLAND

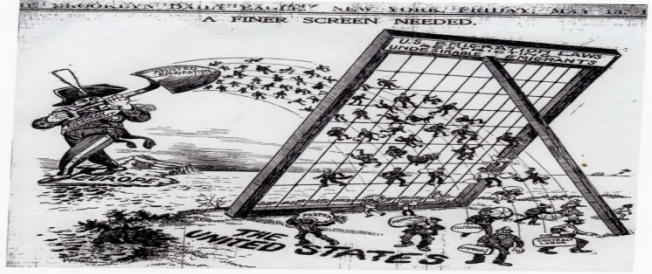
The Extraordinary Story of America's Immigrant Hospital

LORIE CONWAY



Hospital patients in a locked porch of the Contagious Disease Hospital.

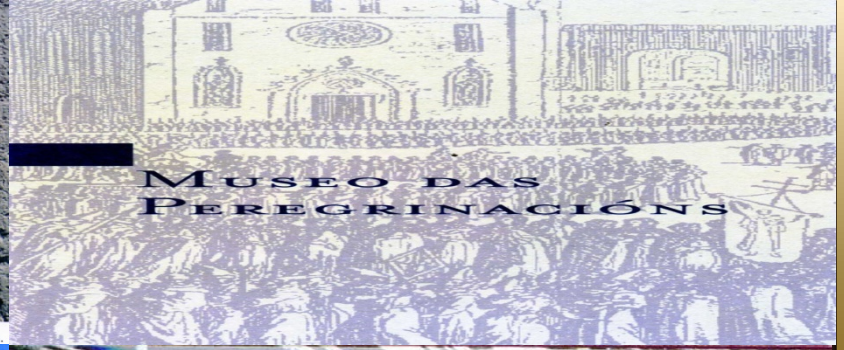
"So far as the restriction of movement is concerned upon the grounds surrounding the hospital, strict attention must be devoted to the retention of patients." DR. EZRA KIMBALL SPRAGUE

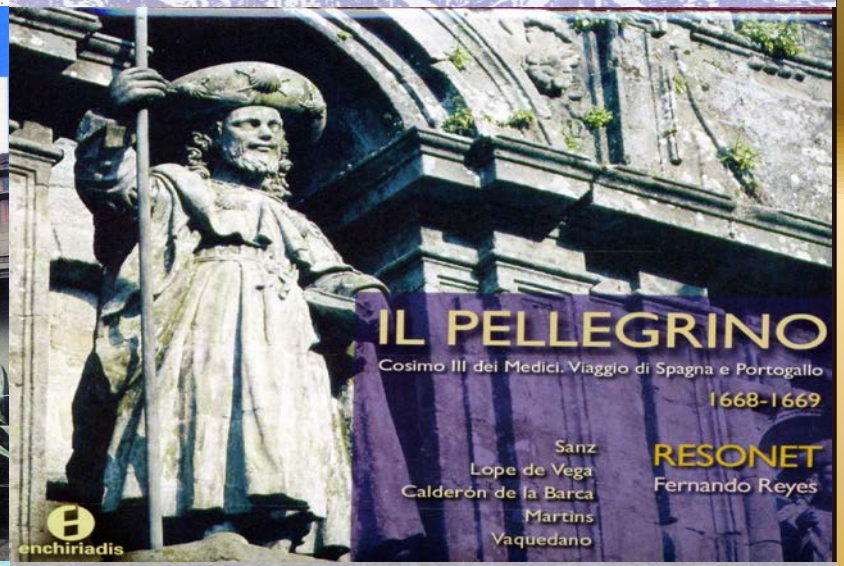


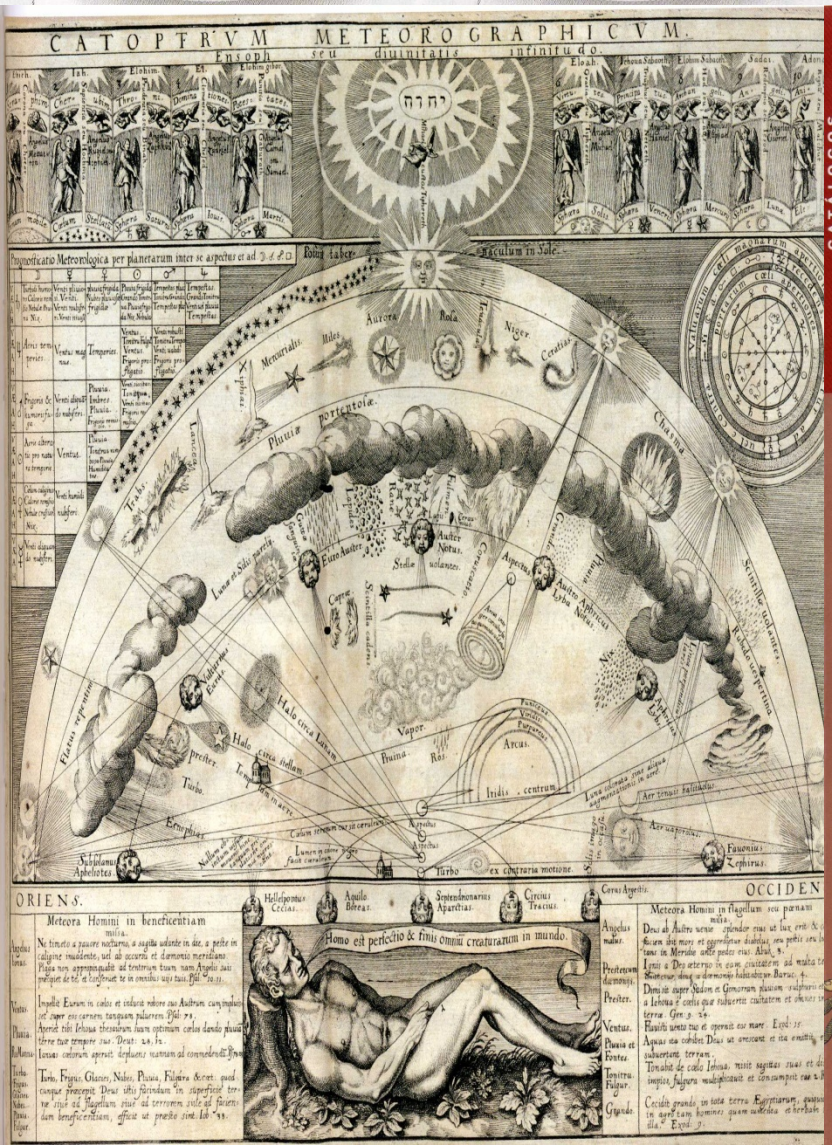
An editorial cartoon calling for a "finer screen" against the increasing numbers of immigrants coming from southern and eastern Europe.

Editorial cartoon illustrating the effects of the quota laws on immigration.

Los peligros del camino eran tales que la muerte no era rara. Las referencias a la muerte son frecuentes durante el trayecto.







CATÁLOGOS

BNP
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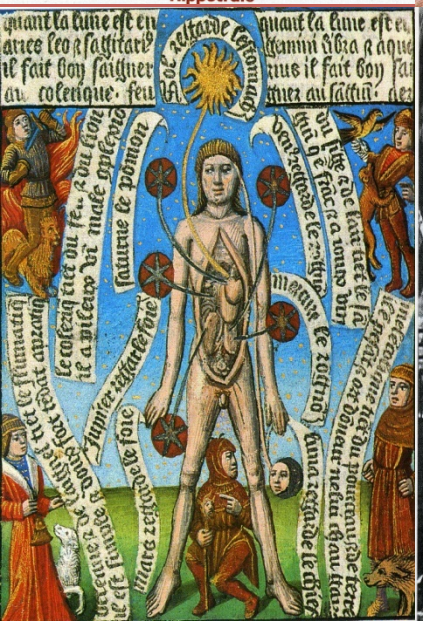
Arte Médica e Imagem do Corpo

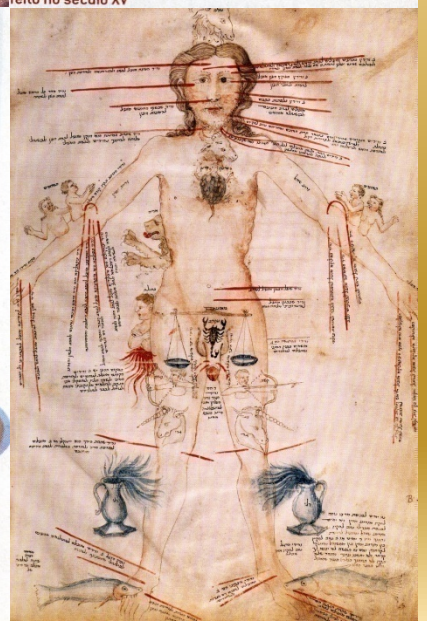
DE HIPÓCRATES AO FINAL DO SÉCULO XVIII

L'AIR DU TEMPS LE RETOUR D'HIPPOCRATE

Hippocrate

RETRATO IMAGINÁRIO de Galeno, provavelmente feito no século XV





VIIIe-XVe siècle

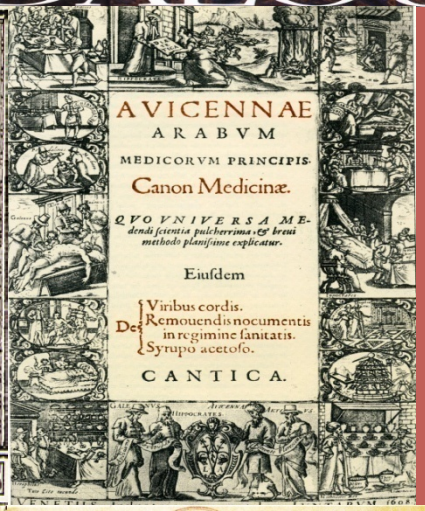
Quand l'Orient civilisait l'Occident

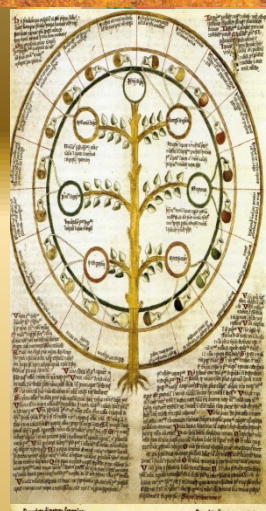
Cordoue, Séville, Grenade...

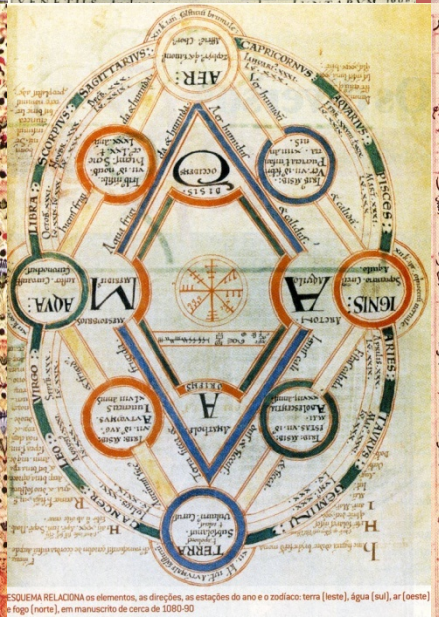
L'ÂGE D'OR DE L'ISLAM ANDALOU

L'âge d'or de la médecine arabe

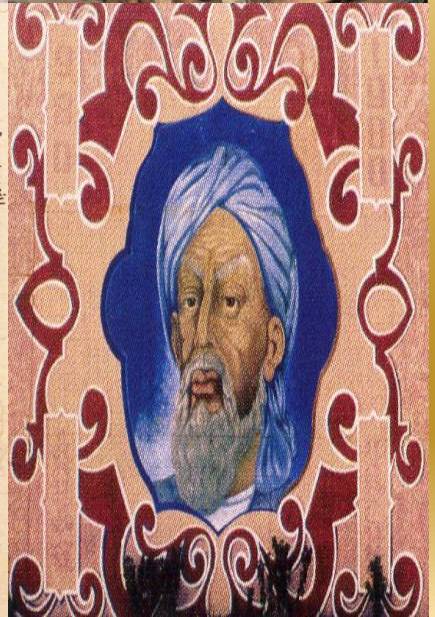
par Françoise Micheau

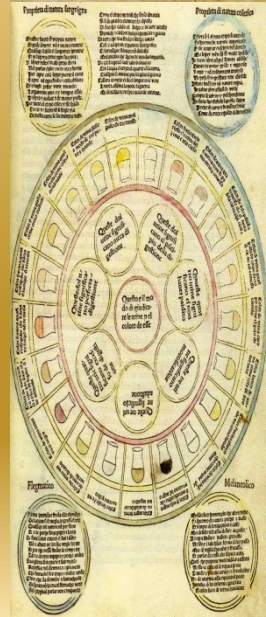






ESQUEMA RELACIONA os elementos, as direções, as estações do ano e o zodíaco: terra (leste), água (sul), ar (oeste) e fogo (norte), em manuscrito de cerca de 1080-90





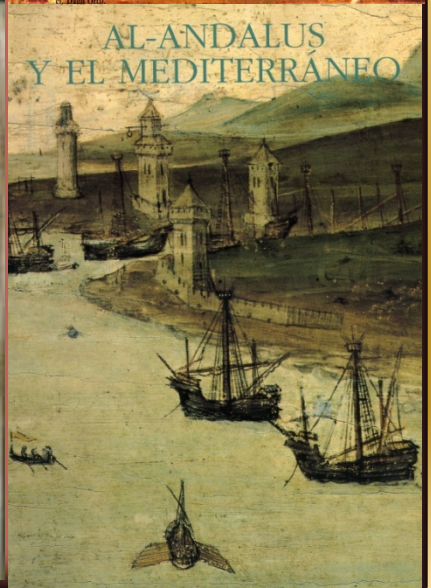
Rediscovering Arabic Science

WRITTEN BY RICHARD COVINGTON

464 *Twelfth-century Moorish philosopher Averroës, learned in philosophy, medicine, and law, offended political and religious authorities and had to hide out among the Jews. Lithograph by Vigneron, courtesy of the Wellcome Trustees*

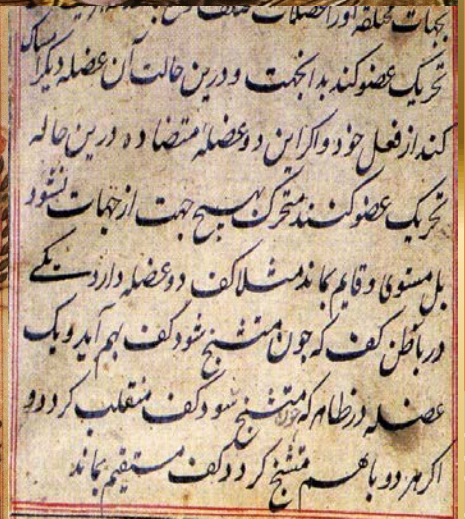
Grâce aux remarquables médecins du monde musulman l'Occident accède à la médecine moderne.

Sur une miniature seldjoukide de 1228, le botaniste grec Dioscoride (ve siècle) explique à un étudiant les propriétés pharmaceutiques des plantes trouvées en Asie Mineure (Istanbul, bibl. de Topkapı ; cl. Dumb Orfit).



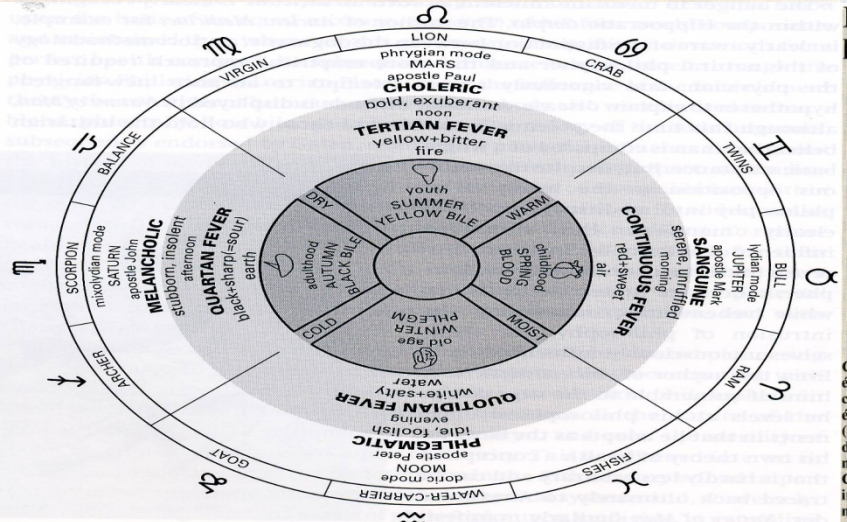
Qantara
Magazine des cultures arabe et méditerranéenne

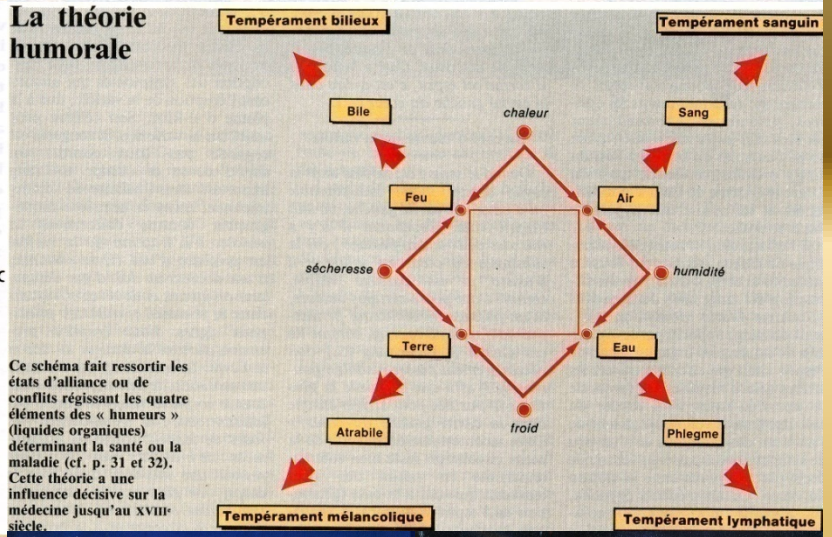
Les Arabes et la Grèce



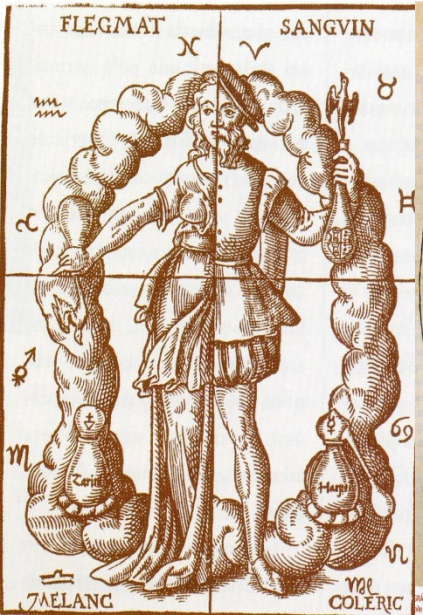
LA SYNTHESE ULTIME

L'utopie du savoir total





Ce schéma fait ressortir les états d'alliance ou de conflits régissant les quatre éléments des « humeurs » (liquides organiques) déterminant la santé ou la maladie (cf. p. 31 et 32). Cette théorie a une influence décisive sur la médecine jusqu'au XVIIIe siècle.



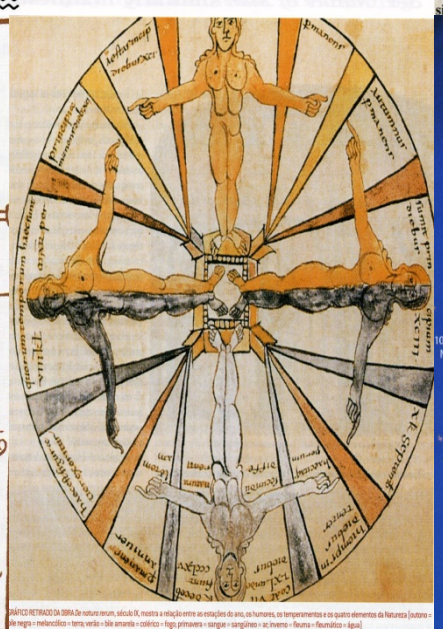
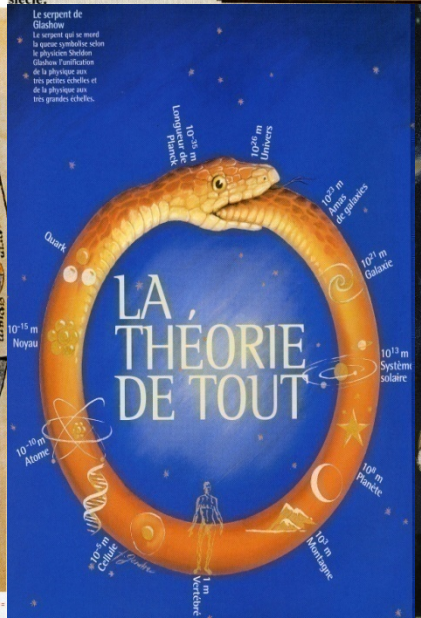
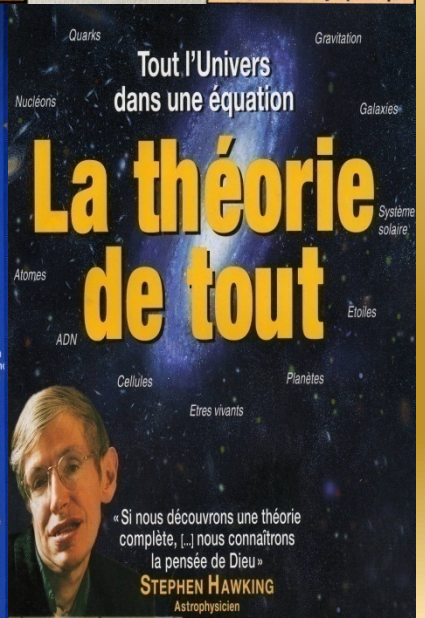


GRÁFICO RETIRADO DA OBRA De natura rerum, século IX, mostra a relação entre as estações do ano, os humores, os temperamentos e os quatro elementos da Natureza [outono = bile negra = melancólico = terra; verão = bile amarela = colérico = fogo; primavera = sangue = sanguíneo = ar; inverno = fleuma = fleumático = água].





Se nourrir, se soigner

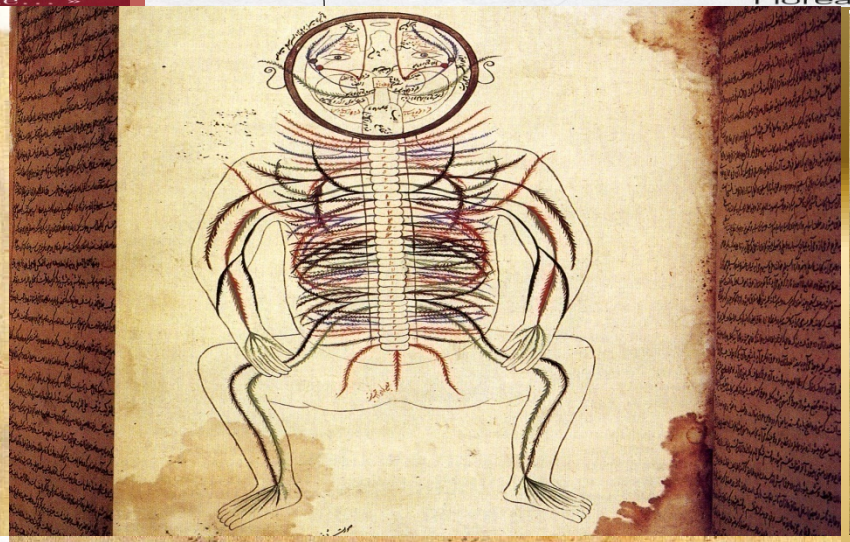
Dioscoride, *De materia medica*
Traduction persane

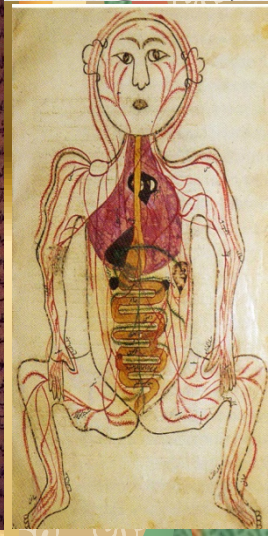
« Il prit une boîte où il y avait plusieurs remèdes [...] et il en tira une petite fiole balsamique dont il frotta longtemps le cou du bossu. Ensuite, il prit dans son étui un ferrement fort propre qu'il lui mit entre les dents ; et, après lui avoir ouvert la bouche, il lui enfonça dans le gosier de petites pincettes, avec quoi il tira le morceau de poisson et l'arête qu'il fit voir à tout le monde. Aussitôt, le bossu étendit les bras et les pieds, ouvrit les yeux, et donna plusieurs autres signes de vie

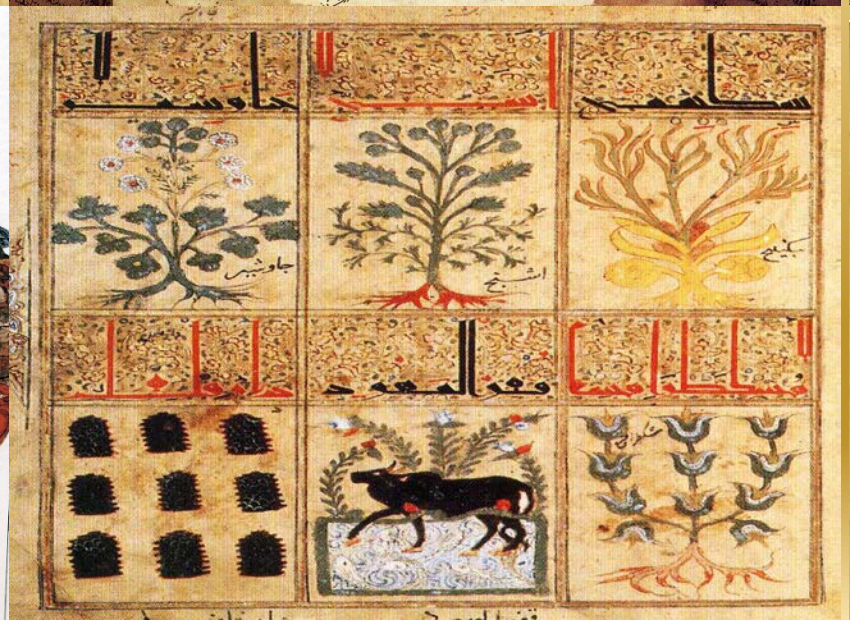
Médecine : l'invention de l'hôpital

Héritière du savoir persan et de l'Antiquité grecque, la médecine au temps des Abbassides a profité de l'essor général des sciences pour se développer de manière remarquable.

Floréal Sanagustin





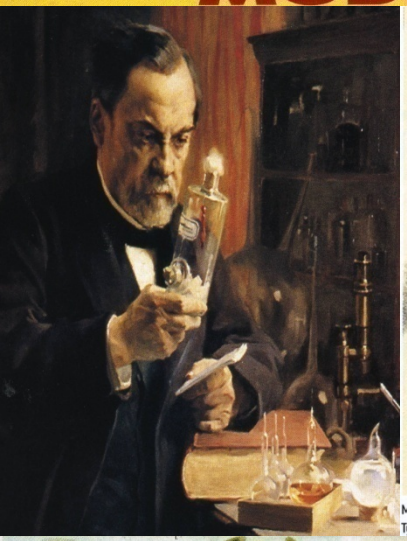


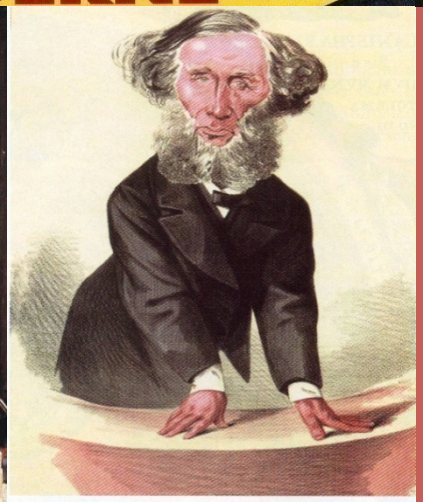
PASTEUR

LA TUMULTUEUSE NAISSANCE DE LA BIOLOGIE MODERNE

PASTEUR

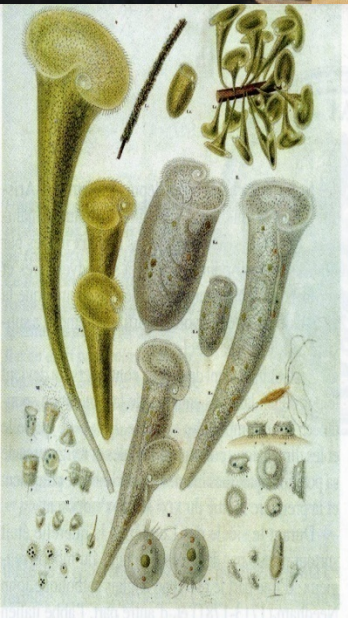
Microbes et controverses

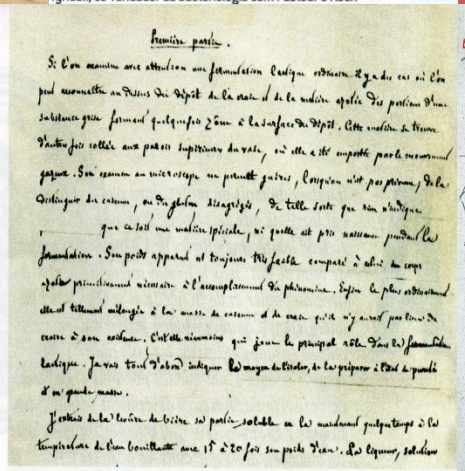




Mesmo seres microscópicos só podem ser gerados por outro ser vivo: John Tyndall, co-fundador da bacteriologia com Pasteur e Koch

- 1857
  - Microrganismos da fermentação
- 1885
  - Vacinação contra a raiva
- Outras doenças que estudou
  - Carbúnculo
  - Erisipela
  - Febre amarela





Première partie.

S'il on examine avec attention une fermentation lactique ordinaire, il y a des cas où l'on peut reconnaître au fond du dépôt de la craie et de la matière azotée des portions d'une substance qui forment quelquefois d'abord à la surface du dépôt. Cette matière se trouve d'autres fois collée aux parois supérieures du vase, où elle a été emportée par le mouvement gazeux. Son examen au microscope ne permet guère, l'origine n'est pas primitive, de la distinguer du caséum, ou du globulin végétal, de telle sorte que rien n'indique que ce soit une matière spéciale, ni quelle ait pris naissance pendant la fermentation. Son poids apparaît et toujours très faible comparé à celui du corps spécial primitivement nécessaire à l'accomplissement du phénomène. Enfin le plus ordinairement elle est tellement mélangée à la masse du caséum et de craie qu'il n'y a rien pour en rendre à son existence. C'est elle cependant qui joue le principal rôle dans la fermentation lactique. Je vais tout d'abord indiquer les moyens de l'isoler, de la préparer à l'état de pureté et en grande masse.

J'extrais de la levure de bière la partie soluble en la maintenant quelque temps à la température de l'eau bouillante avec 15 à 20 fois son poids d'eau. Les liqueurs, solidées

Un extrait du Mémoire sur la fermentation appelée lactique *de Pasteur (1857). À gauche, des infusoires extraits de l'ouvrage* Die Infusionstierchen *(1838) de C. G. Ehrenberg. Ces organismes unicellulaires, aujourd'hui appelés ciliés, furent étudiés au microscope dès le début du XIXe siècle. Pasteur pensait que le vibrion butyrique était l'un d'eux.*

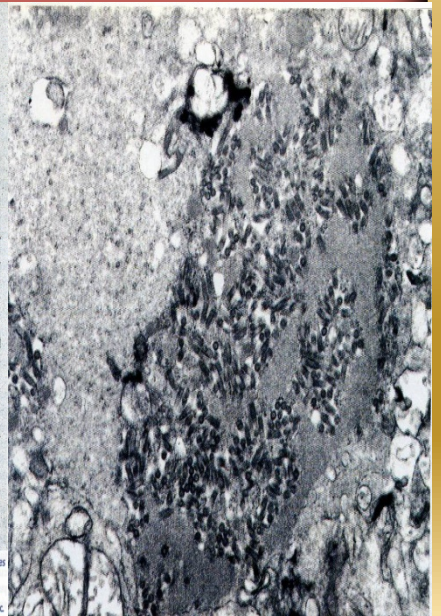
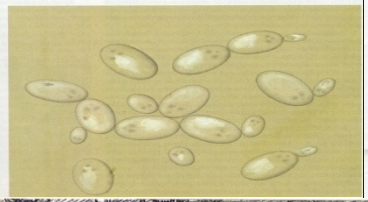


Planche illustrant les travaux de Pasteur sur les générations spontanées, réalisée vers 1875. Y sont rassemblés les dispositifs expérimentaux conçus par le savant pour contrer les arguments de Pouchet et publiés dans son Mémoire sur les corpuscules organisés qui existent dans l'atmosphère (1861), ainsi que les germes observés au microscope. On distingue notamment les schémas des trois expériences clés de Pasteur, respectivement a, b, c.

Dans les années 1850, Pasteur, guidé par ses travaux sur la dissymétrie moléculaire, démontre que la fermentation est un processus initié par des organismes vivants et pose ainsi les fondements de la microbiologie.

Les ferments d'une théorie

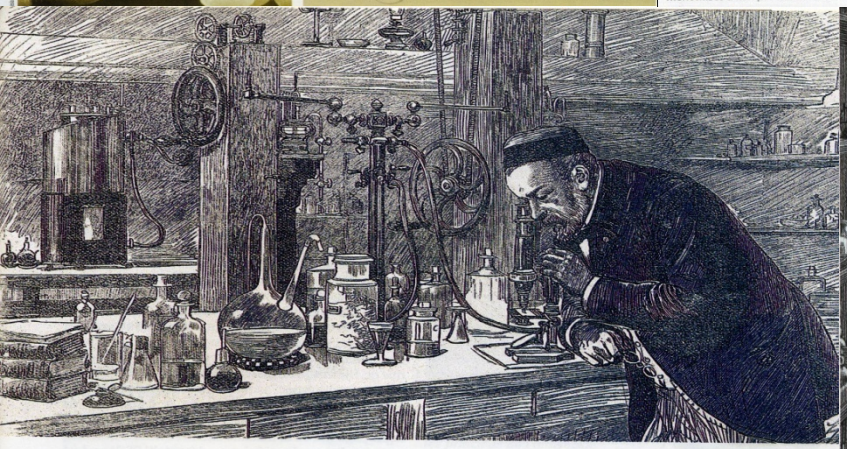


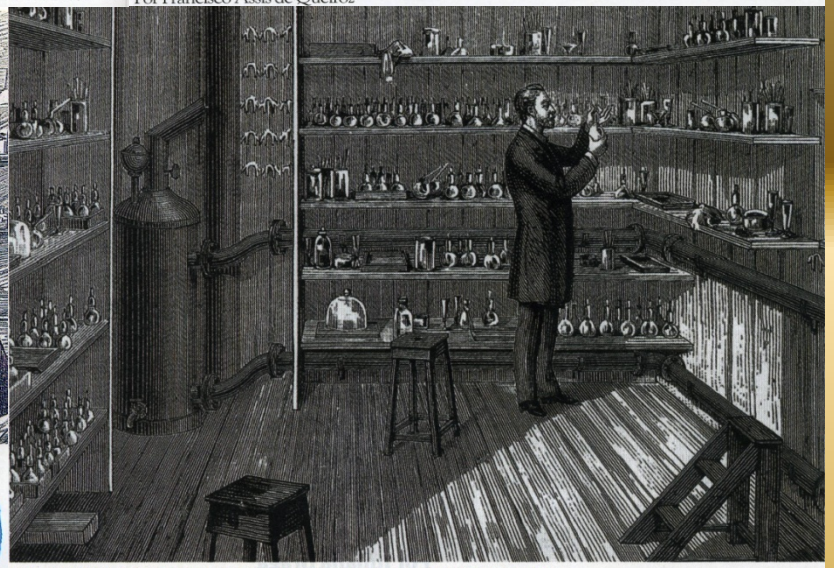
A En 1859, le naturaliste Félix-Archimède Pouchet expose ses thèses spontanéistes dans *Hétérogénie ou Traité de la génération spontanée*. Mais elles seront définitivement mises à mal par Pasteur dans la décennie qui suivra.

A morte da geração espontânea

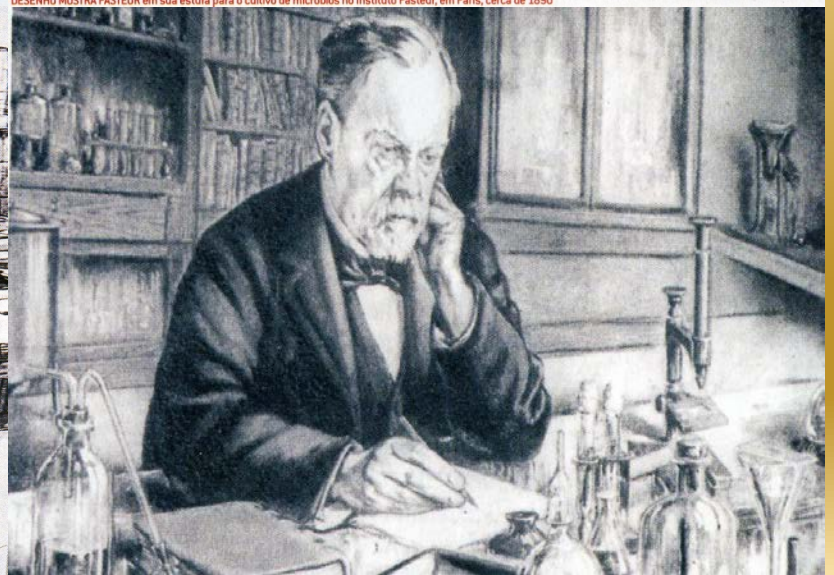
Foram necessários dois séculos de combates vigorosos sobre a origem da vida para que a velha teoria fosse enterrada para sempre

Por Francisco Assis de Queiroz





DESENHO MOSTRA PASTEUR em sua estufa para o cultivo de micróbios no Instituto Pasteur, em Paris, cerca de 1890



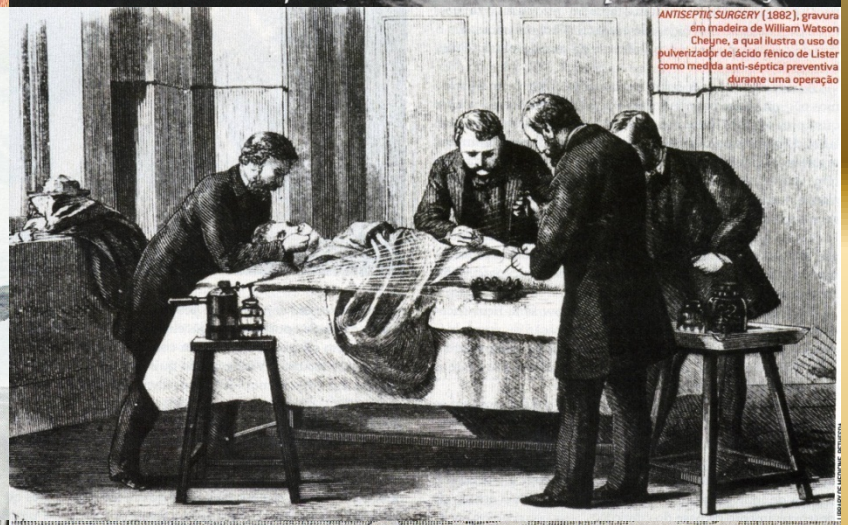
A Doença dos Médicos

Os grandes erros DA CIÊNCIA

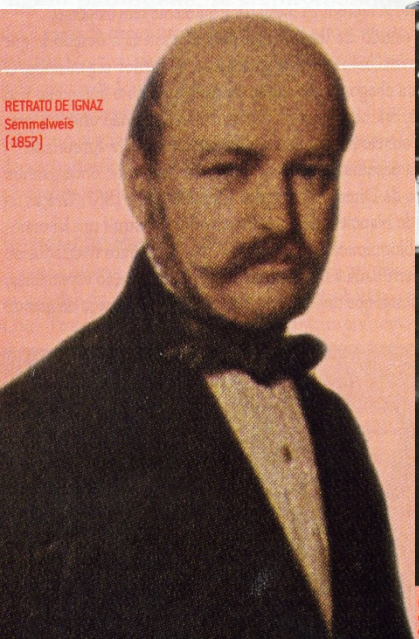
Na atividade científica, errar é a regra, não a exceção. Só aceitando esse fato, o conhecimento pode avançar

Musée d'histoire de la médecine de Zürich

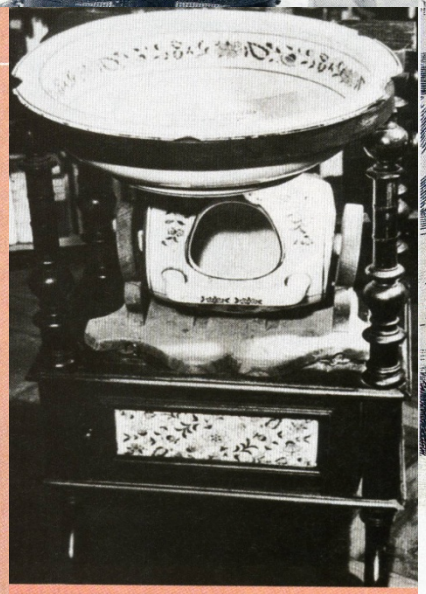
Le médecin anglais Joseph Lister (1827-1912, ci-dessus) découvrit les principes de l'antisepsie dans les années 1860. Il préconisa la vaporisation de phénol sur le champ opératoire à l'aide de l'appareillage ci-contre.



ANTISEPTIC SURGERY (1882), gravura em madeira de William Watson Cheyne, a qual ilustra o uso do pulverizador de ácido fênico de Lister como medida anti-séptica preventiva durante uma operação



RETRATO DE IGNAZ Semmelweis (1857)

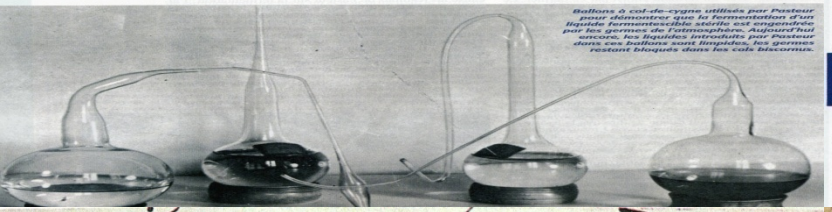


BACIA E SUPORTE usados por Ignaz Semmlweis para lavar as mãos antes de examinar suas pacientes, precaução que impôs a sua equipe e que reduziu drasticamente a taxa de mortalidade obstétrica

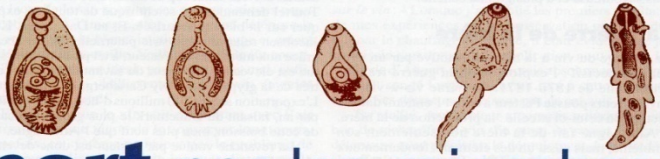
Les principes d'asepsie de Pasteur ont conduit à des découvertes connexes : en 1884, son collaborateur Charles Chamberland (1851-1908) met au point un filtre à eau pour lutter contre la propagation de la fièvre typhoïde qui sévit à Paris. Ce procédé, qui élimine les microbes de l'eau de boisson, sera notamment utilisé par les soldats durant la guerre de 1914-1918 (ci-dessus). Ci-dessous, un nécessaire à trépanation datant de la fin du XIXe siècle. Pasteur montra l'importance de laver et de stériliser les instruments chirurgicaux à la flamme avant leur utilisation.

De l'étude de la fermentation au débat sur la génération spontanée, il n'y a qu'un pas. Pasteur se positionne en détracteur de cette théorie, qu'il anéantit au début des années 1860 en démontrant le rôle de la contamination microbienne.

La vie est le germe



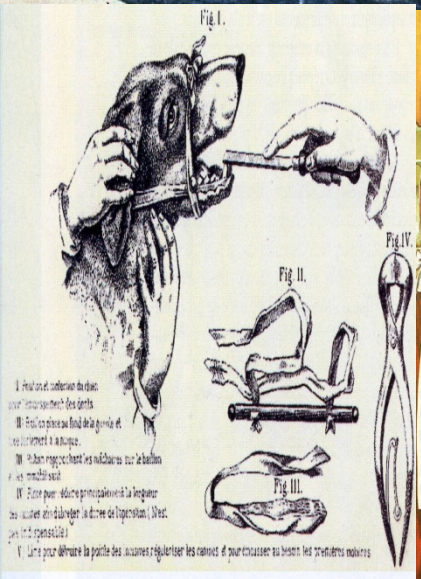
Ballons à col-de-cygne utilisés par Pasteur pour démontrer que la fermentation d'un liquide fermentescible stérile est engendrée par les germes de l'atmosphère. Au-dessus encore, les liquides restent stériles. Au-dessus des ballons sont fissurés, les germes restant bloqués dans les cols biscornus.

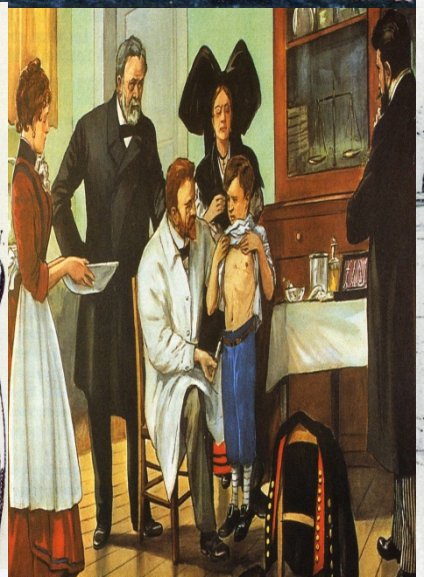


La mort par les microbes

En 1873, malgré l'hostilité de nombreux médecins, Pasteur est élu à l'Académie de médecine. Persuadé que les maladies humaines sont d'origine microbienne, il découvre l'asepsie.

Scène dédiée à la lutte contre la rage, sur une des mosaïques commémoratives qui décorent la crypte où repose Louis Pasteur, à l'Institut Pasteur. En haut à droite est représentée une fiole dans laquelle est suspendue une moelle épinière de lapin rabique desséchée. Cette fiole est l'élément clé qui conduisit Pasteur au vaccin rabique.



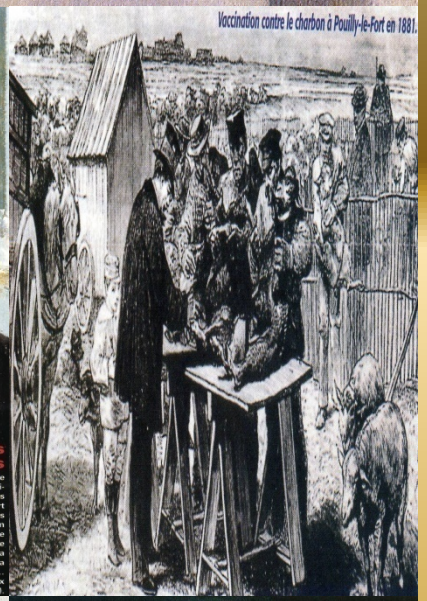


D'OÙ VIENNENT LES MICROBES ?

- 1876
  - Isola o bacilo do carbúnculo
- 1882
  - Isola o bacilo da tuberculose
- 1883
  - Isola o vibrião da cólera
- 1890
  - Inventa a tuberculina
- Outras Doenças que estudou
  - Difteria
  - Tripanosomose
  - Malária
  - Babesiose
  - Febre Tifóide
  - Peste

L'antre des bactéries

Inspiré de celui de Pasteur à Paris, l'Institut pour les maladies infectieuses de Robert Koch ouvre ses portes le 17 août 1891. Un an auparavant, le célèbre bactériologiste allemand annonçait sa découverte de la « tuberculine »... (peinture de Max Pietschman, 1896).



Vaccination contre le charbon à Pouilly-le-Fort en 1881.

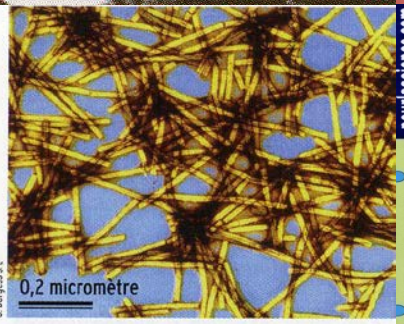
L'expérience historique de Pouilly-le-Fort, symbolisée par des moutons sur une mosaïque de la crypte où repose Pasteur, à l'Institut Pasteur. Ci-contre, Bacillus anthracis, le bacille du charbon (trois à cinq millimètres de longueur). Ci-dessous, Casimir-Joseph Davaine (1812-1882), auteur de nombreux essais sur la maladie du charbon et autres affections parasitaires, et (en bas) le bactériologiste allemand Robert Koch (1843-1910), qui découvrit le bacille de la tuberculose et s'intéressa au charbon.

Ampoules de vaccins contre le charbon et le rouget du porc élaborés dans le laboratoire de Pasteur vers 1880

La découverte d'un nouveau monde

Claude CHASTEL

En découvrant les virus il y a plus d'un siècle, les biologistes abordent un monde original et fascinant. Un nouvel aspect des processus vitaux et des maladies leur est révélé.



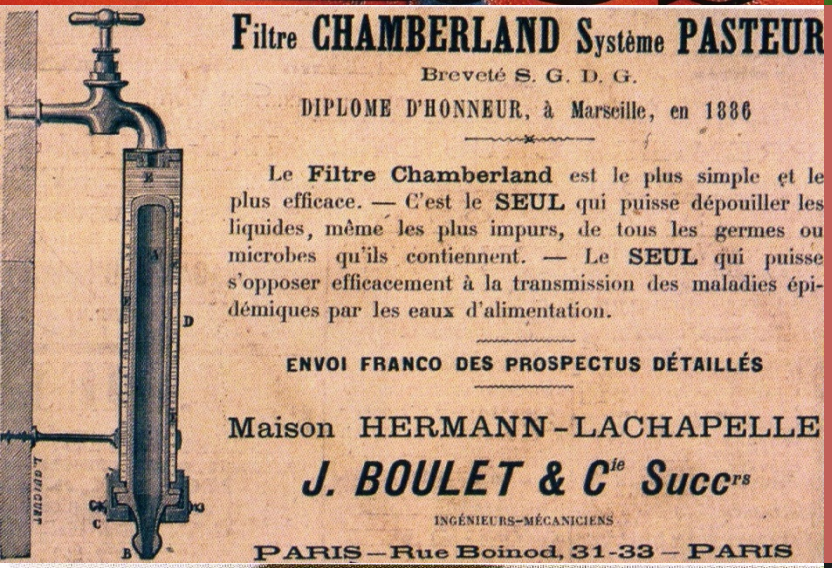
J. Burgess SPL

1. La découverte des virus. Dimitri Ivanovski *(en haut à gauche)* était encore un jeune étudiant russe lorsqu'il mit en évidence les propriétés du virus de la mosaïque du tabac en 1892. Les feuilles de tabac infectées *(en bas à gauche)* se caractérisent par des zones de décoloration et des déformations morphologiques. À l'époque, on pensait que seuls les bactéries, les champignons ou les parasites étaient susceptibles de provoquer de telles infections, et les bougies Chamberland *(au centre)* permettaient de filtrer ces agents infectieux. Malgré ce procédé, aucune entité infectieuse n'était retenue par les filtres lorsque la sève de tabac traversait la bougie Chamberland. Il fallut attendre six ans pour que les travaux d'Ivanovski soient repris et approfondis par le chimiste hollandais Martinus Beijerinck *(en haut à droite)*. Celui-ci écarta définitivement l'hypothèse bactérienne et proposa l'idée d'un agent « vivant », capable de se reproduire et « fluide ». Le virus de la mosaïque du tabac, dont la structure en bâtonnet *(en bas à droite)* fut révélée plus tard par de plus puissants microscopes, est le premier virus découvert par l'homme.

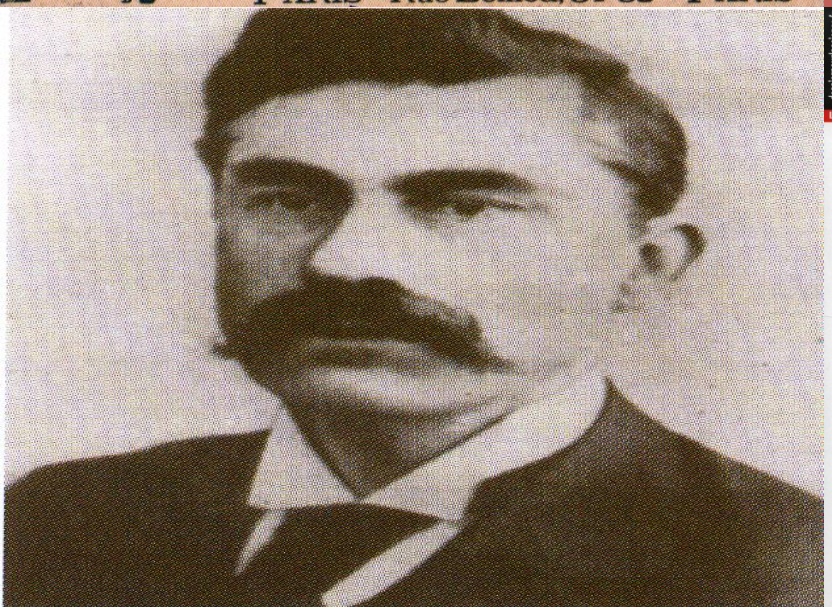
les frontières du vivant

- 1892
  - *Dimitr Ivanovski*
    - Botânico russo
    - Academia de Ciências de S. Petersburgo
      - Vírus do Mosaico do Tabaco

Histoire de virus, de gènes et de chercheurs



- 1898
  - *Martinus Beijerink*
    - Engenheiro químico holandês
      - ***"Contagium vivum fluidum"***



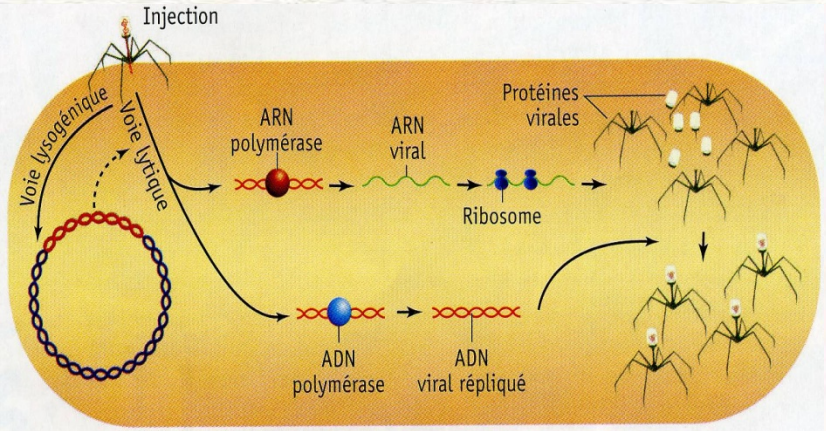
- **1957**
  - ***André Lwoff (Prémio Nobel em 1965)***
    - **1ª Defenição de vírus**
      - **"… trata-se de um elemento, transmissível e potencialmente patogénico, que possui somente um único tipo de ácido nucleico, reproduzindo-se num hospedeiro a partir do seu próprio material genético e desprovido de qualquer metabolismo …" sic.**

Les phages
à l'assaut des bactéries

Laurent DEBARBIEUX

Les phages détruisent les bactéries en s'y reproduisant massivement. Cette caractéristique nous permettra-t-elle de lutter contre des infections devenues résistantes aux antibiotiques?

André Lwoff (à droite) a décrit pour les bactériophages deux voies de reproduction. Ils peuvent soit se multiplier et détruire la bactérie : c'est la lyse ; soit intégrer leurs gènes dans le chromosome de la bactérie. Le prophage ainsi obtenu se multiplie en même temps que la bactérie : c'est la lysogénie.

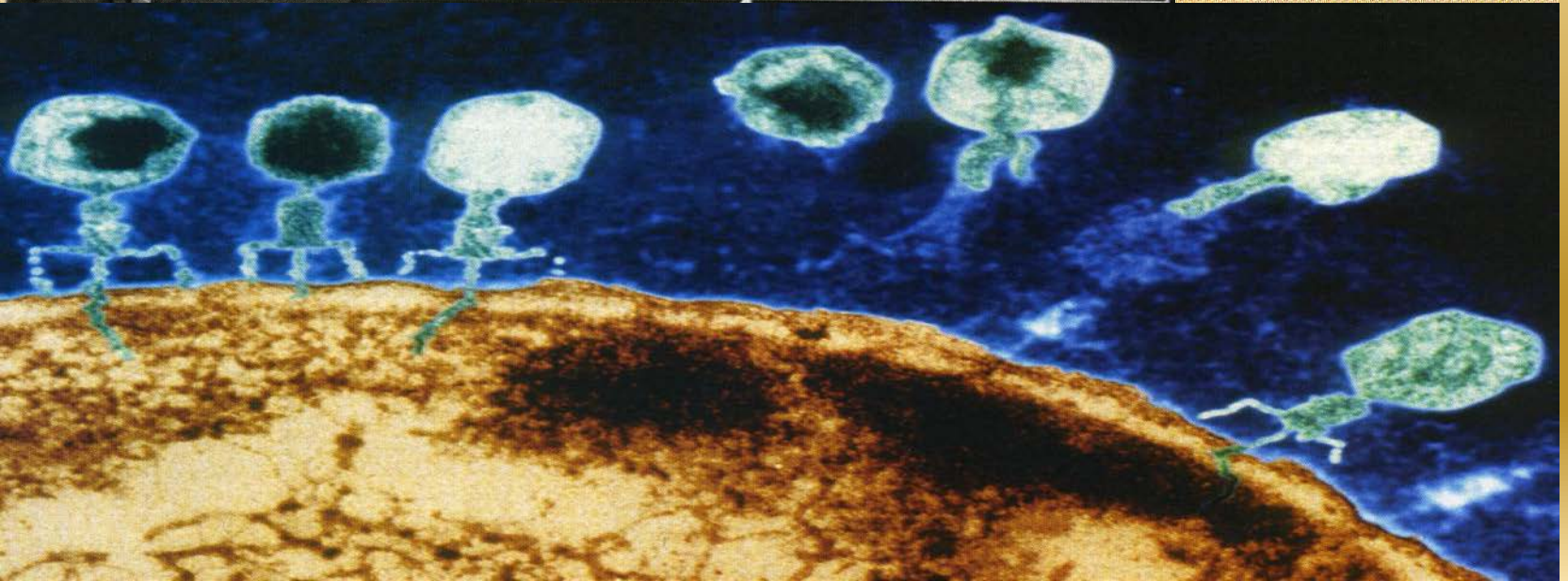


2. Représentation schématique du cycle infectieux des bactériophages. Lorsque le génome des phages pénètre dans le cytoplasme bactérien, deux voies évolutives sont possibles. Soit il entame un cycle lytique où l'usine de reproduction bactérienne est détournée pour produire massivement de nouveaux phages. Soit le génome s'insère dans l'ADN bactérien, il s'agit de la voie lysogénique. Sous certaines conditions, le génome viral intégré à celui de la cellule se réactive, et suit alors la voie lytique.

4. Une bactérie assiégée par des phages. De nombreux phages sont accrochés à la paroi cellulaire. Lorsque l'usine cellulaire aura produit une centaine de phages, des mécanismes de destruction de la paroi libéreront les phages, qui iront infecter d'autres cellules.

Félix D'Herelle e os Vírus do Bem

À ESQ., BACTERIÓFAGOS atacam uma bactéria *Escherichia coli*, que provoca disenteria. Acima, propaganda do Laboratório de Bacteriófagos, onde D'Herelle trabalhou, mostra as diversas terapias possíveis com os fagos. Ao lado, retrato do cientista em 1927



SIDA
état d'urgence

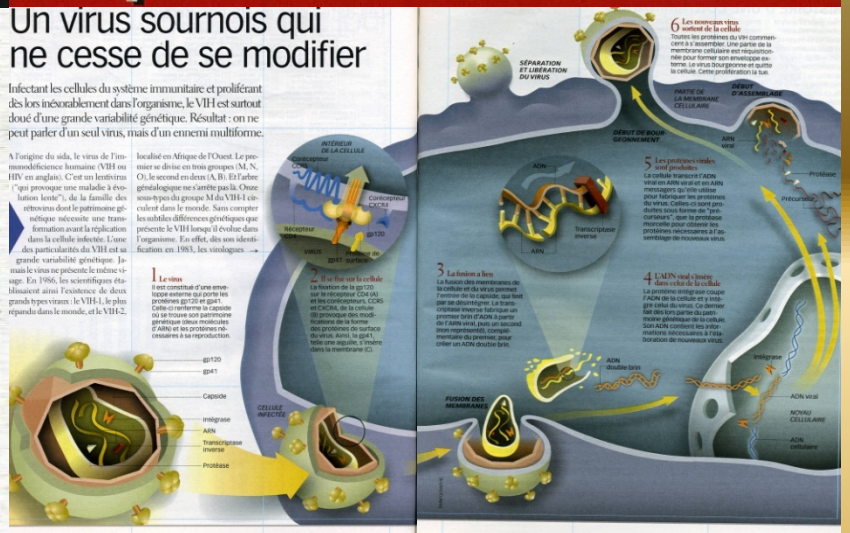
Un Virus qui évolue pour survivre

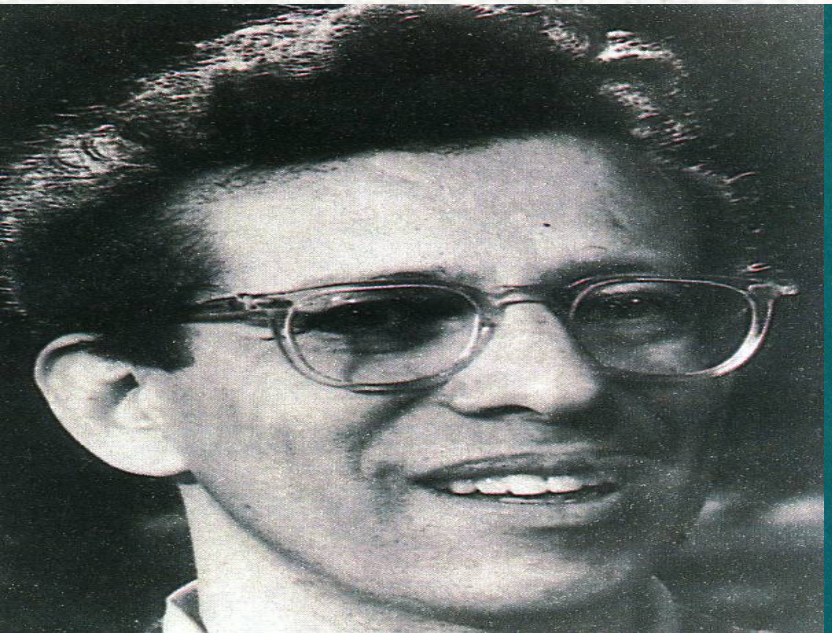
Howard Temin isole en 1970 une enzyme : la transcriptase inverse. Cette découverte transforma notre compréhension de certains phénomènes comme le cancer ou l'organisation de nos chromosomes.

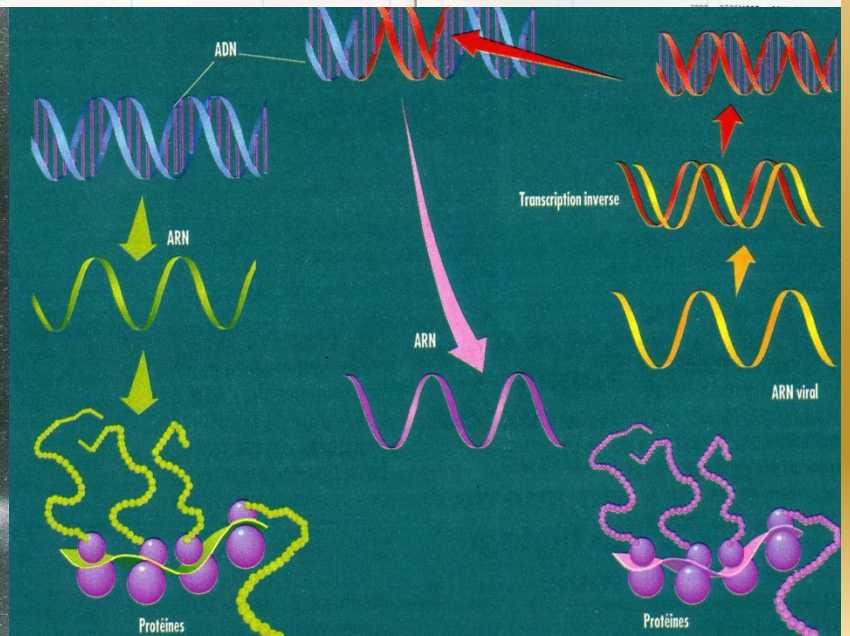
Un virus sournois qui ne cesse de se modifier

Infectant les cellules du système immunitaire et proliférant dès lors inéxorablement dans l'organisme, le VIH est surtout doué d'une grande variabilité génétique. Résultat : on ne peut parler d'un seul virus, mais d'un ennemi multiforme.

A l'origine du sida, le virus de l'immunodéficience humaine (VIH ou HIV en anglais). C'est un lentivirus ("qui provoque une maladie à évolution lente"), de la famille des rétrovirus dont le patrimoine génétique nécessite une transformation avant la réplication dans la cellule infectée. L'une des particularités du VIH est sa grande variabilité génétique. Jamais le virus ne présente le même visage. En 1986, les scientifiques établissaient ainsi l'existence de deux grands types viraux : le VIH-1, le plus répandu dans le monde, et le VIH-2, localisé en Afrique de l'Ouest. Le premier se divise en trois groupes (M, N, O), le second en deux (A, B). Et l'arbre généalogique ne s'arrête pas là. Onze sous-types du groupe M du VIH-1 circulent dans le monde. Sans compter les subtiles différences génétiques que présente le VIH lorsqu'il évolue dans l'organisme. En effet, dès son identification en 1983, les virologues →



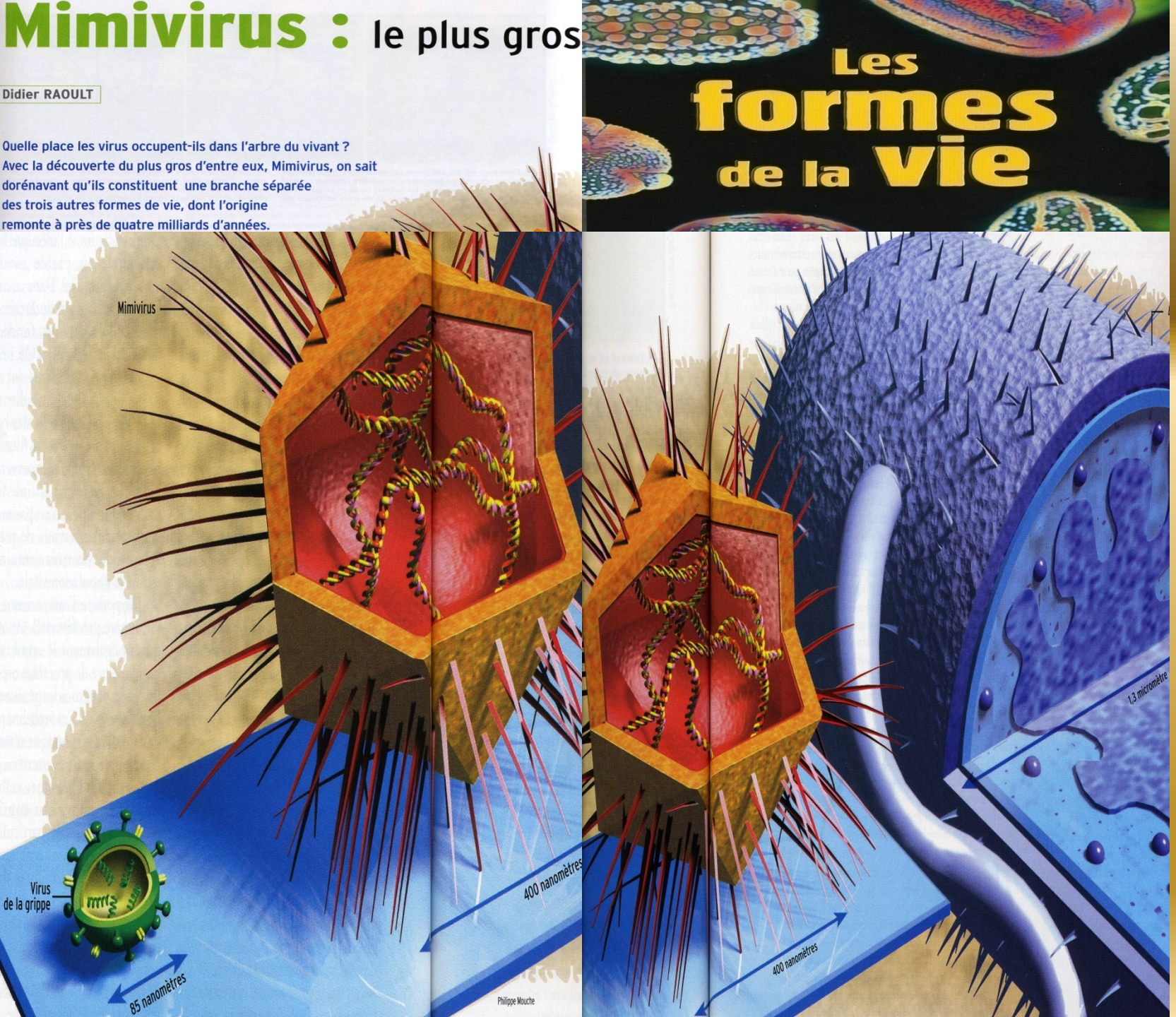




Mimivirus : le plus gros

Didier RAOULT

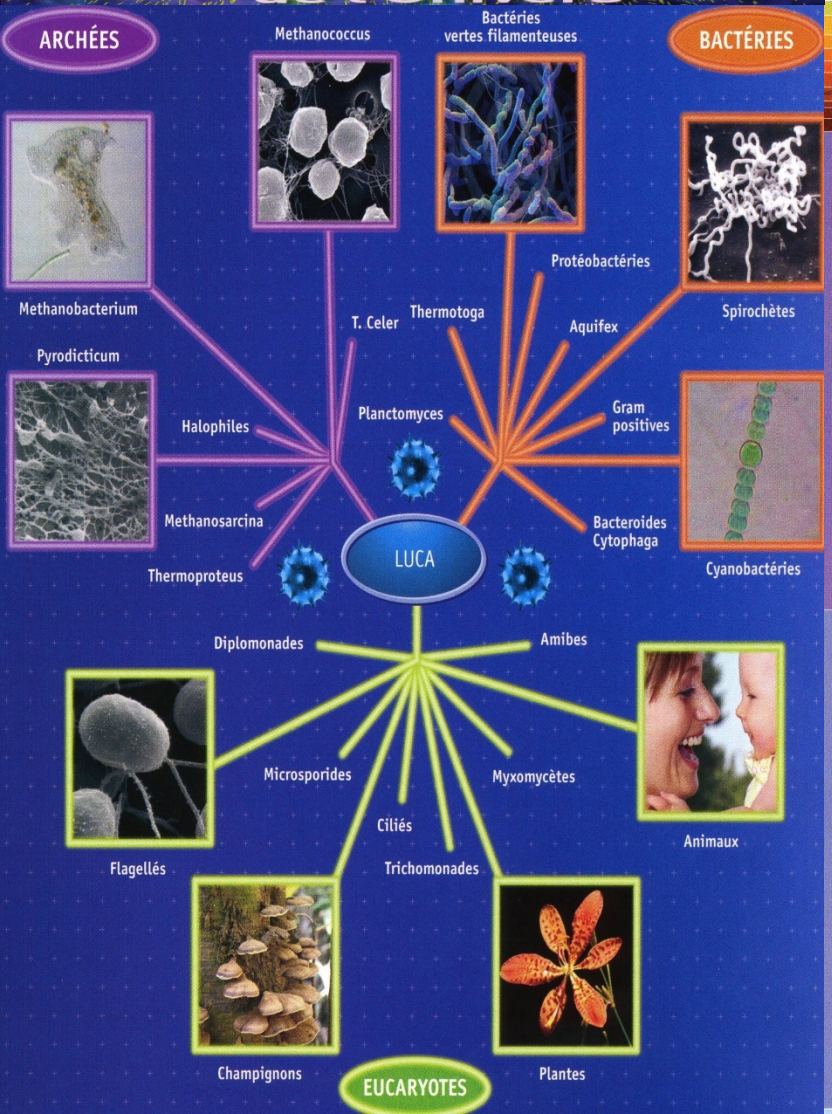
Quelle place les virus occupent-ils dans l'arbre du vivant ? Avec la découverte du plus gros d'entre eux, Mimivirus, on sait dorénavant qu'ils constituent une branche séparée des trois autres formes de vie, dont l'origine remonte à près de quatre milliards d'années.

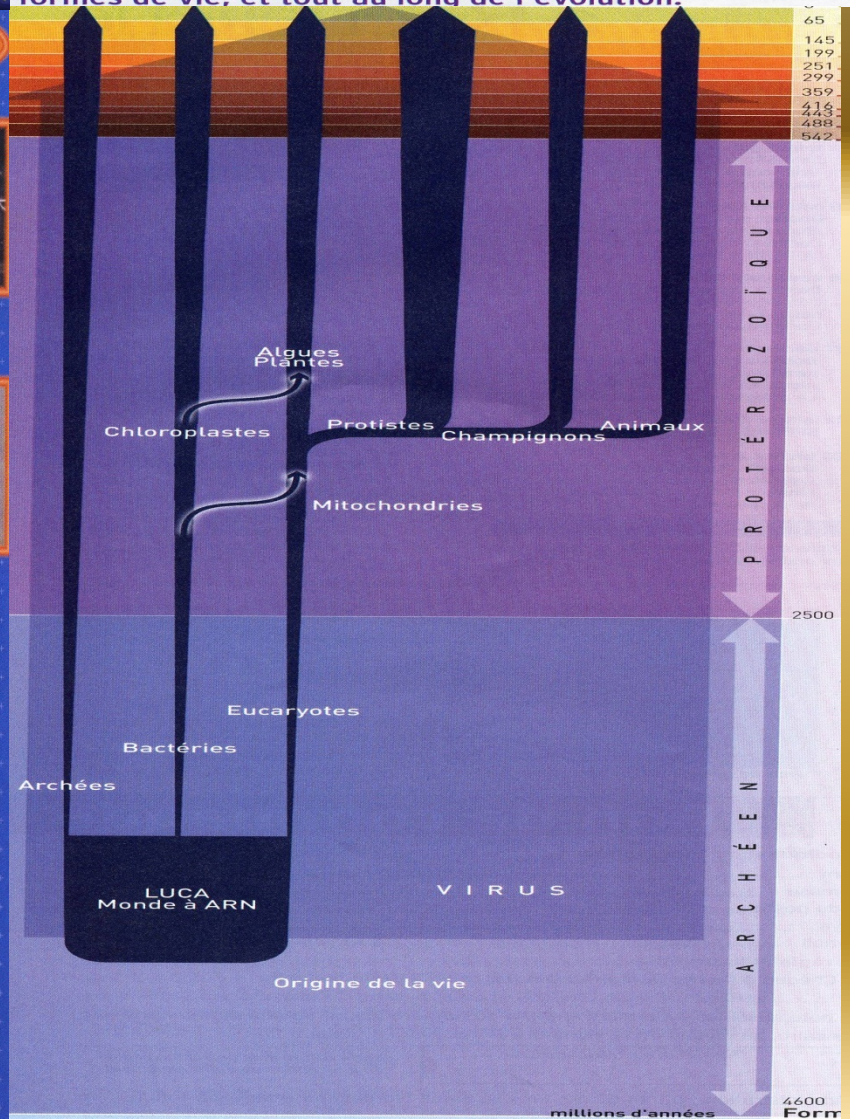


Les virus sont-ils vivants ?

Luis VILLARREAL

Qu'ils soient vivants ou non, les virus semblent avoir joué un rôle essentiel dans l'émergence des différentes formes de vie, et tout au long de l'évolution.



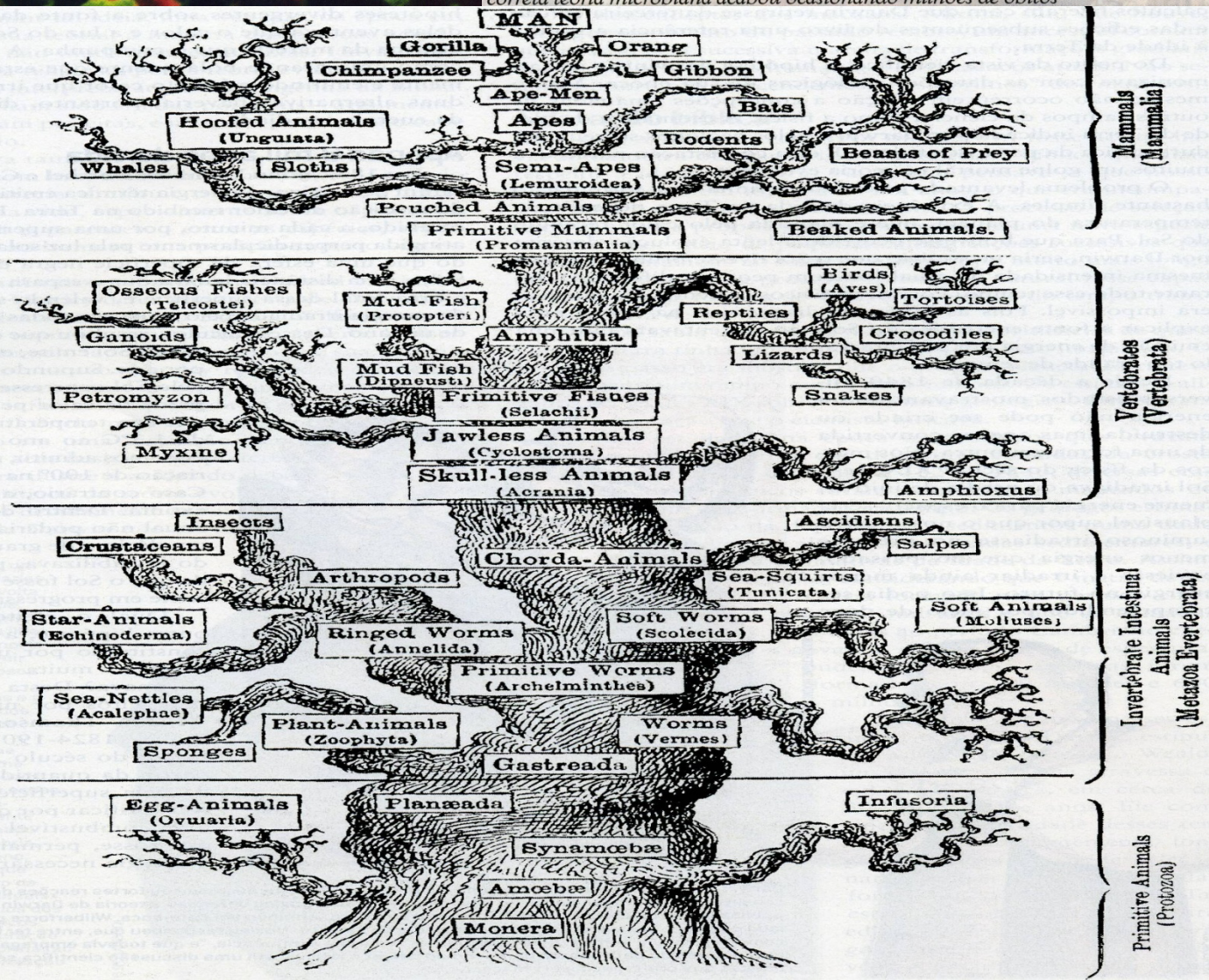


A "geração espontânea" e a origem da vida

Os "miasmas" e a teoria microbiana das doenças

Ironia da história: errônea, a teoria dos miasmas melhorou significativamente a higiene, salvando milhares de vidas; por outro lado, a adoção indiscriminada da correta teoria microbiana acabou ocasionando milhões de óbitos

A árvore evolutiva, segundo ilustração inglesa do séc. XIX. A metáfora utilizada para representar a teoria da evolução das espécies é a árvore evolutiva. As extremidades dos galhos retratam a diversidade da vida atual. As convergências sucessivas dos galhos em direção ao tronco, e ao passado, mapeiam os parentescos, próximos ou longínquos, entre as espécies. Quando se entrelaçam no tronco, os galhos evocam os ancestrais comuns mais remotos. As novas espécies, que surgirão no futuro, poderão aparecer nas ramificações que as extremidades dos galhos vierem a apresentar em qualquer ponto da árvore



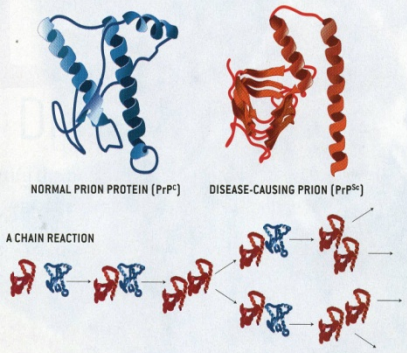
Detecting MAD COW Disease

New tests can rapidly identify the presence of dangerous prions—the agents responsible for the malady—and several compounds offer hope for treatment

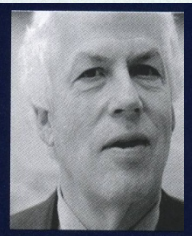
By Stanley B. Prusiner

A BAD INFLUENCE

Prion proteins exist in at least two forms (*below*)—the normal, or cellular, version (PrP^C) and the disease-causing one (PrP^{Sc}). In a process that is not well understood, PrP^{Sc} changes PrP^C into more PrP^{Sc}; the newly altered prions, in turn, can corrupt other normal ones (*bottom*). Usually the body eliminates PrP^{Sc} before too much of it accumulates. But if it does build up and is not successfully removed by the cell's machinery, illness can result.



UNNY DENE RANCH in Mabton, Wash., has been under quarantine since December. This herd and thers in the U.S. are now under surveillance for diseased cattle.



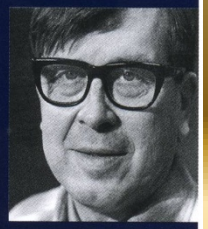
Stanley B. Prusiner

28/05/1942

Des Moines, Iowa, EUA

Título do Prémio

«Priões – um novo princípio biológico de infecção»



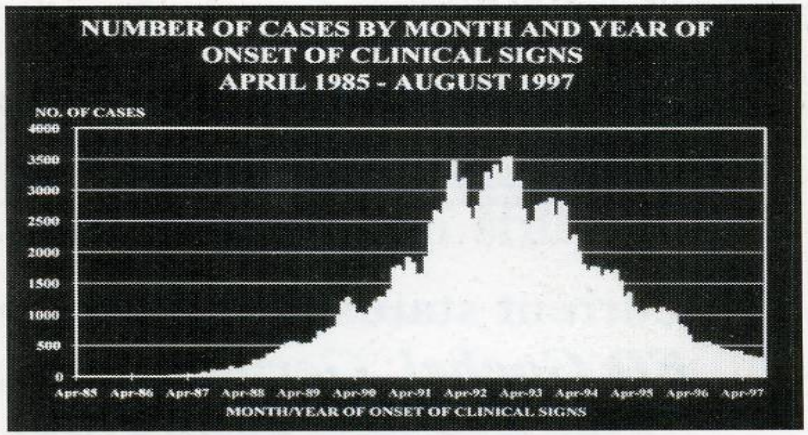
D. Carleton Gadjusek

09/09/1923

Nova Iorque, EUA

Título do Prémio

«Pelas suas descobertas em novos mecanismos da origem e disseminação de doenças infecciosas»



Cases of Bovine Spongiform Encephalopathy in the UK

A WORLDVIEW

Many countries have reported cattle afflicted with BSE, but cases of human infection thought to stem from eating meat from sick cows—variant Creutzfeldt-Jakob disease (vCJD)—remain low, for now at least.

COUNTRY	BSE CASES	vCJD DEATHS (current cases)
Austria	1	0
Belgium	125	0
Canada	2	1
Czech Republic	9	0
Denmark	13	0
Falkland Islands	1	0
Finland	1	0
France	891	6
Germany	312	0
Greece	1	0
Hong Kong	0	1*
Ireland	1,353	1
Israel	1	0
Italy	117	1
Japan	11	0
Lichtenstein	2	0
Luxembourg	2	0
Netherlands	75	0
Oman	2	0
Poland	14	0
Portugal	875	0
Slovakia	15	0
Slovenia	4	0
Spain	412	0
Switzerland	453	0
U.S.	1	0 (1)†
U.K.	183,803	141 (5)
Worldwide		151(6)

*Awaiting confirmation †British subject

A ÚLCERA GASTRODUODENAL

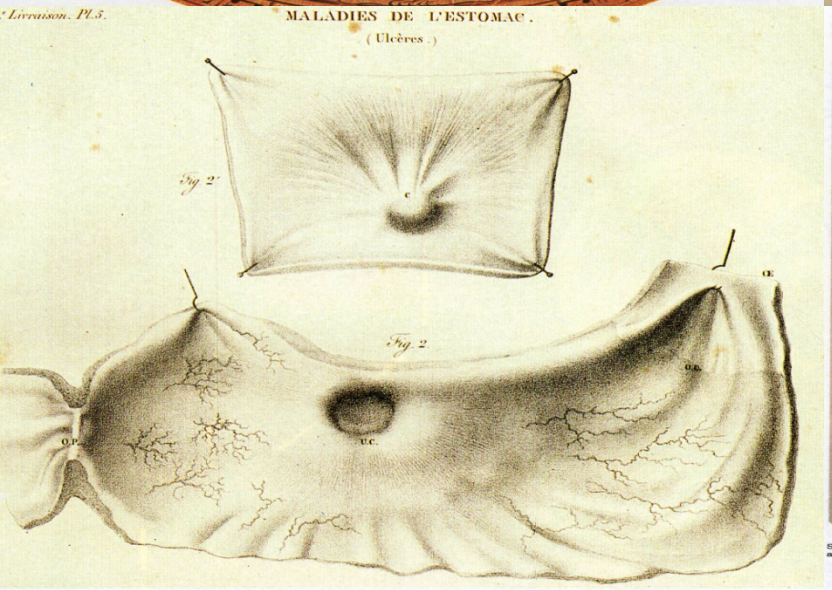
História de uma doença

ELVIRA ARGUIOLA
DELFIN GARCIA-GUERRA
LUIS MONTIEL

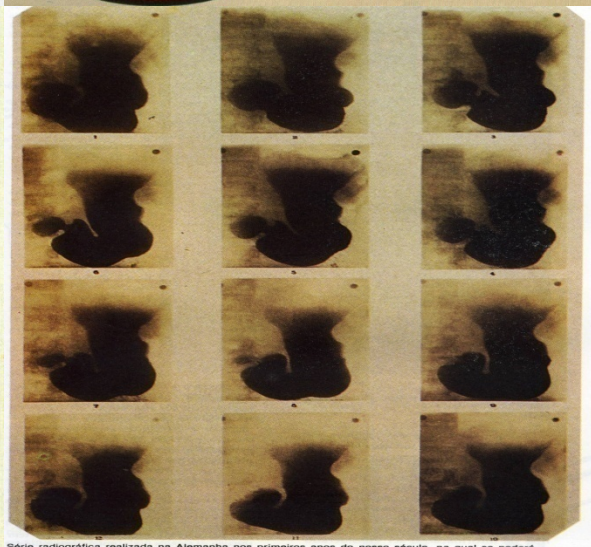
A ÚLCERA GASTRODUODENAL
História de uma doença
ELVIRA ARGUIOLA
DELFIN GARCIA-GUERRA
LUIS MONTIEL

Gastroscopia realizada nos princípios deste século com endoscópio rígido, na Alemanha. Com ela, a endoscopia não só se tinha como ainda atingir o objectivo de permitir a visão directa do estômago, permitindo assim estabelecer um diagnóstico de úlcera fundamentado em muito mais que os sintomas apresentados, mas também era possível obter imagens da úlcera, sem ter de aguardar a autópsia, mediante desenhos da lesão realizados pelo observador.

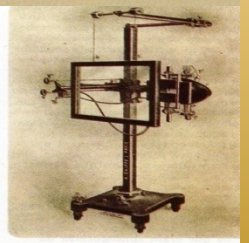
Desenhos realizados através da observação directa da úlcera, situada na pequena curvatura do estômago.

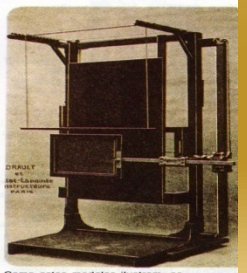


Um dos problemas que se puseram ao tratar da úlcera gastroduodenal foi o diagnóstico diferencial entre esta entidade e o cancro de estômago. Pioneiro em apresentar esta questão foi Cruveilhier, que também definiu o que considerou traços diferenciais de ambas as entidades.

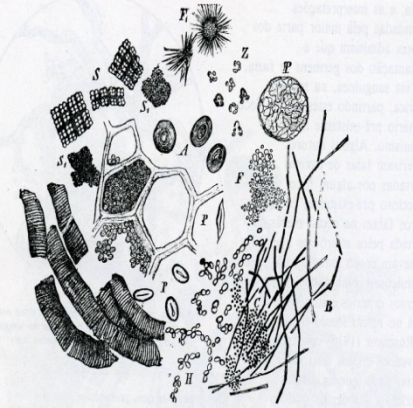


Série radiográfica realizada na Alemanha nos primeiros anos do nosso século, na qual se poderá apreciar a utilização de substâncias de contraste para tornar opacas as zonas a radiografar.

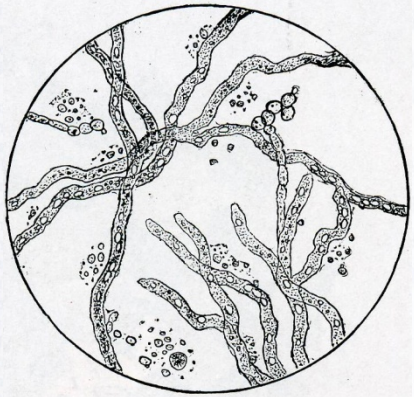




Como estes modelos ilustram, as esperanças depositadas na capacidade da radiografia para o diagnóstico de úlcera foram secundadas pelo progresso técnico dos instrumentos.
Em cima: Pé porta-lâmpada de Gaiffe. *Em baixo:* porta-lâmpada com dispositivo para fixação dos quadros, especialmente concebido para a exploração radiográfica do tubo digestivo.



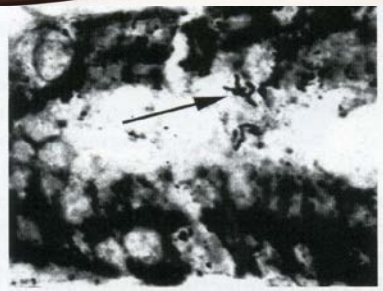
Achados microscópicos na ectasia gástrica, destacando-se a presença de bacilos do género *Leptotrix* (B) e micrococos (C), que na segunda metade do século passado foram incriminados pela patogenia da úlcera, de acordo com a teoria infecciosa que se debateu naquela altura. Tomado Da obra *The essentials of Histology*, de E.A. Shafer(1887)



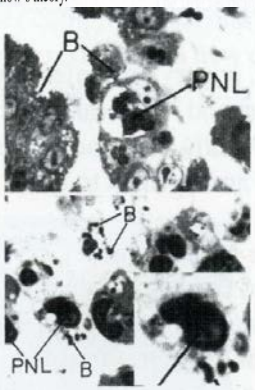
Autores como Einhorsn, a quem se deve esta ilustração, detectaram a presença de fungos no conteúdo gástrico de doentes com hipercloridria

MÜNCHENER
MEDICINISCHE WOCHENSCHRIFT
ORGAN FÜR AMTLICHE UND PRAKTISCHE ÄRZTE
№ 38. 17. September 1895.
Originalien.
Mykotisch-peptisches Magengeschwür.

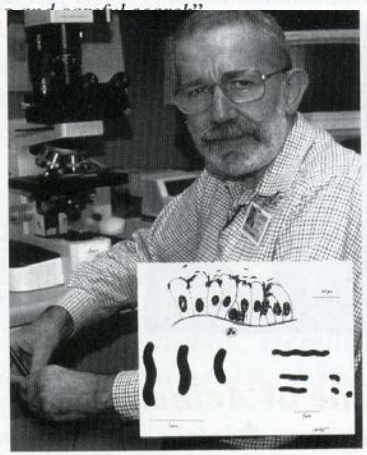
In 1895, Nauwerck in his publication "Mykotisch-peptisches Magengeschwür" described a microbial infiltration of gastric ulcers, trying to synthesize his findings with Virchow's theory.



In 1940, Freedberg and Baron in "The presence of Spirochetes in human gastric mucosa" described detection of spirochetes in "14.2 per cent in non-ulcerating stomachs as compared with 52.3 per cent where ulceration was present". *"The organisms were found with difficulty and frequently required*



In 1975 Steer and Colin-Jones described bacteria *"3 µm long and about 0.5 µm wide, .. related to the gastric mucus-secreting cells in patients with gastric ulceration ... these bacteria have not been seen in the biopsies from normal stomachs"*. Unfortunately they grew a contaminant identified as *Pseudomonas aeruginosa.*



Robin Warren's first observations of spiral campylobacter-like organisms in a gastric biopsy in 1979, and their successful culture after the easter holidays in 1982 provided the unexpected breakthrough for the idea of an infectious origin of gastritis and peptic ulceration.

HP: Prémio Nobel em 2005

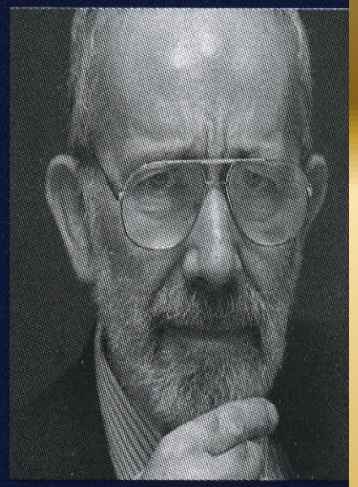
Barry J. Marshall

30/09/1951

Kalgoorlie, AUSTRÁLIA

Título do Prémio

«Pela sua descoberta da bactéria Helicobacter pylori e do seu papel na gastrite e doença ulcerosa péptica»



J. Robin Warren

11/6/1937

Adelaide, AUSTRÁLIA

Título do Prémio

«Pela sua descoberta da bactéria Helicobacter pylori e do seu papel na gastrite e doença ulcerosa péptica»

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

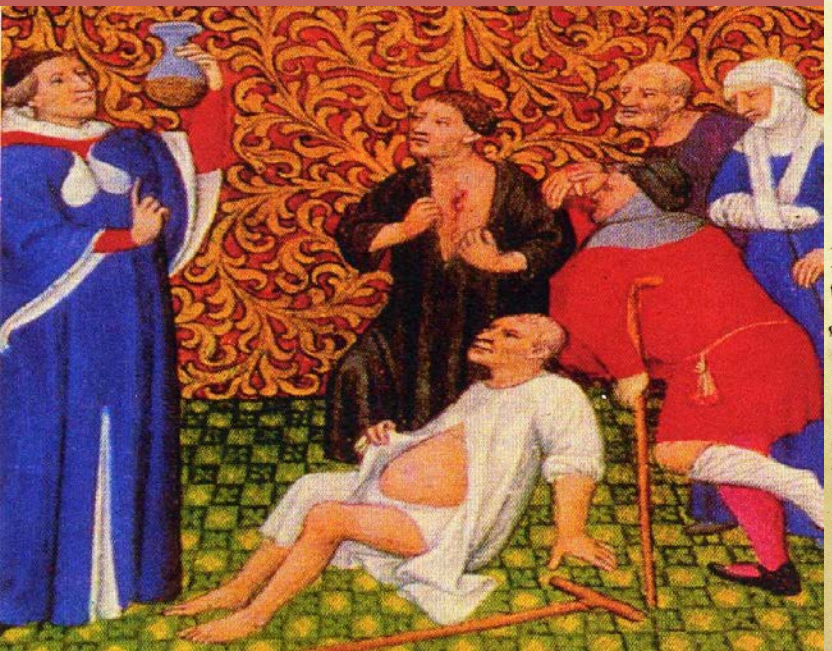
Whipple's Disease

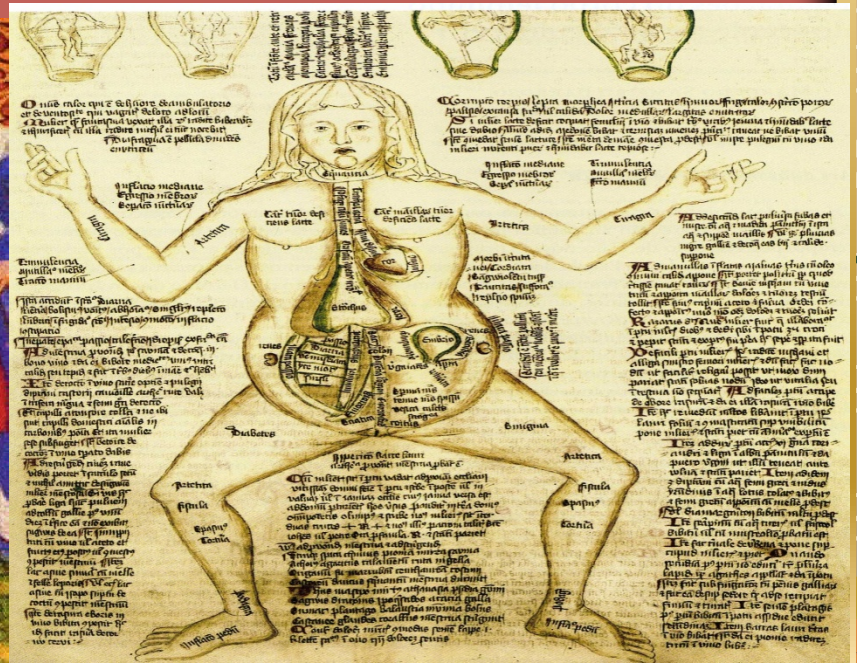
Florence Fenollar, M.D., Ph.D., Xavier Puéchal, M.D., Ph.D., and Didier Raoult, M.D., Ph.D.

Table 1. Milestones in the History of Whipple's Disease and *Tropheryma whipplei*.

Date	Investigators	Advance
1907	Whipple[1]	First description of the disease
1947	Oliver-Pascual et al.[2]	First diagnosis before the death of a patient
1949	Black-Schaffer[3]	Development of periodic acid–Schiff staining for diagnosis
1952	Paulley[4]	First reported efficacy of antibiotic treatment
1961	Chears and Ashworth,[5] Yardley and Hendrix[6]	Detection of bacteria in macrophages by electron microscopy
1991	Wilson et al.[7]	Partial sequencing of 16S rRNA of an unknown bacterium
1992	Relman et al.[8]	Confirmation and extension of the 16S rRNA sequence; first naming of the bacterium: *T. whippelii*
2000	Raoult et al.[9]	First cultivation of the Whipple bacillus
2001	La Scola et al.[10]	First phenotypic characterization of the Whipple bacillus; renaming of the bacterium: *T. whipplei*
2003	Bentley et al.,[11] Raoult et al.[12]	Full sequencing of two genomes from two different strains of *T. whipplei*

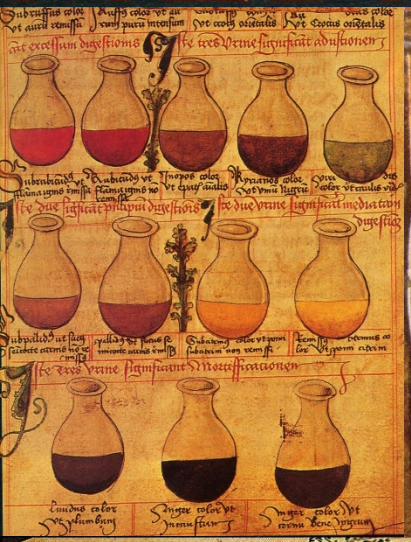
O DIAGNÓSTICO

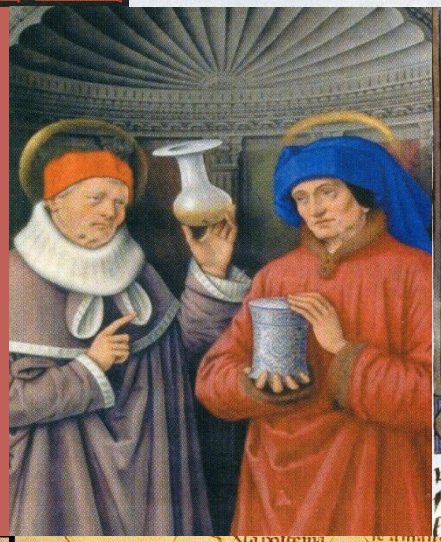


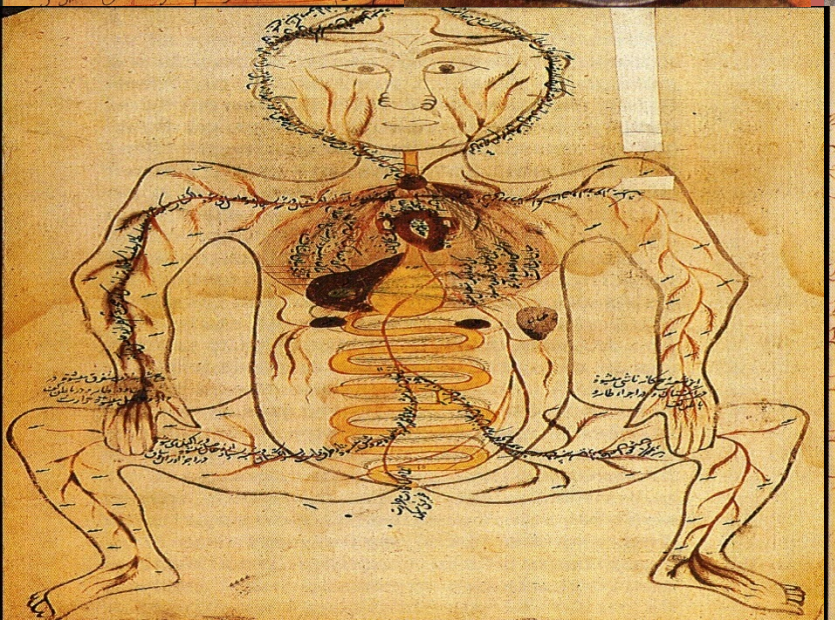


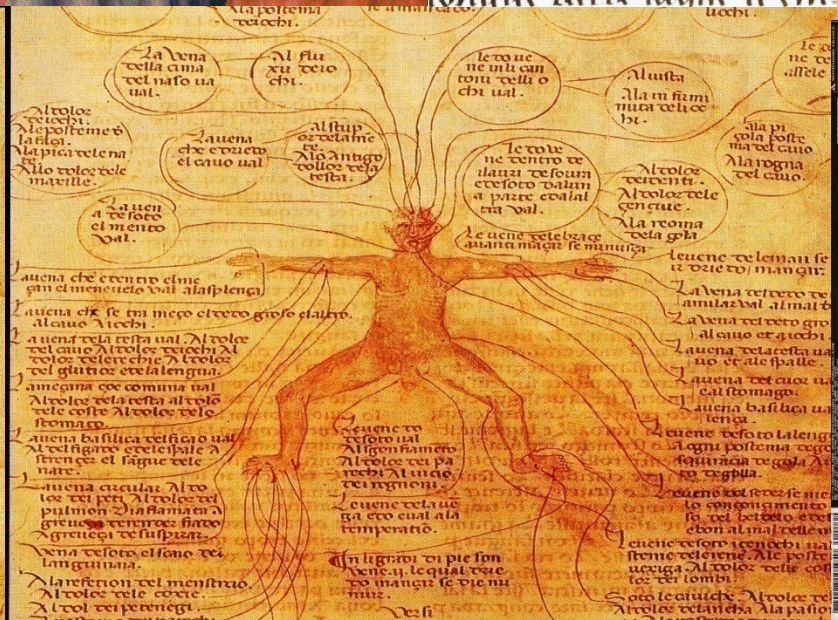
Les Grands Principes de la Médecine Médiévale

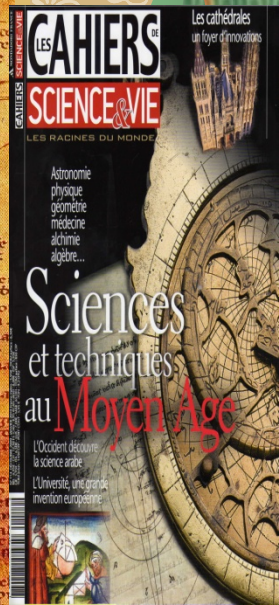
Medicina de laboratório





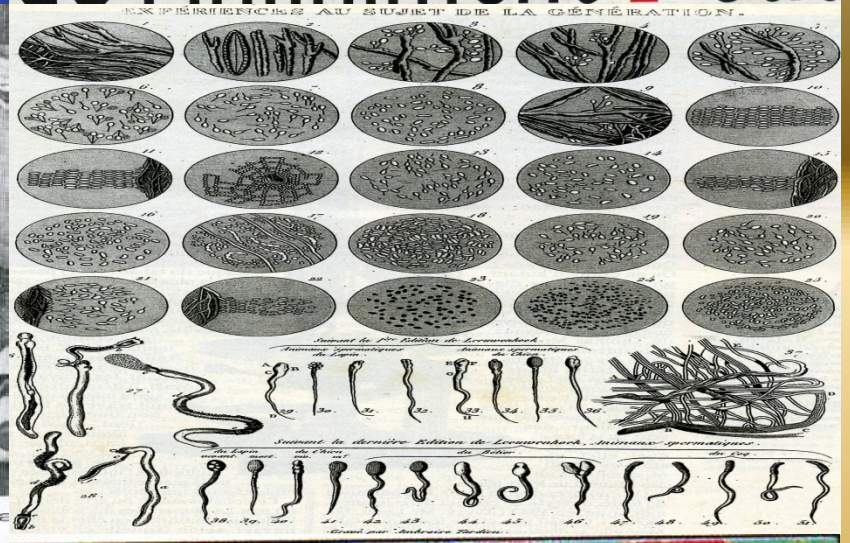


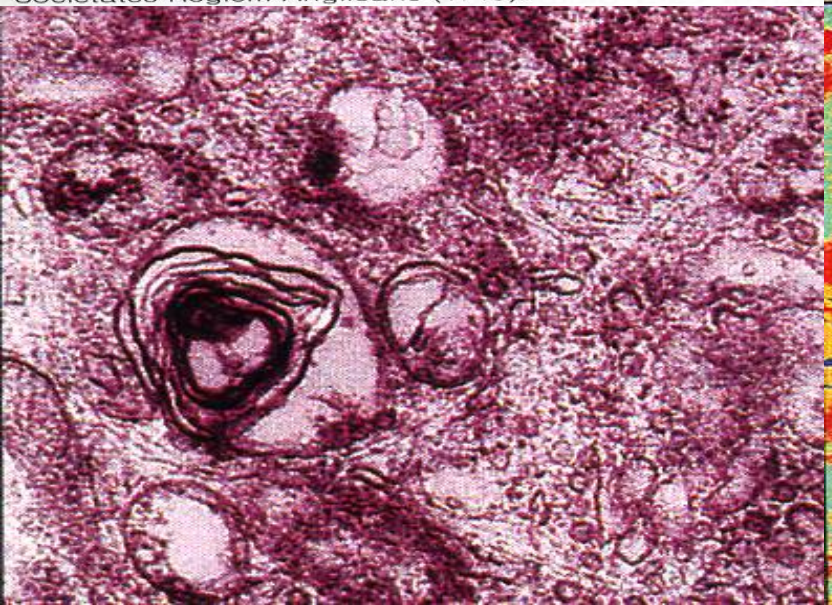


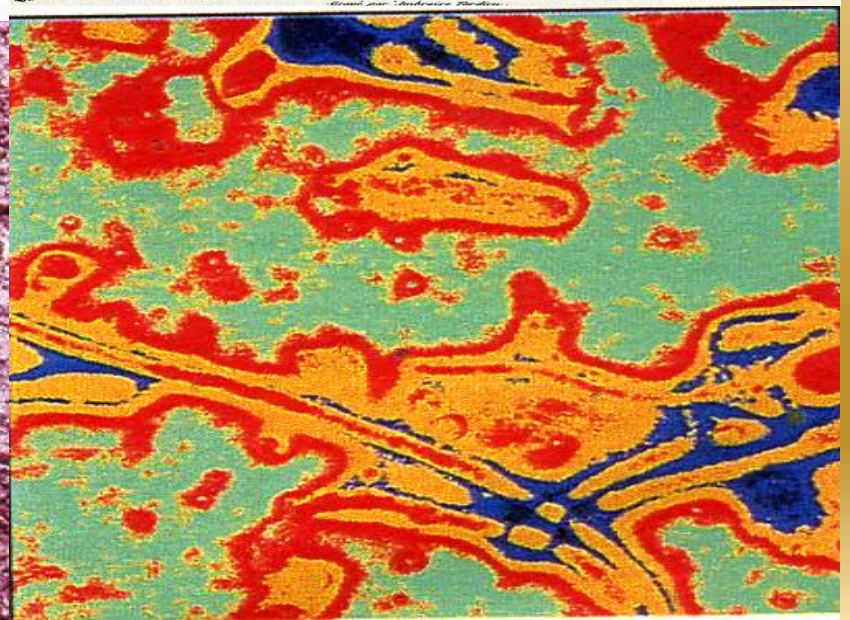


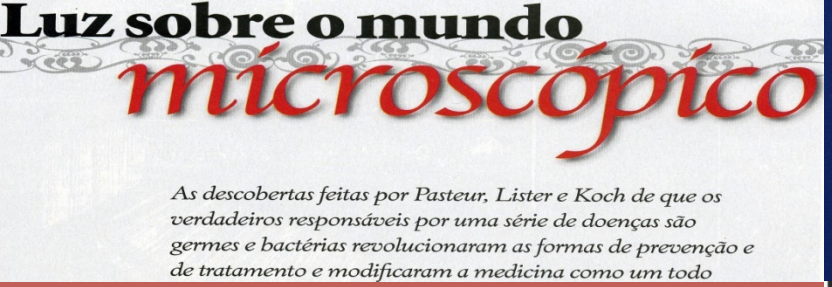
Une brève histoire de l'infiniment Petit

Fig. 25 – Anthony Von Lewenhoek. Retrato na Epístola Societates Regiem Anglicans (1719).









- **1939**
  - ***Ernst Ruska***
    - **Microscópio electrónico**
      - **Primeiras observações de vírus**

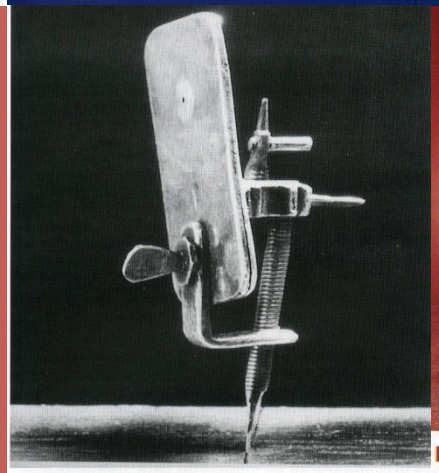
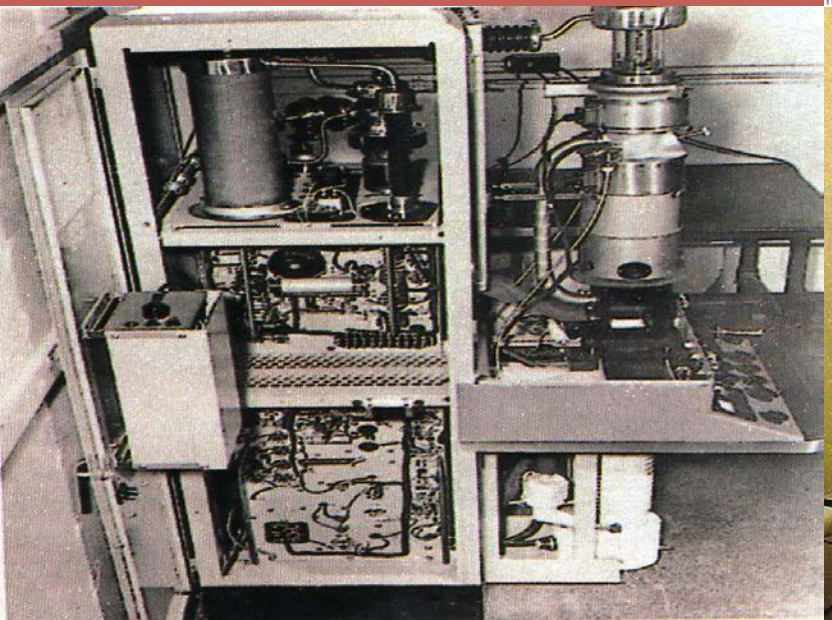
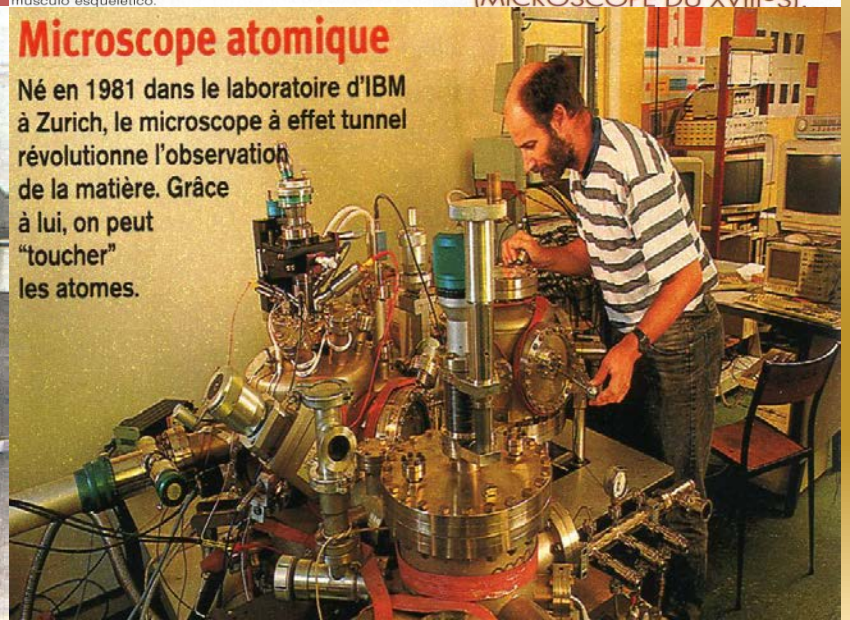


Fig. 24 – Microscópio de Lewenhoek, através do qual pela primeira vez viu os corpúsculos de sangue (glóbulos vermelhos) que pensou serem agentes de doença. Estudou os espermatozóides e descreveu a natureza estriada do músculo esquelético.

L'UTILISATION DU MICROSCOPE REPOSE LA QUESTION : LES PETITS ORGANISMES NE NAISSENT-ILS PAS DE LA MATIÈRE INERTE ? (MICROSCOPE DU XVIIIe S.)





ISSN 1157-4887

LES CAHIERS DE SCIENCE & VIE

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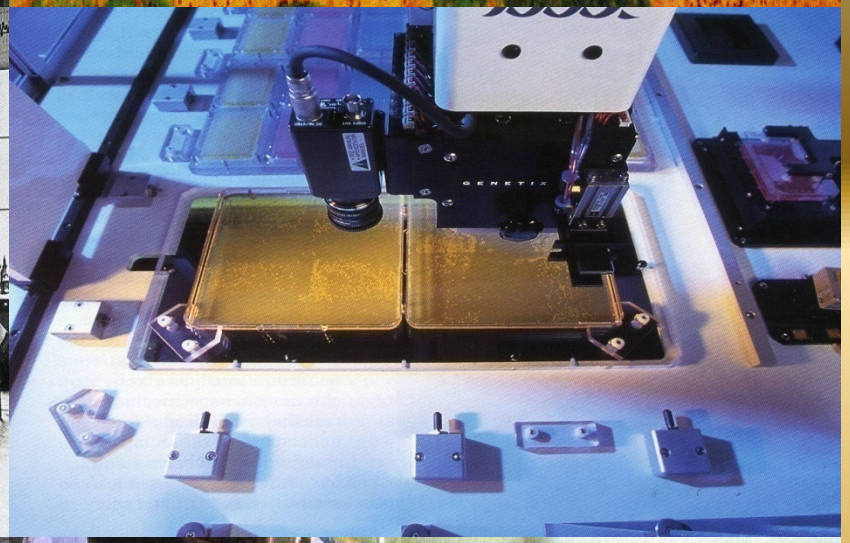
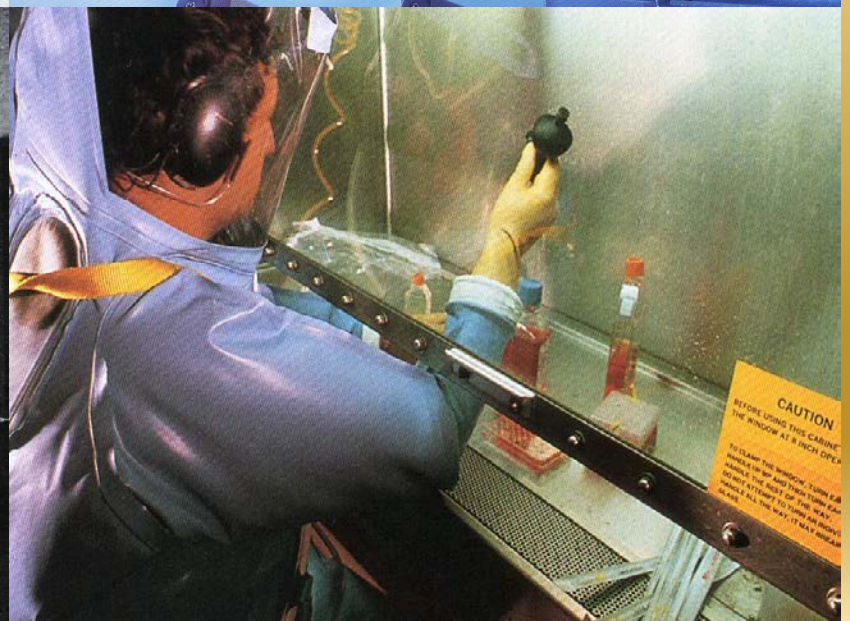
1000 ANS DE SCIENCES

IX – XIXe siècle

Les premiers grands laboratoires

BIOTECHNOLOGY AND PUBLIC CONTROVERSY



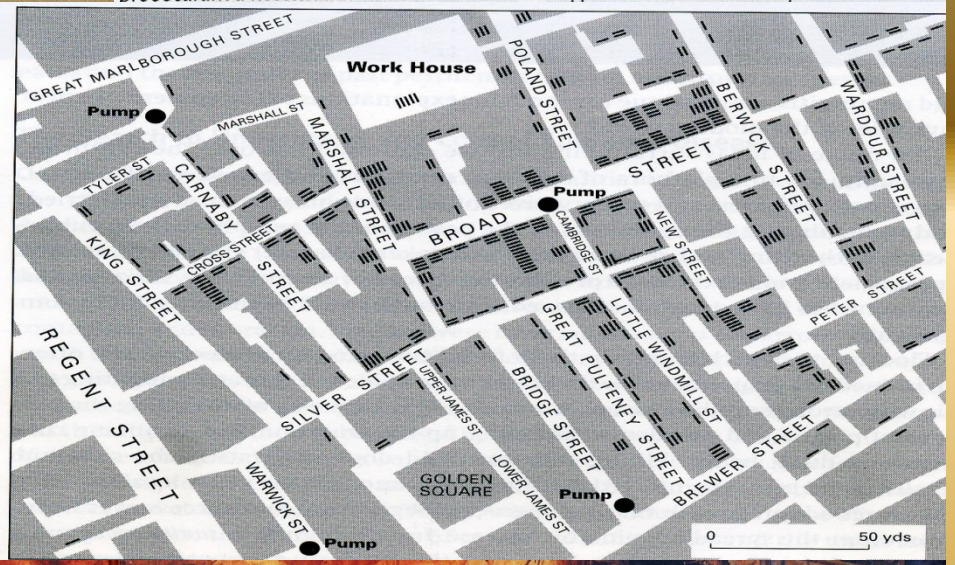


Epidemias e o Estado

Surtos freqüentes de peste, cólera, febre amarela e malária ao longo do século XIX provocaram a necessidade de saneamento e ao surgimento de um sistema público de saúde

EM CIMA John Snow era não só um eminente higienista como também o anestesista que introduziu o éter na Inglaterra. O encerramento da bomba da Broad Street controlou o surto de cólera em Londres em 1854.

John Snow drew a mark or bar on the houses where deaths from cholera took place in Soho during a period of eleven days in 1854. He noted that the people who had drunk water from the Broad Street pump fell ill, and when the pump handle was removed the epidemic ceased.



DESDE A IDADE MÉDIA muitos artistas retrataram em suas obras a morte relacionada às ondas epidêmicas da Europa. Aqui Brueghel representa a Peste Negra de 1332, que afetou quase a quarta parte da população européia, como se as forças da escuridão houvessem caído sobre a humanidade. *O Triunfo da Morte* (cerca de 1556)

Ditadura da Saúde

A TERAPÊUTICA

La vie quotidienne dans les hôpitaux du Moyen Age

par Annie Saunier

L'existence des hôpitaux au Moyen Age est bien connue. Ce qui l'est moins, ce sont les soins, l'alimentation, les traitements et la chirurgie qu'on y pratiquait.

Le lazaret de Venise

ANTIBIOTIQUES : UNE RÉVOLUTION

QUELS ANTIBACTÉRIENS POUR APRÈS-DEMAIN ?

Jean-François Desnottes

Outils et concepts nouveaux relancent la recherche industrielle

Science botanique médiévale

Au Moyen Age, l'apothicaire et l'herboriste se déclarent l'un et l'autre aussi capables de fabriquer des remèdes.

MÉDICO LÉ RECEITA de medicamento para seu ajudante, em iluminura do livro *La grande chirurgie*, do cirurgião Guy of Chauliac. Manuscrito de cerca de 1450

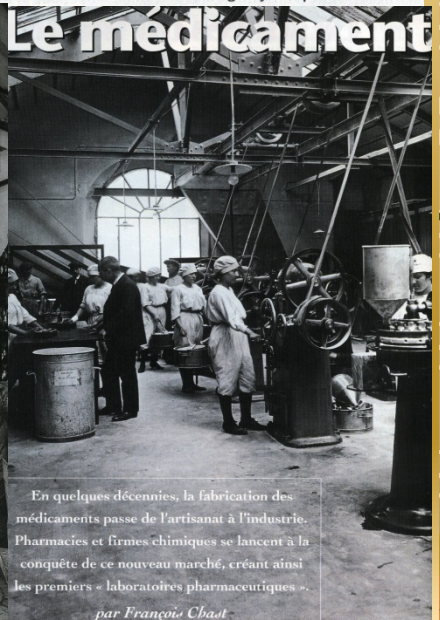
Pharmaciens des Lumières

En 1777, Louis XVI accorde le monopole de la vente des médicaments aux seuls membres du Collège royal de pharmacie.

HERBÁRIO DO SÉCULO XII, em que eram indicadas as propriedades medicinais das plantas

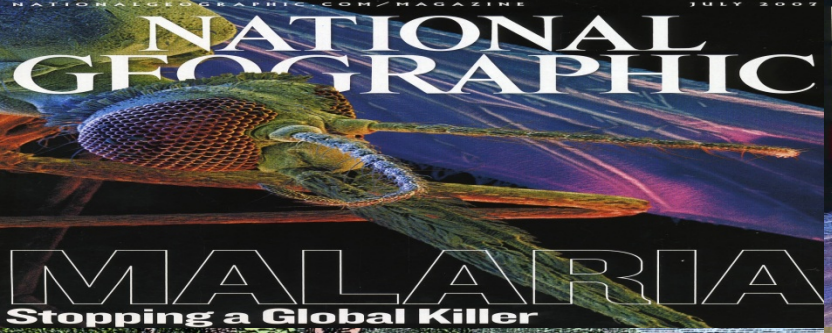
Jusqu'à la Première Guerre mondiale, la pharmacie reste artisanale (ci-contre une herboristerie en 1905).

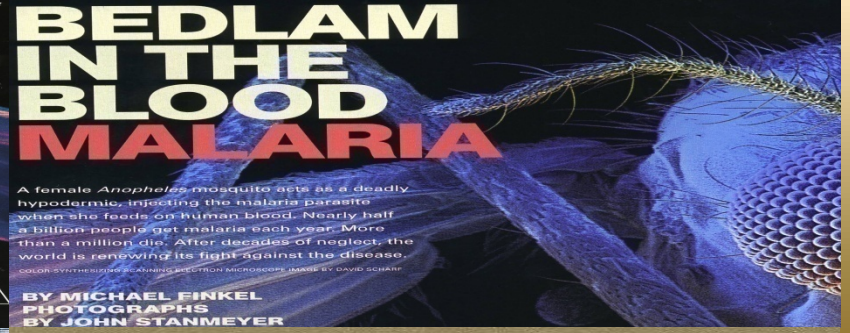
Le médicament



En quelques décennies, la fabrication des médicaments passe de l'artisanat à l'industrie. Pharmacies et firmes chimiques se lancent à la conquête de ce nouveau marché, créant ainsi les premiers « laboratoires pharmaceutiques ».

par François Chast





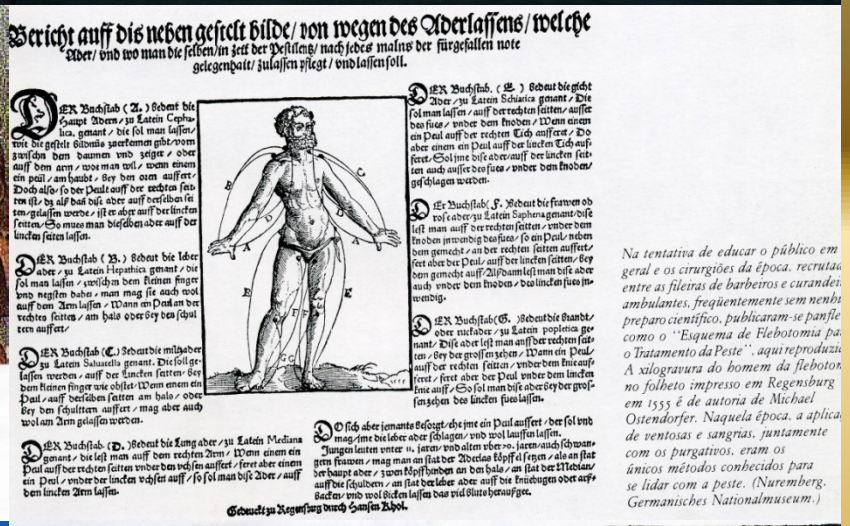
La légende veut que la comtesse d'el Chichon (ci-dessous) guérie du paludisme, ait introduit la poudre de quinquina en Europe. Mais c'est à Joseph Caventou (à g.) et Joseph Pelletier (à dr.) que l'on doit la découverte de la quinine, extraite de l'écorce du quinquina (à gauche).

Joaquim Barradas

A ARTE DE SANGRAR

DE CIRURGIÕES E BARBEIROS

EM CIMA A sangria – uma terapia em que é aberta uma veia para extrair determinada quantidade de sangue – tem uma longa história médica.



Bericht auff dis neben gesetzt bilde/ von wegen des Aderlassens/ welche Ader/ vnd wo man die selben/in zeit der Pestilenz/ nach jedes malns der fürgefallen note gelegenhait/ zulassen pflegt/ vnd lassen soll.

DER Buchstab (A.) bedeut die Haupt Adern/ zu Latein Cephalica, genant/ die sol man lassen/ wie die gesetzt bildnis zuerkennen gibt/ vom zwischen dem daumen vnd zeiger/ oder auff den arm/ wo man wil/ wenn einem ein peul/ am haubt/ bey den oren auffert/ Doch also/ so der Peule auff der rechten seiten ist/ vs alß das dise ader auff derselben seiten/ gelassen werde/ ist er ahrt auff der lincken seiten/ So muss man dieselben ader auff der lincken seiten lassen.

DER Buchstab (B.) bedeut die leber ader/ zu Latein Hepatica genant/ die sol man lassen/ zwischen dem kleinen finger vnd negsten daben/ man mag sie auch wol auff dem Arm lassen/ Wann ein Peul an der rechten seiten/ am halß oder bey den schulteren auffert/

DER Buchstab (C.) bedeut die milzader zu Latein Sahuatilla genant. Die soll gelassen werden/ auff der lincken seiten/ bey dem kleinen finger vse oblet/ Wenn einem ein Peul/ auff derselben seiten am halß/ oder bey den schultern auffert/ mag aber auch wol am Arm gelassen werden.

DER Buchstab (D.) bedeut die Lung ader/ zu Latein Mediana genant/ die lest man auff dem rechten Arm/ Wenn einem ein Peul auff der rechten seiten vnder den vchsen auffert/ feret aber einem ein Peul/ vnder der lincken vchsen auff/ so sol man dise Ader/ auff dem lincken Arm lassen.

DER Buchstab (E.) bedeut die gicht Ader/ zu Latein Schiatica genant/ Die sol man lassen/ auff der rechten seiten/ auffer das fuss/ vnder dem knoden/ Wenn einem ein Peul auff der rechten Tich aufferet/ Do aber einem ein Peul auff der lincken Tich aufferet. Sol jme dise ader/ auff der lincken seiten auch auffer des fuss/ vnder dem knoden/ geschlagen werden.

DER Buchstab (F.) bedeut die frawen ordre ader/ zu Latein Saphena genant/ diese lest man auff der rechten seiten/ vnder dem knoden inwendig das fuss/ so ein Peul/ neben dem gemecht/ an der rechten seiten auffert/ feret aber der Peul/ auff der lincken seiten/ bey dem gemecht auff/ Alßdann lest man dise ader auch vnder dem knoden/ bey lincken fuss inwendig.

DER Buchstab (G.) bedeut die Brandt/ oder nickader/ zu Latein popletica genant/ Dise ader lest man auff der rechten seiten/ bey der grossen zehen/ Wenn ein Peul/ auff der rechten seiten/ vnder dem knie aufferet/ feret aber der Peul vnder dem lincken knie auff/ So sol man dise ader bey der grossen zehen des lincken fuss lassen.

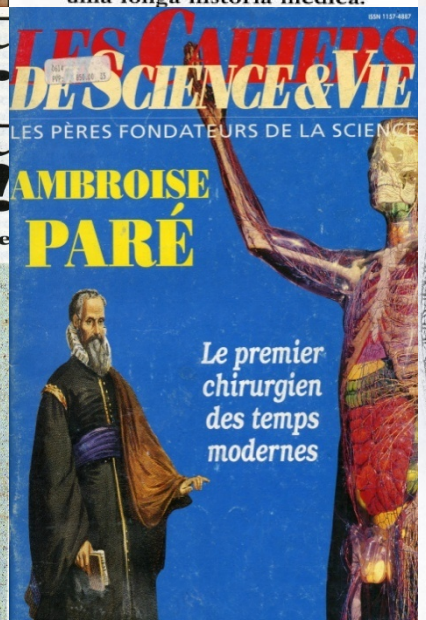
Do sich aber jemants besorgt/ ehe jme ein Peul auffert/ der sol vnd mag jme die leber ader schlagen/ vnd wol lassen lassen. Jungen leuten vnter 11. jaren/ vnd alten vber 70. jaren/ auch schwangern frawen/ mag man an stat der Aderlas köpff setzen/ als an stat der haupt ader/ zwen köpff hinden an den hals/ an stat der Mediana/ auff die schulderen/ an stat der leber ader auff die knieübugen oder auff backen/ vnd wol dicken lassen das vid blute heraussfüret.

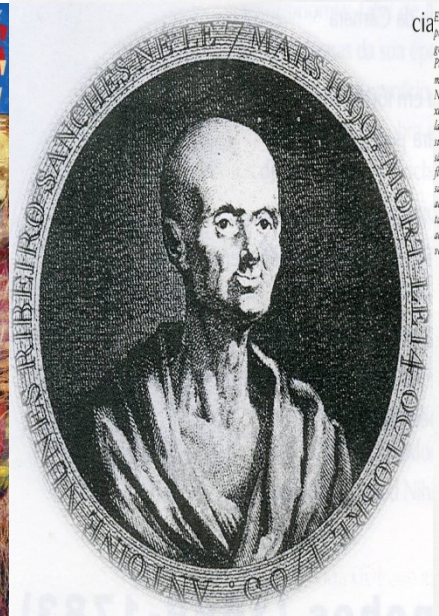
Gedruckt zu Regenspurg durch Hansen Khol.

Na tentativa de educar o público em geral e os cirurgiões da época, recrutados entre as fileiras de barbeiros e curandeiros ambulantes, freqüentemente sem nenhum preparo científico, publicaram-se panfletos como o "Esquema de Flebotomia para o Tratamento da Peste", aqui reproduzido. A xilogravura do homem da flebotomia no folheto impresso em Regensburg em 1555 é de autoria de Michael Ostendorfer. Naquela época, a aplicação de ventosas e sangrias, juntamente com os purgativos, eram os únicos métodos conhecidos para se lidar com a peste. (Nuremberg. Germanisches Nationalmuseum.)

Et saigner et purger !

par Arlette Lebigre





Entre as descrições do tratamento da peste no século XVI, ocupa lugar de grande destaque o "Poema da Pestilência", de Hans Folz (1450-1515), mestre cantor e cirurgião-barbeiro de Nuremberg, também ilustrado por uma xilogravura. Nela aparece um médico lancetando bubões. Os gânglios linfáticos supurados no pescoço, axilas e virilha são lancetados com o bisturi ou o flebótomo, instrumento utilizado para sangria, ou cauterizados com ferros aquecidos ao rubro. Aplicavam-se também sapos sobre os bubões, acreditando-se que eles sugavam o veneno. A xilogravura data de 1482.

Recherche

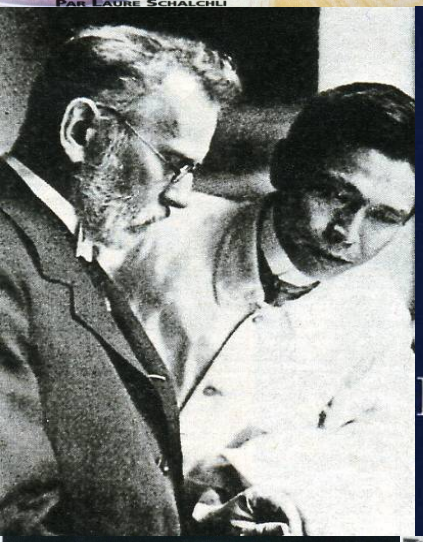
LES GRANDS MÉDICAMENTS DU XXe SIÈCLE

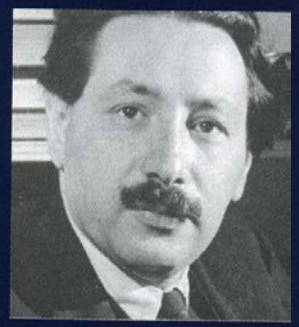
Pénicilline, sulfamides, cortisone, tous ont vu le jour dans la première moitié du siècle dernier. Des découvertes qui ont bouleversé notre vie ...

Par Laure Schalchli

O avanço da penicilina

A descoberta, a produção e o consumo de drogas antibióticas mudaram completamente a relação da medicina com as doenças infecciosas que mais mataram durante toda a história da humanidade





Ernst Boris Chain

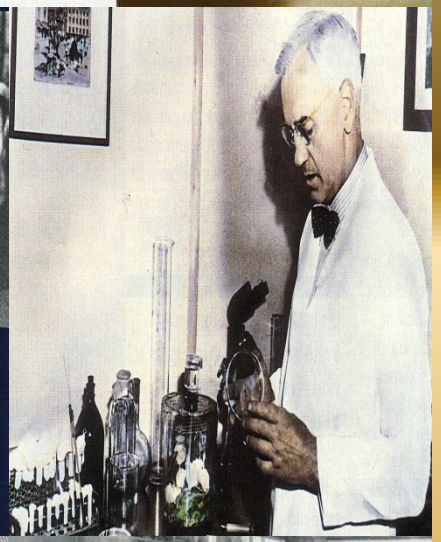
19/06/1906 - 12/08/1979

Berlim, ALEMANHA

Sir Howard Walter Florey

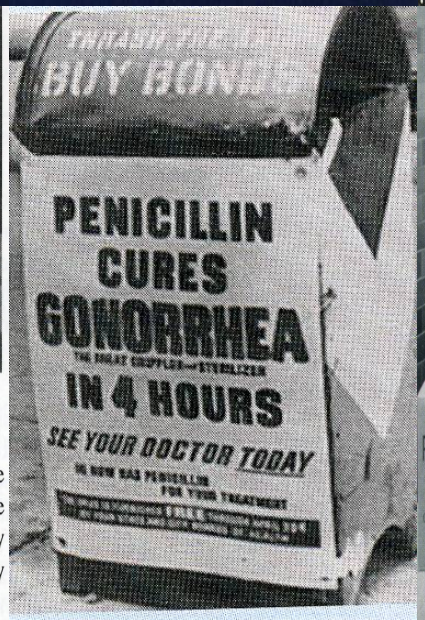
24/09/1898 - 21/02/1968

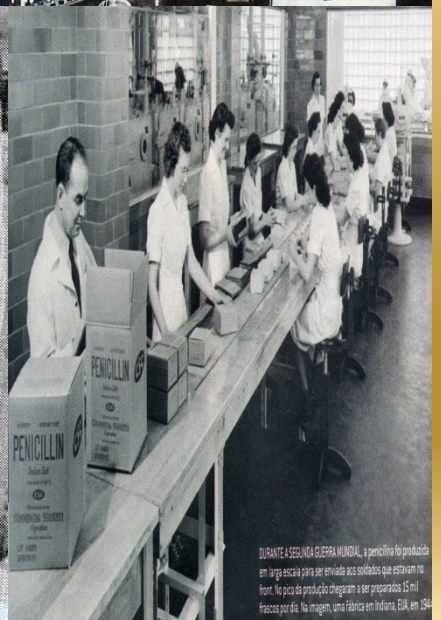
Adelaide, AUSTRÁLIA



PLACA ORIGINAL DE CULTURA do fungo *Penicillium notatum* feita por Fleming enquanto ele trabalhava no Hospital Saint Mary, em Londres. A imagem vista aqui foi refotografada 25 anos após sua descoberta em 1928

In March 1945 penicillin became available in the USA on a large scale. Antibiotics once was once more costly than gold but are available every where now. Dosages however differ significantly from country to country.





DURANTE A SEGUNDA GUERRA MUNDIAL, a penicilina foi produzida em larga escala para ser enviada aos soldados que estavam no front. No pico da produção chegaram a ser preparados 15 mil frascos por dia. Na imagem, uma fábrica em Indiana, EUA, em 1944

LA FIN DE L'ÂGE D'OR DES ANTIBIOTIQUES

Jacques Acar et Patrice Courvalin

Il est grand temps d'agir : certaines bactéries échappent à tous les traitements

- **1901**
  - **Prémio Nobel**
    - **Seroterapia (tétano e difteria)**
- ***(Emil von Bhering)***

- **1939**
  - **Prémio Nobel**
    - **Sulfamidas**
- ***(Gerhard Domagk)***

ILUSTRES DESCONHECIDOS ...

Donnerstag № 49. 4. December 1890.

DEUTSCHE
MEDICINISCHE WOCHENSCHRIFT.

Mit Berücksichtigung des deutschen Medicinalwesens nach amtlichen Mittheilungen, der öffentlichen Gesundheitspflege und der Interessen des ärztlichen Standes.

Begründet von Dr. Paul Börner.

Sechszehnter Jahrgang.

Redacteur Sanitäts-Rath Dr. S. Guttmann in Berlin W. Verlag von Georg Thieme, Leipzig-Berlin.

Nachdruck nur unter Quellenangabe gestattet.

I. Aus dem hygienischen Institut des Herrn Geheimerath Koch in Berlin.

Ueber das Zustandekommen der Diphtherie-Immunität und der Tetanus-Immunität bei Thieren.

Von Stabsarzt Dr. Behring, Assistenten am Institut, und Dr. Kitasato aus Tokio.

Bei unseren seit längerer Zeit fortgesetzten Studien über Diphtherie (Behring) und Tetanus (Kitasato) sind wir auch der therapeutischen und der Immunisirungsfrage nähergetreten, und bei beiden Infectionskrankheiten ist es uns gelungen, sowohl inficirte Thiere zu heilen, wie die gesunden derartig vorzubehandeln, dass sie später nicht mehr an Diphtherie bezw. am Tetanus erkranken.

Auf welche Weise die Heilung und die Immunisirung zu erreichen ist, darauf soll an dieser Stelle nur soweit eingegangen werden,[1]) als nothwendig ist, um die Richtigkeit des folgenden Satzes zu beweisen.

„Die Immunität von Kaninchen und Mäusen, die gegen Tetanus immunisirt sind, beruht auf der Fähigkeit der zellenfreien Blutflüssigkeit, die toxischen Substanzen, welche die Tetanusbacillen produciren, unschädlich zu machen."

Die Erklärung für die Immunität, welche im vorstehenden Satz zum Ausdruck gebracht ist, wurde in denjenigen Arbeiten, die in neuerer Zeit sich mit der Immunitätsfrage beschäftigten, noch nicht in Erwägung gezogen.

Ausser mit der Phagocytosenlehre, die in der vitalen Thätigkeit der Zellen die Erklärung suchte, wurde noch mit der bacterienfeindlichen Wirkung des Blutes und mit der Giftgewöhnung des thierischen Organismus gerechnet.

Wenn eins dieser Erklärungsprincipien nicht ausreichte, oder von experimentell arbeitenden Autoren als unrichtig erkannt wurde, so glaubte man auf dem Wege der Ausschliessung die anderen in Anspruch nehmen zu dürfen. So sagte Bouchard in seiner Rede auf dem X. internationalen medicinischen Congress, die vielleicht am prägnantesten den bisherigen Stand der Immunitätsfrage wiedergiebt, Folgendes: „Ne parlons donc plus d'entraînement des leucocytes et d'accoutumance des cellules nerveuses aux poisons bactériens: c'est pure rhétorique" und: „C'est en effet cet état bactéricide qui constitue la vaccination ou l'immunité acquise."

Diese positive Erklärung kommt auf dasselbe hinaus, was Roger[2]) früher mit folgenden Worten ausdrückte: „La vaccination détermine dans l'organisme des modifications chimiques qui rendent les humeurs et les tissus peu favorables à la végétation du microbe, contre lequel on a prémuni l'animal."

Nun konnte der eine von uns (Behring) bei seinen Studien an diphtherieimmunen Ratten und an immunisirten Meerschweinchen feststellen, dass keine der oben erwähnten Theorieen uns die Immunität dieser Thiere zu erklären vermag, und er sah sich genöthigt, nach einem anderen Erklärungsprincip zu suchen. Nach mannichfachen vergeblichen Bemühungen zeigte sich in der diphtheriegift-zerstörenden Wirkung des Blutes von diphtherieimmunen Thieren die Richtung, in welcher die Unempfänglichkeit für Diphtherie zu suchen ist. Aber erst bei der Anwendung der bei der Diphtherie gemachten Erfahrungen auf den Tetanus sind wir zu Ergebnissen gelangt, die, soweit wir erkennen können, an Beweiskraft nichts zu wünschen übrig lassen.

Die im folgenden angeführten Experimente beweisen:

1. Das Blut des tetanusimmunen Kaninchens besitzt tetanusgiftzerstörende Eigenschaften.

2. Diese Eigenschaften sind auch im extravasculären Blut und in dem daraus gewonnenen zellenfreien Serum nachweisbar.

3. Diese Eigenschaften sind so dauerhafter Natur, dass sie auch im Organismus anderer Thiere wirksam bleiben, so dass man imstande ist, durch die Blut- bezw. Serumtransfusion hervorragende therapeutische Wirkungen zu erzielen.

4. Die tetanusgiftzerstörenden Eigenschaften fehlen im Blut solcher Thiere, die gegen Tetanus nicht immun sind, und wenn man das Tetanusgift nicht immunen Thieren einverleibt hat, so lässt sich dasselbe auch noch nach dem Tode der Thiere im Blut und in sonstigen Körperflüssigkeiten nachweisen.

Wir theilen zum Beweise für diese Behauptungen folgende grössere Versuchsreihe mit:

Auf eine Art, die an anderer Stelle genau beschrieben werden wird[1]), wurde ein Kaninchen gegen Tetanus immunisirt. Bei der Prüfung des Grades der Immunität erhielt dasselbe 10 ccm einer keimhaltigen virulenten Tetanusbacillen-Cultur, von der für normale Kaninchen 0,5 ccm genügten, um dieselben ganz sicher am Tetanus zu Grunde gehen zu lassen. Jenes Kaninchen blieb ganz gesund.

[1]) Genauere Mittheilungen hierüber werden in der Zeitschrift für Hygiene erfolgen.

[2]) „Contribution à l'étude de l'immunité acquise." 1890.

[1]) In einer demnächst in der Zeitschrift für Hygiene erscheinenden Arbeit: Ueber die Eigenschaften des Tetanusgiftes, von Kitasato.

In Praise of Antibiotics

The Advent of Modern Microbiology

These "wonder drugs" revolutionized the treatment of infectious diseases—but they cannot be taken for granted

Julian Davies

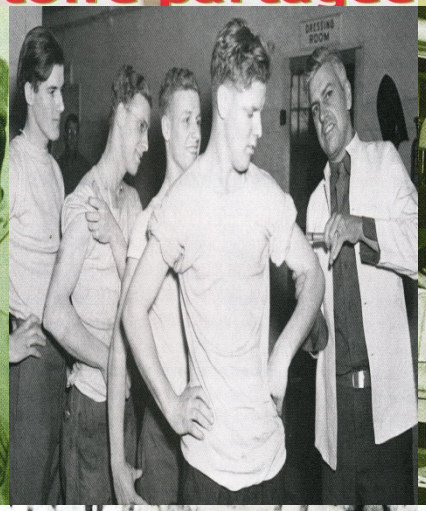
Table 1. Overview of important antibiotics

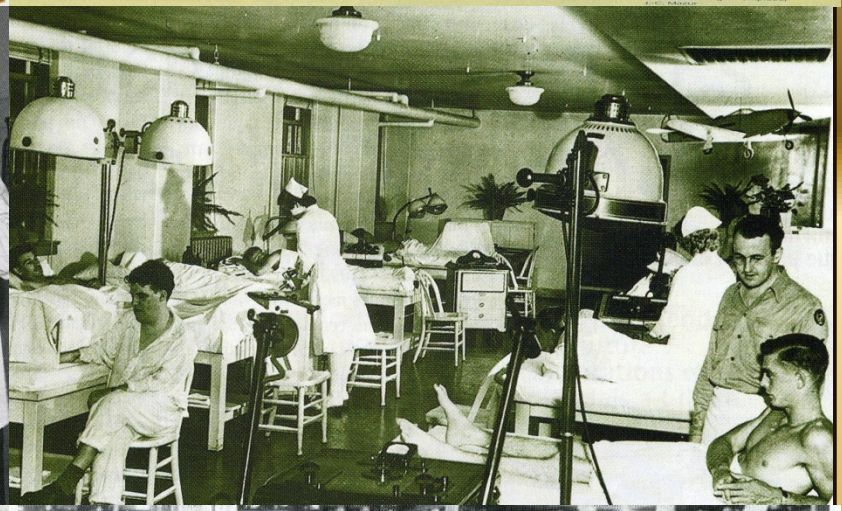
Year discovered	Antibiotic*	Class	Comments
1929	Penicillin	β-Lactam	Identification of activity—not isolated
1932	Sulfapyridine*	Sulfonamide	Many derivatives have been developed and remain useful drugs
1939	Polymixin	Peptide	Employed for topical application ('triple antibiotic cream')
1940	Penicillin G	β-Lactam (penicillin)	The forerunner of a large class of antibiotics
1944	Streptomycin	Aminoglycoside (streptamine)	Important drug for TB treatment
1945	Cephalosporin C	β-Lactam (cephalosporin)	First of its class.
1947	Chloramphenicol	Phenylpropanoid	In spite of toxicity (bone marrow suppression), widely used for typhoid, diarrheas
1948	Chlortetracycline	Tetracycline (type II polyketide)	Broad spectrum, extensively used in humans, but also for animal growth promotion
1950	Erythromycin	Macrolide (type I polyketide)	Modern derivatives (clarithromycin, azithromycin) used widely for gram-positive infections
1955	Vancomycin	Glycopeptide	Little used until the 1980s when it was introduced to treat multiply-resistant gram-positive bacterial pathogens; the 'V' in VRE
1955	Amphotericin B	Polyene	First generally effective antifungal agent
1955	Virginiamycin	Streptogramins (two-component agent: macrocyclic peptolide and depsipeptide	Introduced for animal use, closely related to Synercid now used in humans
1955	Lincomycin	Lincosamide	Long-time standby for certain gram-positive infections
1959	Rifamycin	Ansamycin	Front-line drug for TB treatment
1960	Methicillin	β-Lactam (penicillin)	The 'M' in MRSA
1962	Cephalothin	β-Lactam (cephalosporin)	
1962	Nalidixic acid*	Quinolones	The forerunner of the potent 4-fluoroquinolones (e.g., ciprofloxacin* 1983)
1962	Trimethoprim*	Substituted pyridinediamine	Often used in combination with sulfa drug.
1963	Gentamicin	Aminoglycoside (2-deoxystreptamine)	First broad-spectrum aminogycloside widely used for nosocomial infections
1969	Fosfomycin	Phosphonate	Recently introduced in North America
1973	Cefoxitin	Cephamycin	
1973	Aztreonam	Monobactam	
1976	Thienamycin	Carbapenem	All β-lactam antibiotics, the 'modern' replacements for penicillin
1980	Daptomycin	Lipopeptide	Presently in advanced trials for VRE, MRSA treatment

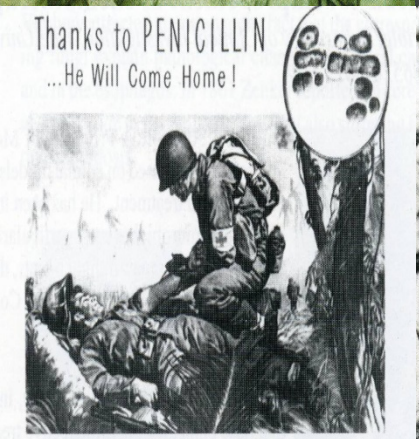
*Not derived from natural products.

LA SCIENCE ET LA GUERRE

400 ans d'histoire partagée







On the 28th of December 1940, penicillinase was born. The issue of *Nature* of that date contained a short paper by E. P. Abraham and E. Chain reporting that extracts from several Gram-negative rods including *B. coli* destroyed penicillin.

On the 8th of September 1939, just after the declaration of Second World War, Florey obtained a grant of only 25 pounds from the Medical Research Council : *"to produce a single end-result-penicillin"*. Fortunately in November of the same year, he received more substantial support from the Rockefeller Foundation.

ELSEVIER SAUNDERS

Infect Dis Clin N Am 18 (2004) 341–368

INFECTIOUS DISEASE CLINICS OF NORTH AMERICA

Impact of infectious diseases on war

Matthew R. Smallman-Raynor, PhD[a,*], Andrew D. Cliff, DSc[b]

[a]School of Geography, University of Nottingham, University Park, Nottingham, NG7 2RD, UK

[b]Department of Geography, University of Cambridge, Downing Place, Cambridge, CB2 3EN, UK

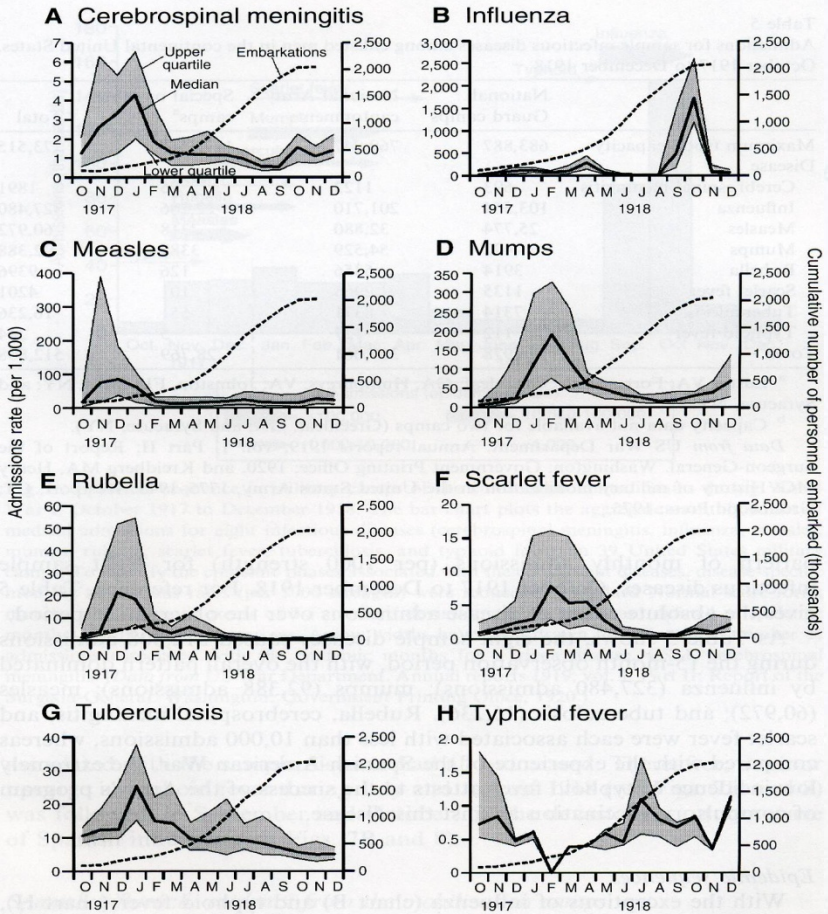


Fig. 7. Infectious diseases in military camps, continental United States, World War I. Graphs plot, as a heavy line trace, the median value of the monthly admission rate (per 1000 strength) for sample diseases in 39 military camps. On each graph the shaded area forms an envelope, which delimits the interquartile range of the corresponding admission rates. (*A*) Cerebrospinal meningitis. (*B*) Influenza. (*C*) Measles. (*D*) Mumps. (*E*) Rubella. (*F*) Scarlet fever. (*G*) Tuberculosis. (*H*) Typhoid fever. The broken line trace on each graph plots the cumulative monthly count of Army personnel embarked for Europe. (*Data from* US War Department. Annual reports 1919, vol. 1. Part II: Report of the Surgeon-General. Washington: Government Printing Office; 1920; and Kreidberg MA, Henry MG. History of military mobilization in the United States Army, 1775–1945. Westport, CT: Greenwood Press; 1975.)

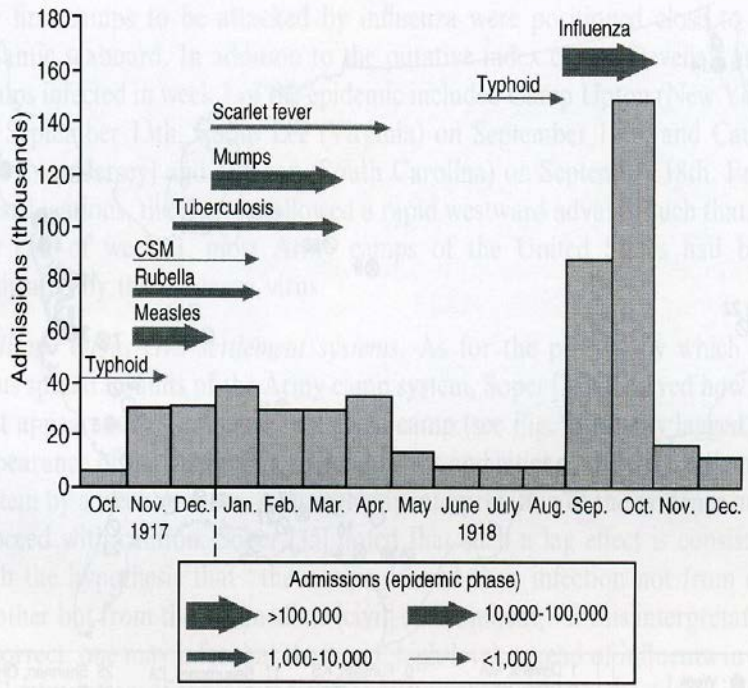


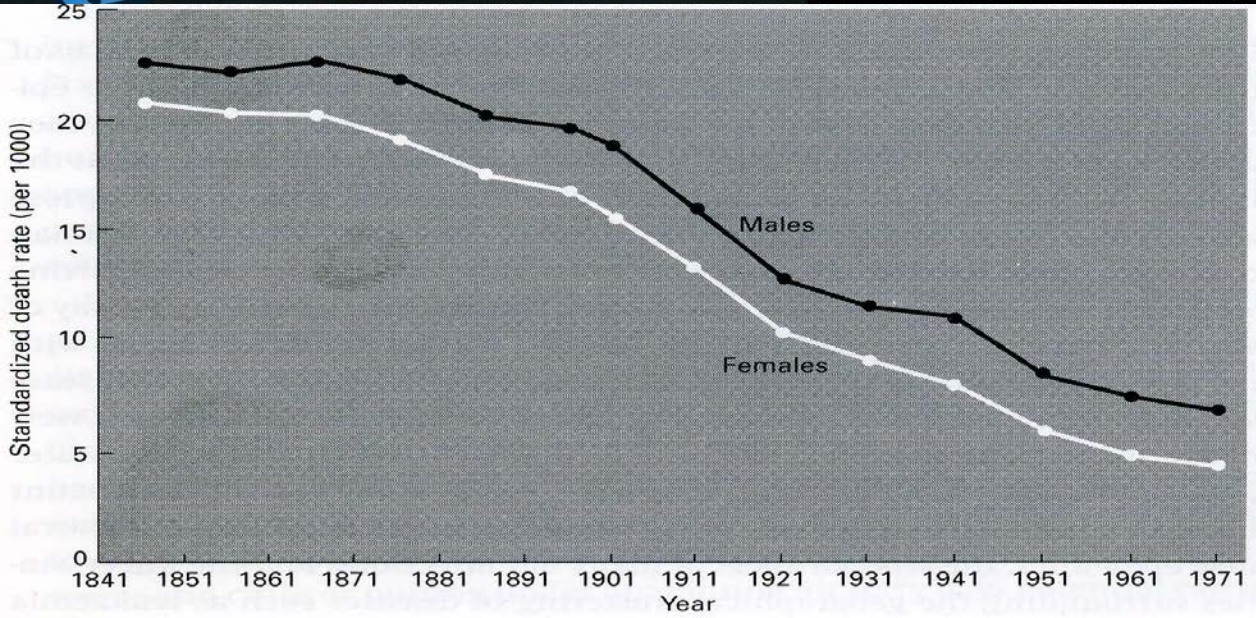
Fig. 8. Epidemic sequence in military camps of the continental United States during World War I, October 1917 to December 1918. The bar chart plots the aggregate monthly count of medical admissions for eight infectious diseases (cerebrospinal meningitis, influenza, measles, mumps, rubella, scarlet fever, tuberculosis, and typhoid fever) in 39 United States military camps. To identify the epidemic phases associated with the constituent diseases, disease-specific monthly admissions rates (per 1000 strength) were reduced to standard Normal score form; months with scores in excess of 0.5 standard deviations above the mean (defined as epidemic months) are indicated by arrows. Arrow widths have been drawn to indicate the number of admissions associated with the epidemic months for a given disease. CSM, cerebrospinal meningitis. (*Data from* US War Department. Annual reports 1919, vol. 1. Part II: Report of the Surgeon-General. Washington: Government Printing Office; 1920.)

OXFORD

WESTERN MEDICINE

An Illustrated History

Edited by IRVINE LOUDON



Death-rates in the Western world have fallen substantially since the mid-nineteenth century. The cause of this mortality decline remains a subject of debate amongst historians. It has been argued that immunization, medical therapies, and other scientific advances made little contribution to the mortability decline, except possibly in the case of smallpox and vaccination.

GLOBAL HEALTH

Designing Tomorrow's Vaccines

Gary J. Nabel, M.D., Ph.D.

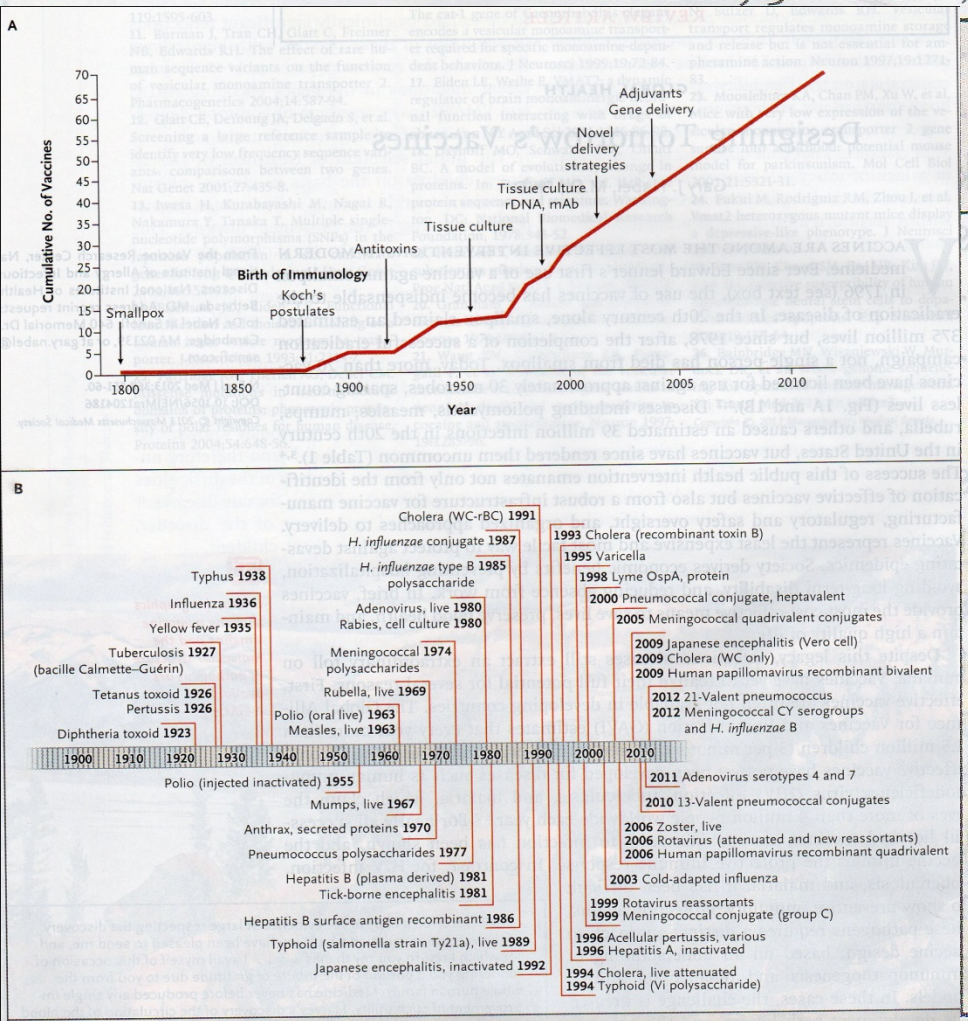


Figure 1. Timelines for Vaccine Development and Licensure of Commercial Vaccines.

Panel A shows major milestones and advances in vaccine development and the cumulative number of licensed vaccines since the time of Edward Jenner's first use of a vaccination against smallpox in 1796.[1] Panel B shows the timeline for licensure of commercial vaccines against the indicated pathogens.[2] The abbreviation mAb denotes monoclonal antibody, OspA outer surface protein A, rBS recombinant B subunit of cholera toxin, rDNA recombinant DNA, and WC whole-cell *Vibrio cholerae* O1.

Table 1. Estimated Cumulative Number of Cases of Selected Infectious Diseases in the United States in the 20th Century before the Advent of a Vaccine, as Compared with Mortality after Utilization.*

Disease	Estimated Prevaccine Cases in 20th Century	Deaths in 2002
	number	
Smallpox	4.81 million	0
Poliomyelitis	1.63 million	0
Diphtheria	17.60 million	2
Haemophilus influenzae	2.00 million	22
Measles	5.03 million	36
Mumps	1.52 million	236
Pertussis	1.47 million	6632
Rubella	4.77 million	20
Tetanus	0.13 million	13

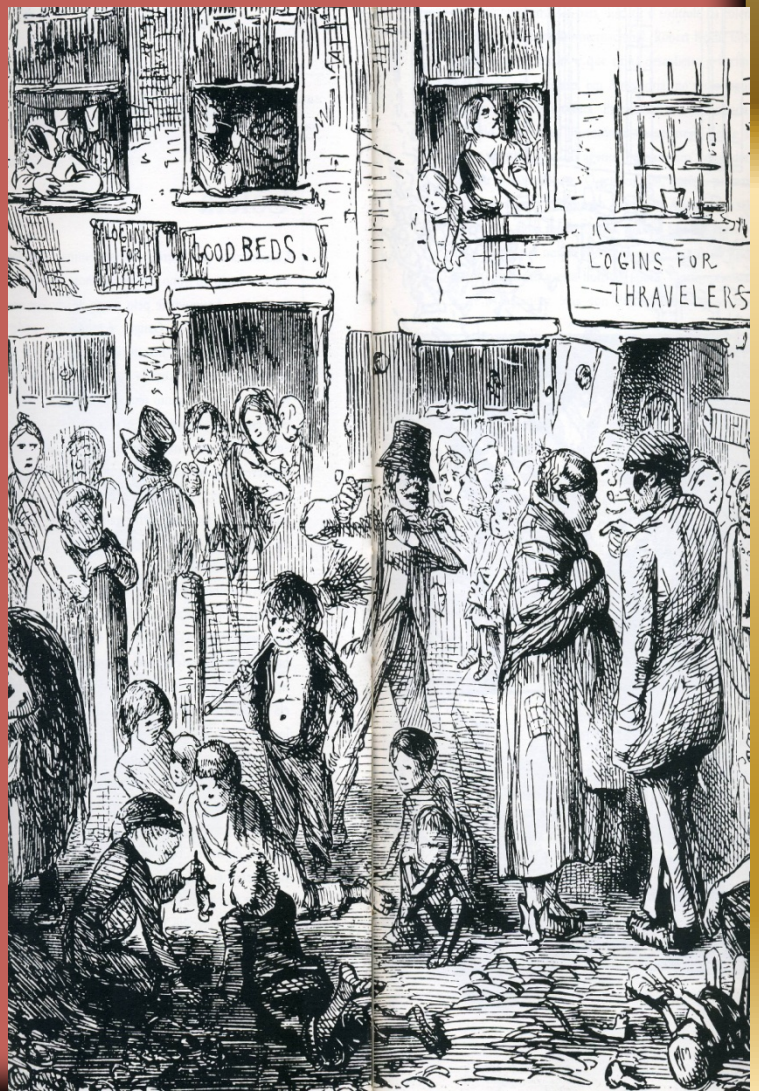
* Data are from the Centers for Disease Control and Prevention[3] and Roush and Murphy.[4]

AS NOSOLOGIAS e os AGENTES INFECCIOSOS

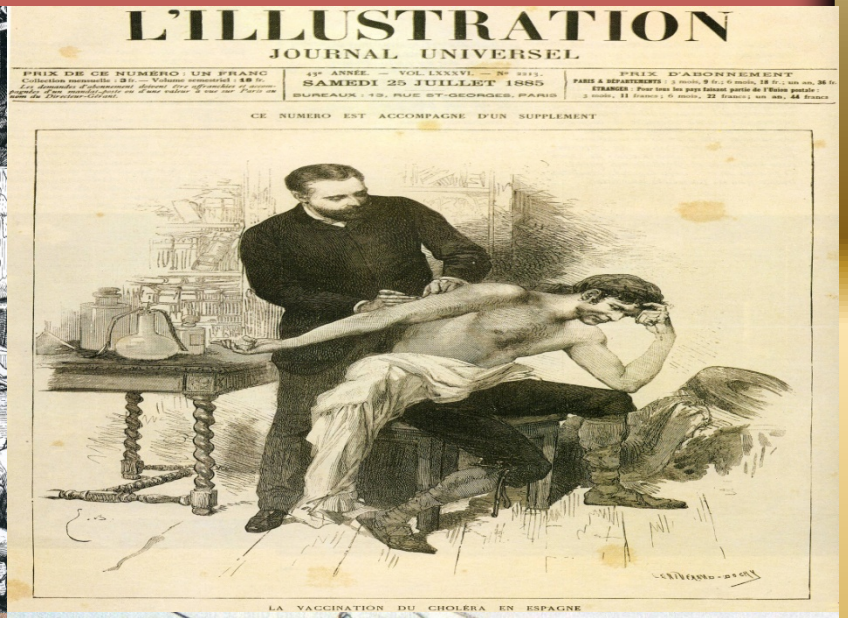
Provérbios flamengos, de Pieter Bruegel, o Velho (c. 1525-1569). Em contraste com os cuidados tomados na antiga Roma, durante a Idade Média e no período posterior, não existiam esgotos e havia pouca preocupação com o destino dos dejetos, que eram atirados nas ruas ou em outros logradouros públicos

CÓLERA

- 1817 – 1963
  - Sete Pandemias
- 1817
  - Primeiras Descrições
    - Índia
- 1885
  - *Jaime Ferrán*
    - Primeira Vacina
- Primeiras Vacinações em Massa
  - 1890
    - Índia e NY (USA)
- Vítimas Ilustres
  - *Peter Tchaikovsky*
  - *Georg Hegel*
  - *Jean-François Champollion*



CÓLERA



L'ILLUSTRATION

JOURNAL UNIVERSEL

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45e ANNÉE. — VOL. LXXXVI. — N° 2213.

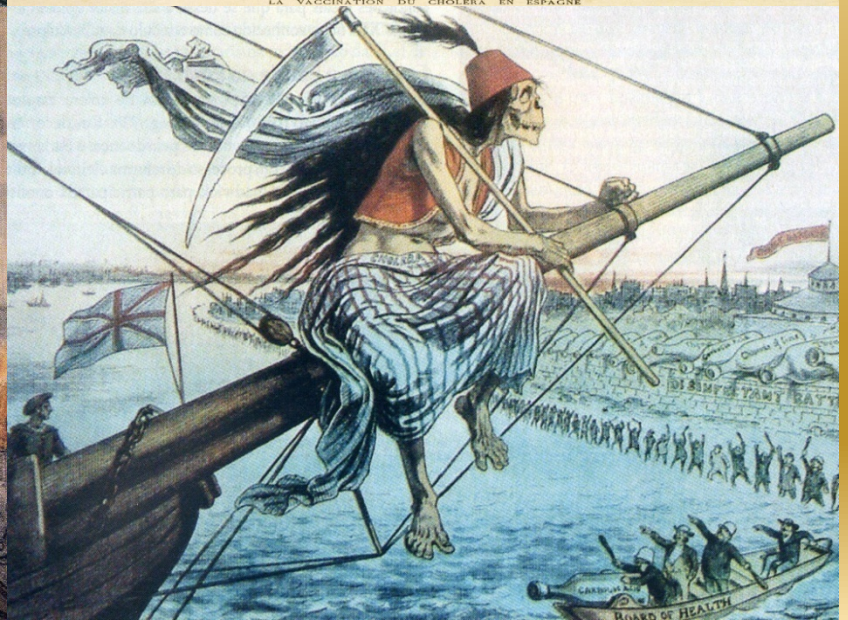
SAMEDI 25 JUILLET 1885

BUREAUX : 13, RUE ST-GEORGES, PARIS

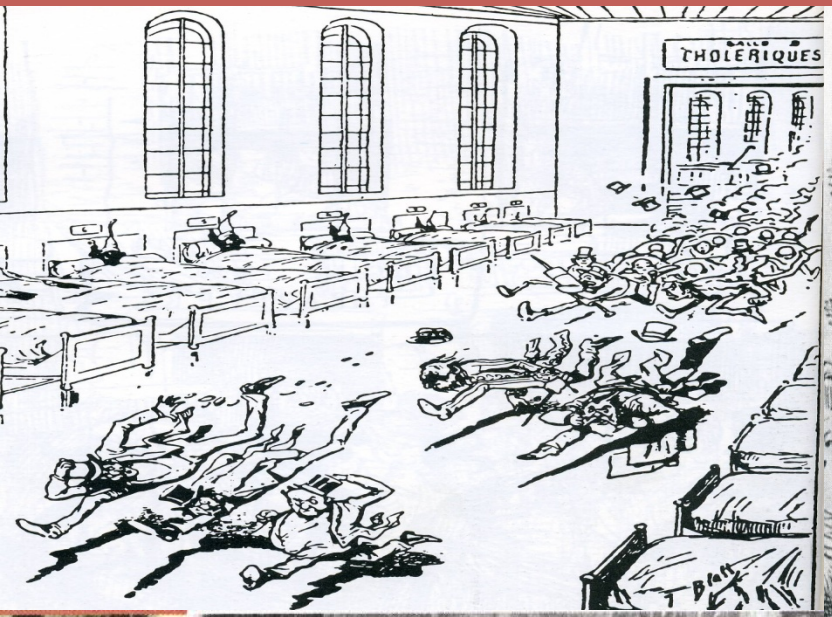
PRIX D'ABONNEMENT

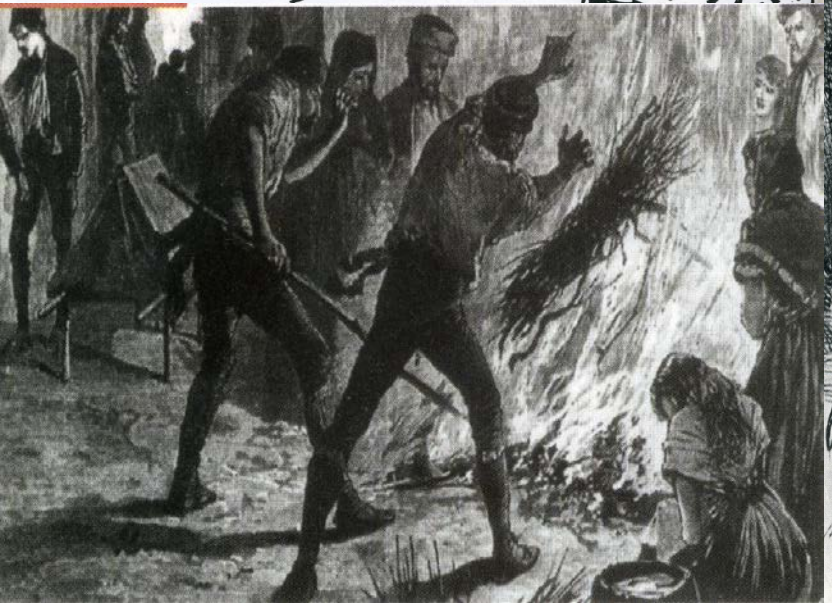
CE NUMERO EST ACCOMPAGNE D'UN SUPPLEMENT

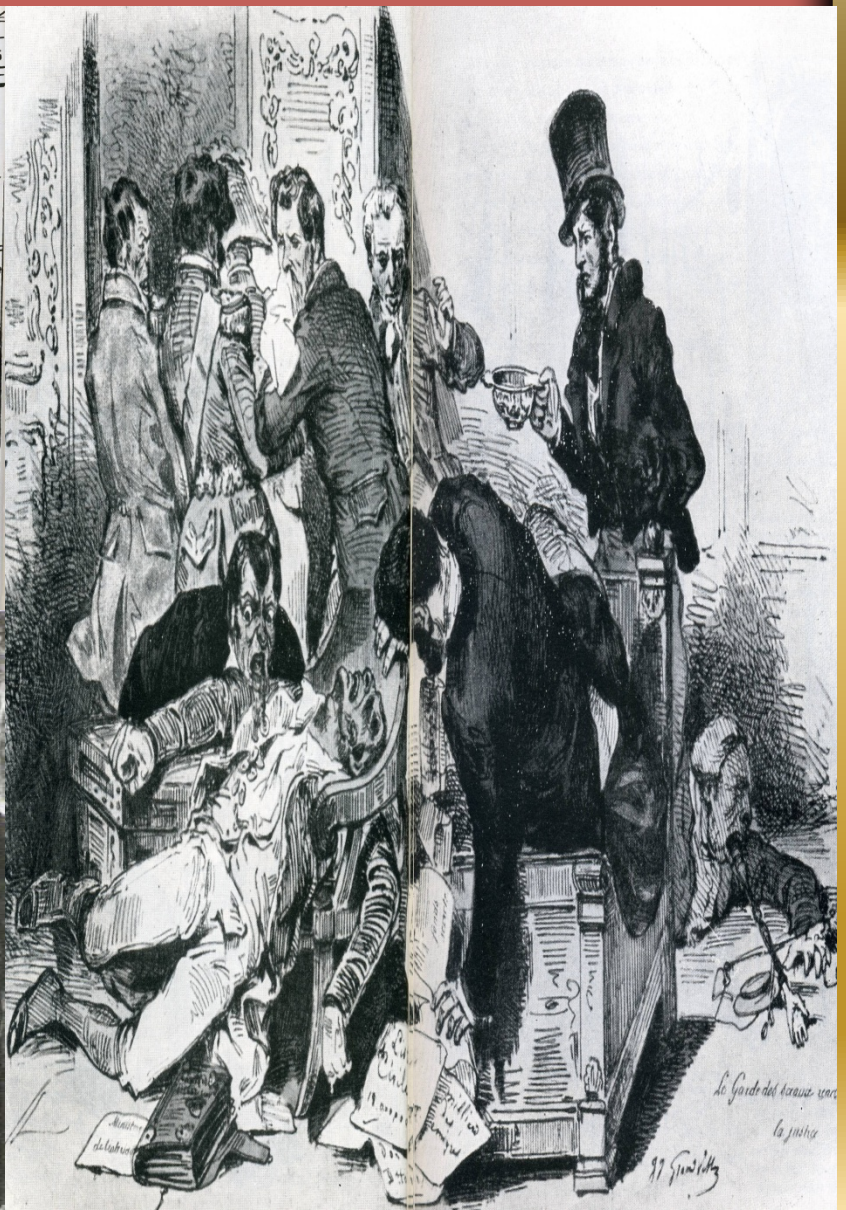
LA VACCINATION DU CHOLÉRA EN ESPAGNE



CÓLERA



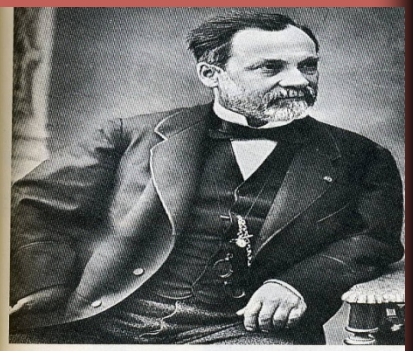




Febre Amarela

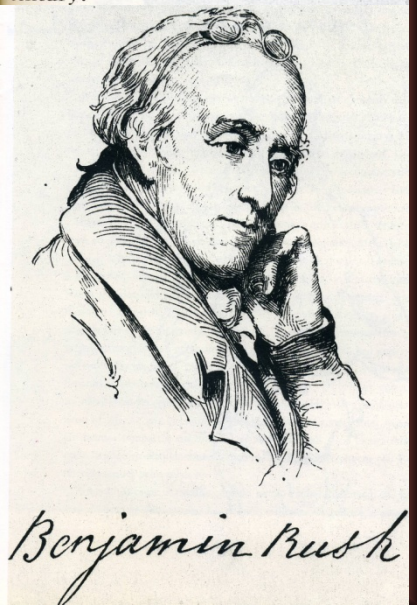
- **Séc. XVII**
  - **Continente Americano**
    - **Griffin Huges Primeira Descrição nos Barbados**
- **1881**
  - ***Carlos Finley***
    - **Vector (*aedes aegypti*)**
- **1901**
  - ***William Gorgas***
    - **"Kerosene" na desinfestação dos pântanos**
- **1927**
  - **Walter Reed**
    - **Isolamento do Vírus**

George Miller Sternberg



BELOW FAR RIGHT *Gorgas.* General William Crawford Gorgas (1845–1920), a military doctor from Mobile, Alabama, played a major part in the control of yellow fever in Cuba and Panama, using the techniques of the new tropical medicine. Photograph, late nineteenth century.

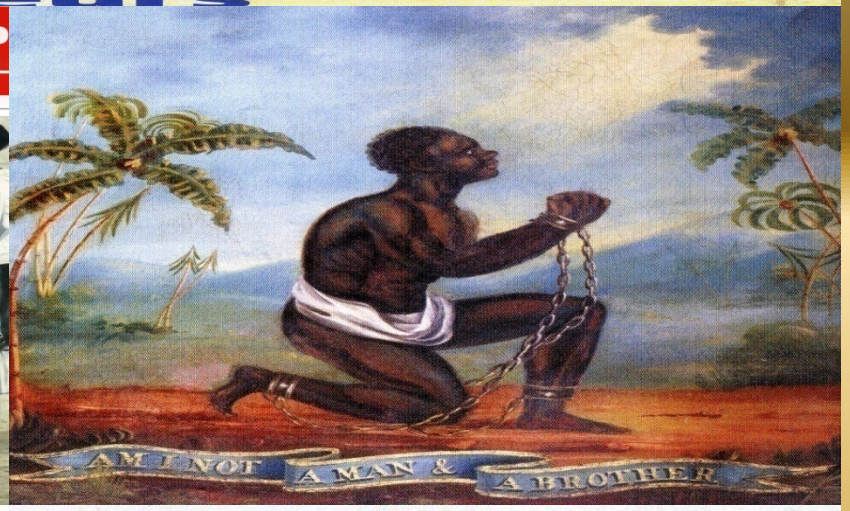
Walter Reed (1851–1902) and his team confirmed the theory that yellow fever is transmitted by mosquitoes



Qu'est-ce que transmettre ?

Savoir
Mémoire
Culture
Valeurs

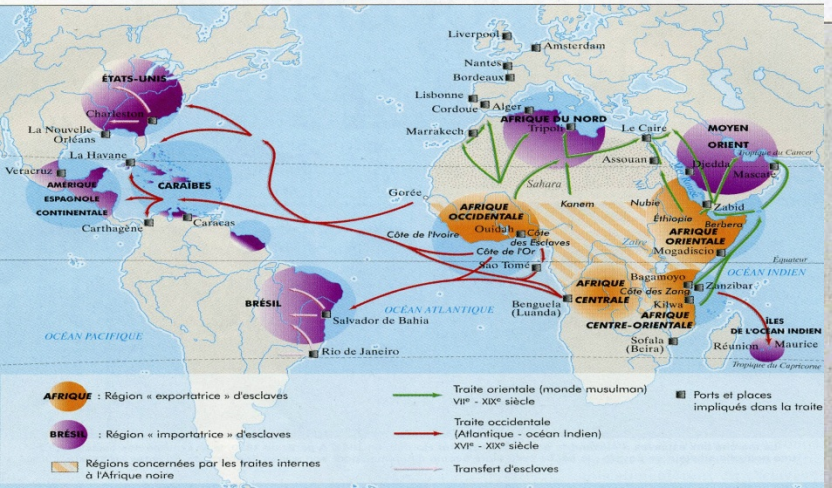
L'ESCLAVAGE



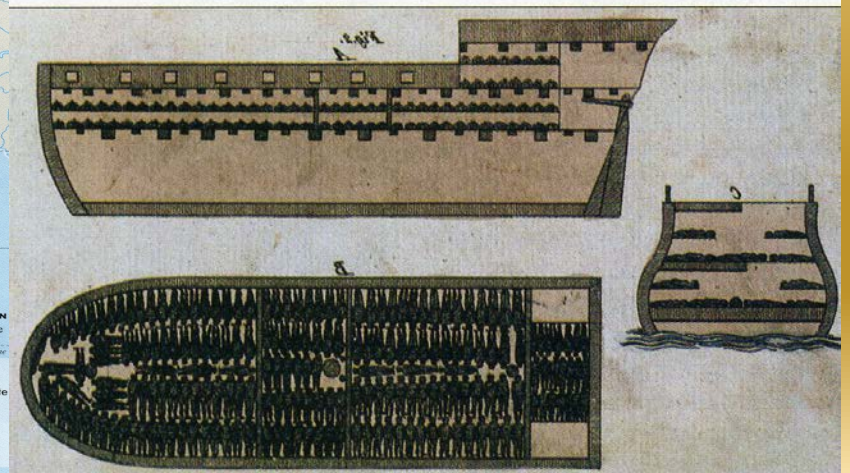
IMAGES

REPÈRES CARTOGRAPHIQUES

Les traites négrières, VIIe-XIXe siècle

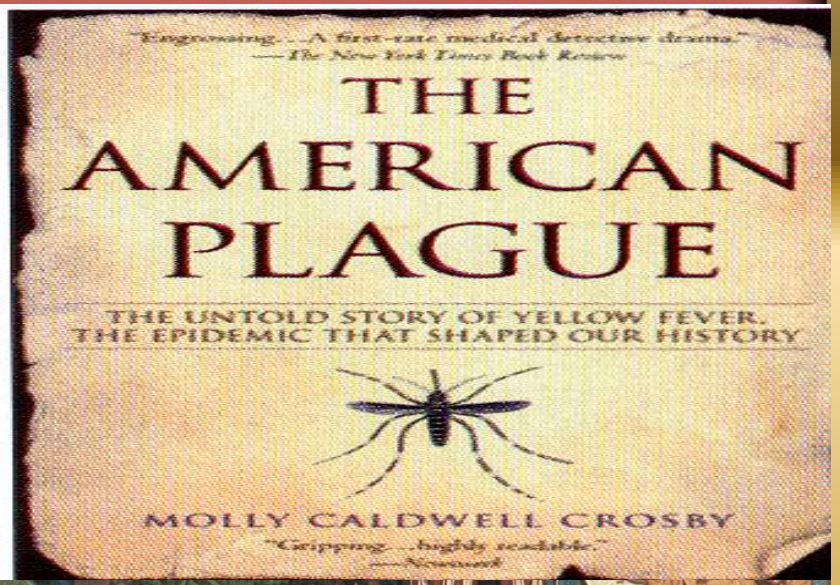


A bord des navires négriers



FEBRE AMARELA

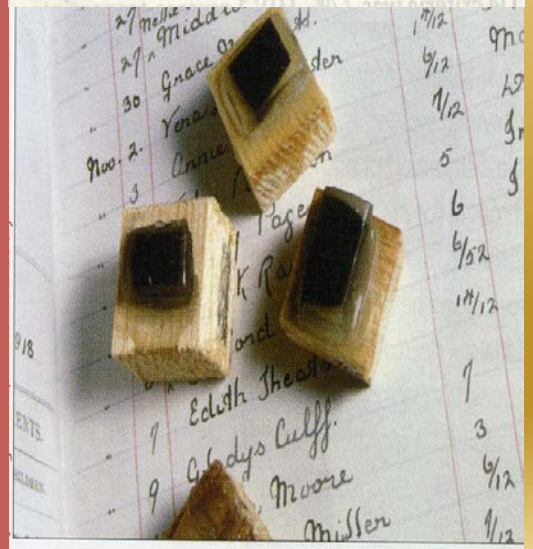
S. Burt Wolbach and John L. Todd Crossing Kandong Bolon, a Creek near Somita, Gambia, Where They Were Researching Yellow Fever and Other Tropical Diseases, in February 1911.



INFLUENZA

- Séc. XVIII
  - Três grandes epidemias
- Séc. IX
  - Quatro grandes epidemias
- 1918 – 1920
  - “Gripe Espanhola”
    - 20.000.000 – 40.000.000 mortos
- 1957
  - “Gripe Asiática”
    - 4.000.000 mortos
- 1968
  - “Gripe de Hong Kong”
    - 1.000.000 mortos

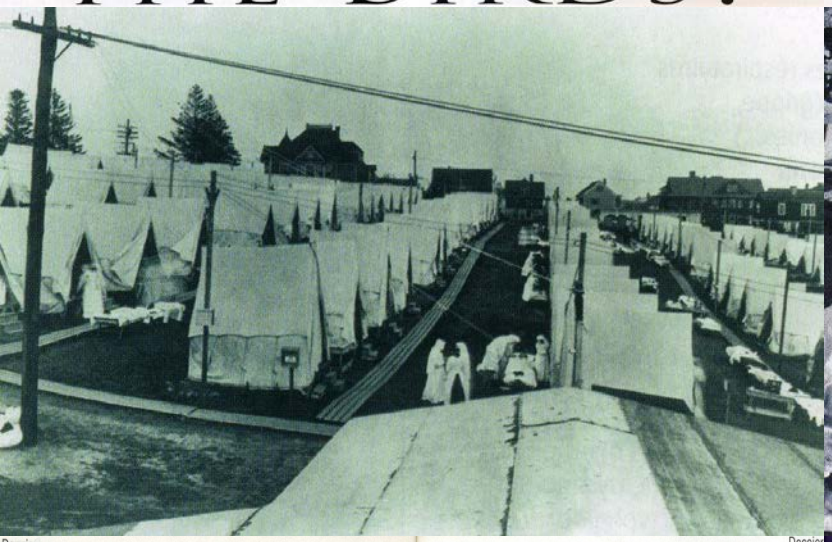
Seattle Police Officers Wearing Protective Face Masks during the Influenza Epidemic of 1918.

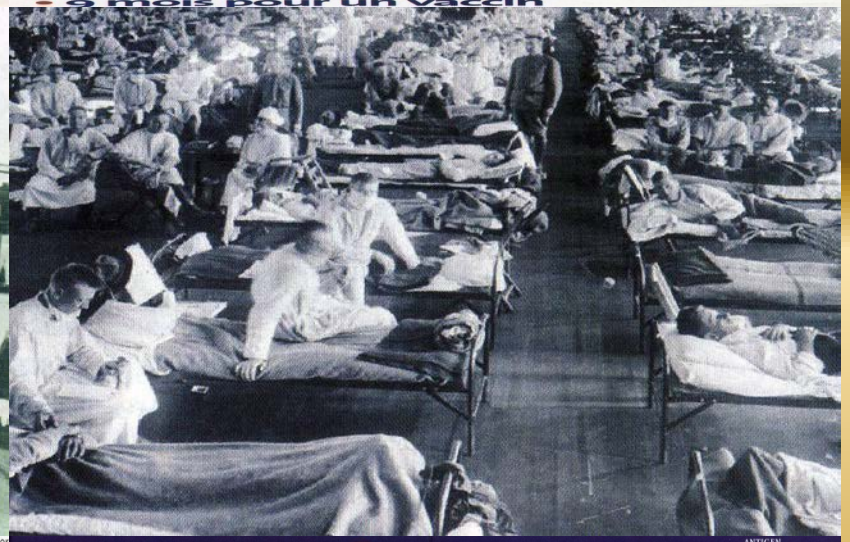


Tissue samples and a list of child victims of the 1918 influenza pandemic

UNDERSTANDING THE SECRET LIFE OF INFLUENZA VIRUSES

STRICTLY FOR THE BIRDS?





MALADIES ÉMERGENTES

MALADIES ÉMERGENTES

Grippe: les tribulations d'un virus en Chine

1 Canards et mouettes migrateurs
porteurs sains du virus de la grippe de type A (virus digestif), **non transmissible** à l'homme

infection entre oiseaux migrateurs

2 Canards d'élevage
porteurs sains : énorme et premier réservoir animal (virus digestif), **non transmissible** à l'homme

infection entre canards

CHINE

les poussières de fientes porteuses du virus de la grippe, contaminent les voies respiratoires des porcs

3 Porcs d'élevage
porteurs sains : 2e énorme réservoir animal (virus respiratoire), **transmissible** à l'homme

poumon

infection entre porcs

antigènes inconnus chez l'homme et chez les autres mammifères

hémagglutinine neuraminidase

8 segments d'ADN

cellule respiratoire infectée

noyau

virus grippal d'origine aviaire

autre virus de mammifère

réassortiment génétique

4 Fermiers chinois
(virus inconnu au plan antigénique : pas d'anticorps protecteurs chez l'homme)

infection entre fermiers

5 Citadins chinois
contamination par voie aérienne à l'occasion d'un marché d'animaux par exemple, dans une grande ville chinoise

infection entre citadins

avion

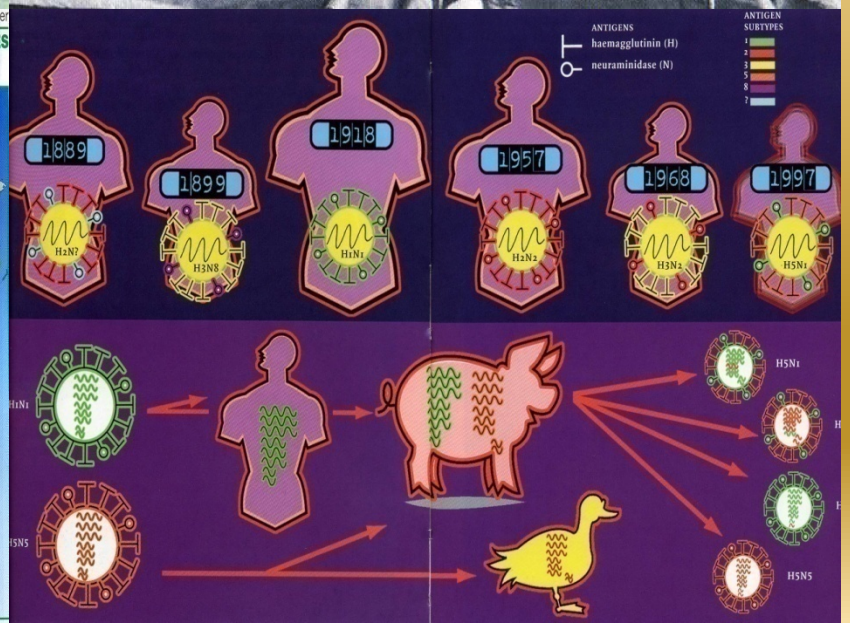
voiture

bateau

CHINE

6 Épidémie mondiale
contamination interhumaine par voie respiratoire

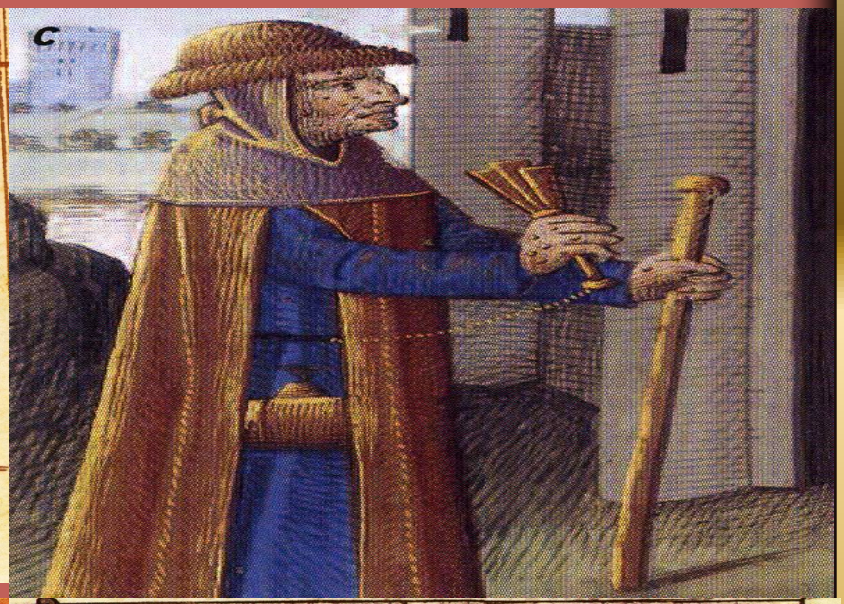
La grippe est potentiellement l'ennemi public numéro 1. Celle de 1918-1919 a entraîné 20 millions de morts dans le monde. Celle de 1889-1890, 4000 décès en France. Elle est provoquée par la pénétration, au niveau respiratoire, d'un Influenzavirus. Trois types existent. Le A, le plus dangereux pour l'homme, a la particularité de se modifier génétiquement au fil du temps, si bien que l'organisme n'est pas préparé pour se défendre. Il existe deux grands réservoirs d'Influenzavirus A: le canard et l'homme, sans transmission directe entre les deux groupes. « C'est une hypothèse hautement probable que le cochon soit l'hôte intermédiaire (un lieu de mélange entre les Influenzavirus aviaires et des virus humains) et que la Chine soit l'épicentre des nouvelles pandémies humaines », confirme Jean-Claude Manuguerra, médecin et chef de l'unité grippe de l'Institut Pasteur (Paris). Les variations majeures du virus laissent les populations et les responsables sanitaires désarmés car il faut six mois pour fabriquer un vaccin protecteur. ❑



LEPRA

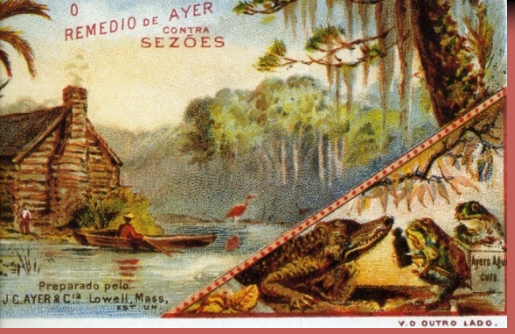
- Bíblia
  - Velho Testamento
    - Primeiras referências
- 800 ac
  - China
    - Primeiras descrições
- Europa
  - Sec. XIII
    - 19.000 Lazaretos
  - Sec. XVI
    - Início do seu rápido desaparecimento por razões não muito bem esclarecidas
- 1875
  - *Armauer Hansen*
    - Agente

LEPRA



la roial compagnie alast deuant li & q
il alast la ou il voulsit & commanda de
ligeaument as menuldres que nulle cho
se orde ne puant il ne lessassent venir de
uant li. mes comanda que li demoustrast
toute loieuse dise & bone. & commandout

LEPRA



PALUDISMO

- Sinónimos
  - Sazonismo
  - Febre Palustre
  - Malária
    - "Mau ar" (Itália Séc. XVIII)
    - "Mãe das Febres"
- 300.000.000 anos
  - Mosquitos parasitados
    - Fósseis
- Primeiras Descrição
  - 427 ac – 200 dc
    - Reino Visigótico, Índia, China
    - Platão
    - Aristóteles
    - Hipocrates
    - Galeno
- Descoberta
  - *Ronald Ross*
    - Nobel 1902 (Vector: Anopheles)
  - *Charles Lavaran*
    - Nobel 1907 (Agente: Plasmodio)
- *Ricardo Jorge* (1903)
  - *"… esta é, como poucas, uma questão patriótica. Não será temeridade afirmar-se que a infecção sezonal avulta entre as piores pragas colectivas que flagelam a população portuguesa …"* (sic)
- 1624 – 1689
  - *Thomas Sydenham*
    - Casca de Quina
- Terapêutica
  - Quinino: 1914
  - Cloroquina: 1934
  - Proguanil: 1944
  - Primaquina: 1950
  - Pririmatamina: 1951
  - Mefloquina: 1985
  - Artemisina: 1980
  - Halofantrina: 1989
  - 1998: Malarone
- Vítimas Ilustres
  - *Homero*
  - *Hipócrates*
  - *Alexandre da Macedónia*
  - *Albert Durer*
  - *Jaime I*
  - *Olivier Cromwell*

PALUDISMO

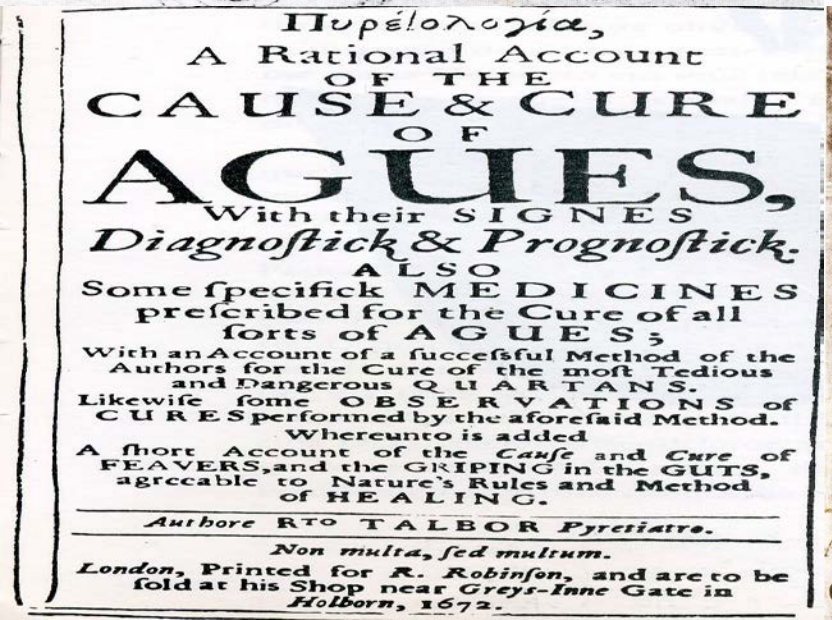
THOMÆ SYDENHAM
Med. Doct.
METHODUS
CURANDI FEBRES
Propriis Obſervationibus
Superſtructa.

Editio Secunda, priori multò auctior ac emendatior; cui etiam acceſſit Sectio Quinta de *Peſte* ſive *Febre Peſtilentiali*.

Multa egerunt qui ante nos fuerunt, ſed non peregerunt: multum adhuc reſtat operæ, multumque reſtabit: neque ulli nato poſt mille ſæcula præcidetur occaſio aliquid adhuc adjiciendi. Seneca.

LONDINI,
Impenſis *J. Crook*, apud quem veneunt in Vico vocato *Duck*-lane propè *Little Brittain*, MDCLXVIII.

Thomas Sydenham (1624-1689) - o

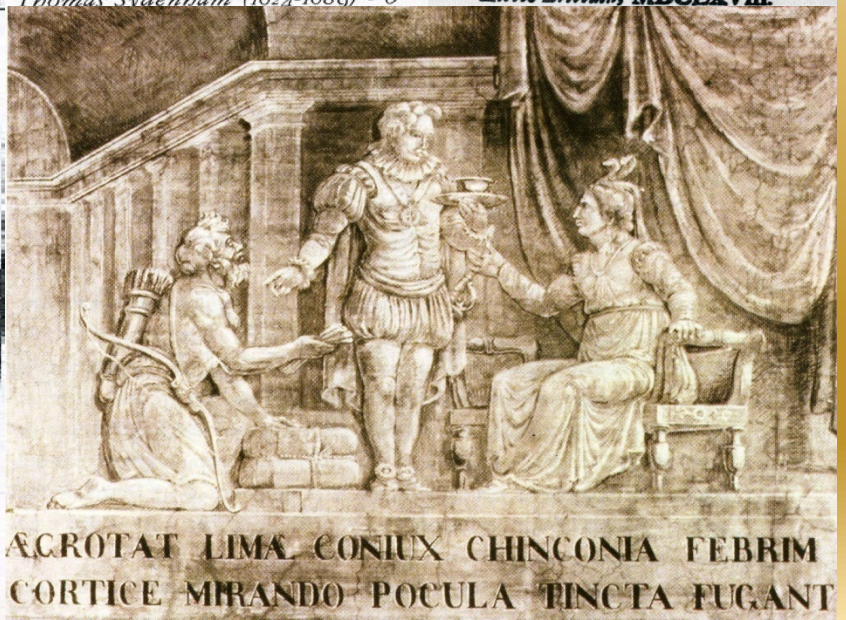


Πυρέτολογία,
A Rational Account
OF THE
CAUSE & CURE
OF
AGUES,
With their SIGNES
Diagnoſtick & Prognoſtick.
ALSO
Some ſpecifick MEDICINES
preſcribed for the Cure of all
ſorts of AGUES;
With an Account of a ſucceſsful Method of the Authors for the Cure of the moſt Tedious and Dangerous QUARTANS.
Likewiſe ſome OBSERVATIONS of CURES performed by the aforeſaid Method.
Whereunto is added
A ſhort Account of the *Cauſe* and *Cure* of FEAVERS, and the GRIPING in the GUTS, agreeable to Nature's Rules and Method of HEALING.

Authore RTO TALBOR *Pyretiatro.*

Non multa, ſed multum.

London, Printed for *R. Robinſon*, and are to be ſold at his Shop near *Greys-Inne* Gate in *Holborn*, 1672.



PALUDISMO

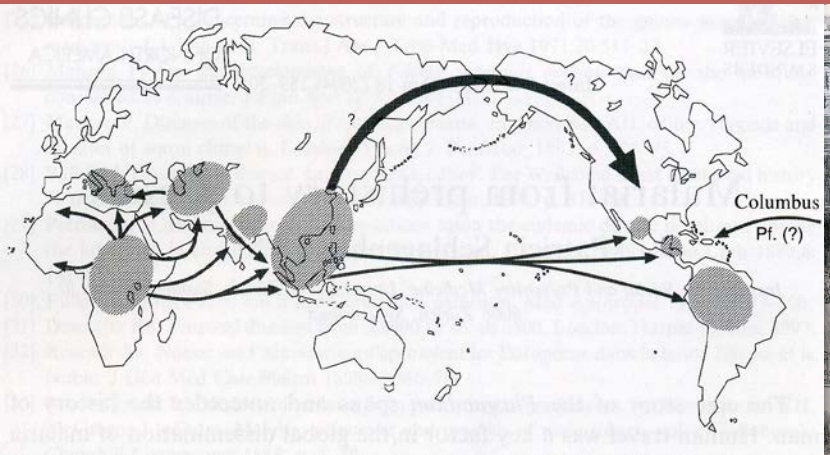
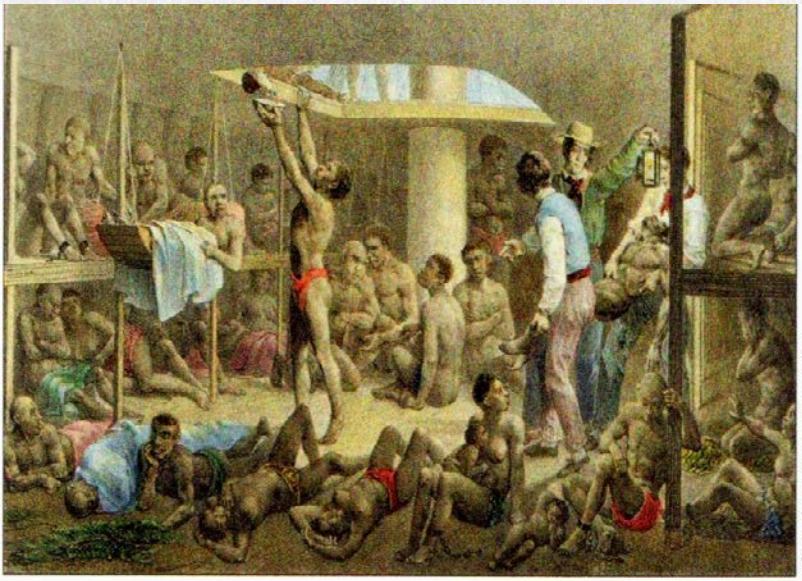
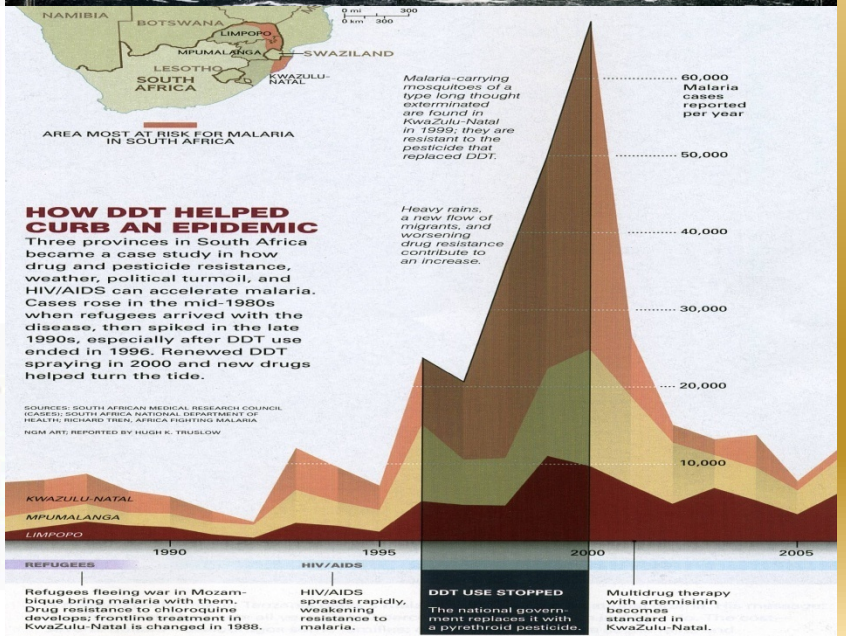


Fig. 1. Probable routes of the spread of malaria in prehistoric and early historic times. (*Adapted from* Bruce-Chwatt LJ. Paleogenesis and paleo-epidemiology of primate malaria. Bull World Health Organ 1965;2:363–87; with permission.)



After Johann Moritz Rugendas

P falciparum in South America came from Africa during the transatlantic slave trade



INSTITUTO DE MALARIOLOGIA
ÁGUAS DE MOURA — PORTUGAL

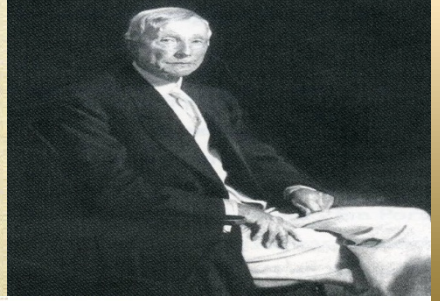
Temos o prazer de anunciar que, com a autorização de Sua Excelência o Ministro do Interior, e da Direcção Geral de Saúde Pública, o Doutor Francisco José C. Cambournac foi nomeado Director do Instituto de Malariologia, e tomará posse do novo cargo no dia 2 do próximo mês de Dezembro.

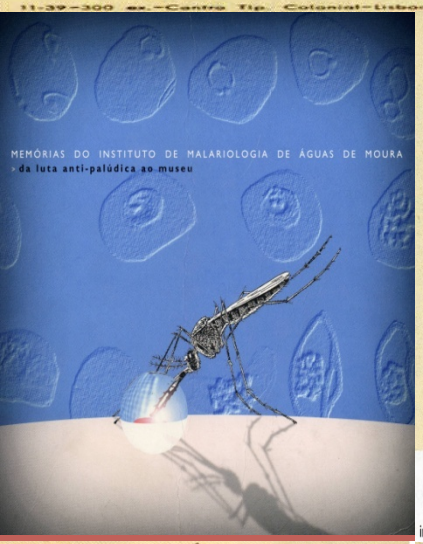
We are pleased to announce that Doctor Francisco José C. Cambournac has been appointed Director of the Malaria Institute, as of December 2, 1939.

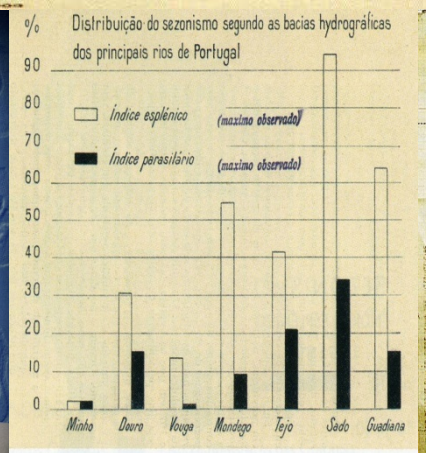
ÁGUAS DE MOURA
November 15, 1939.

Dr. Rolla B. Hill
Retiring Director

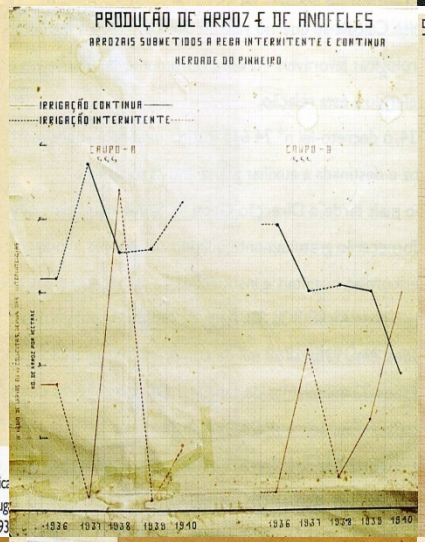
11-39-300 ex.—Centro Tip. Colonial—Lisboa

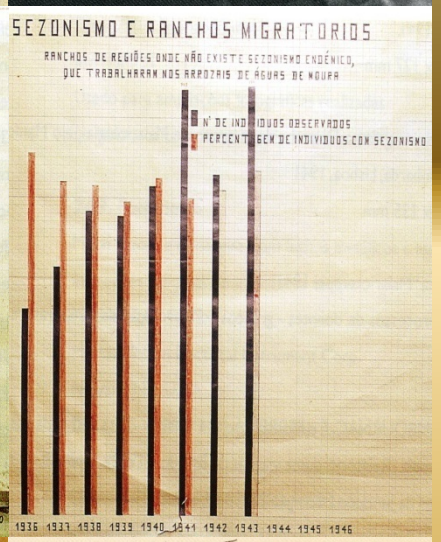


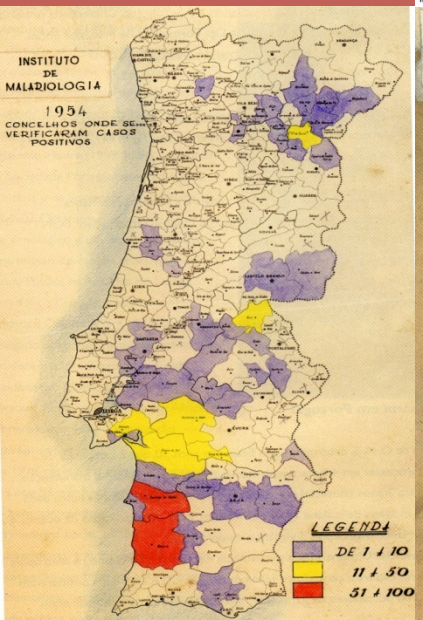


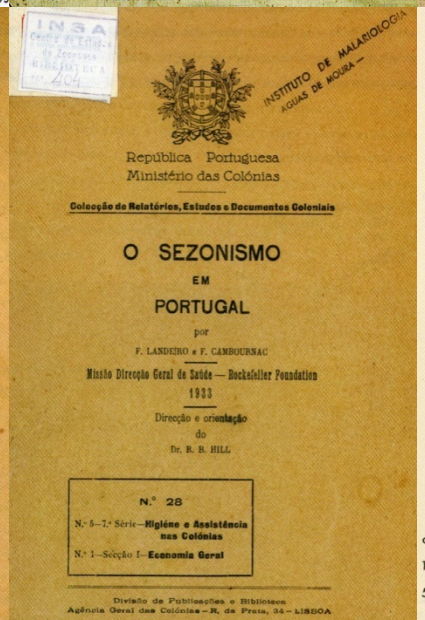


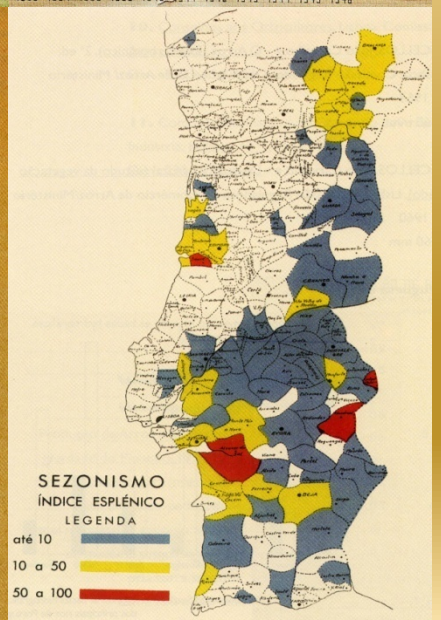
Distribuição do Sezonismo segundo as bacias hidrográfic
dos principais rios de Portug
in CAMBOURNAC, Francisco e LANDEIRO, Fausto - O Sezonismo em Portugal, 193

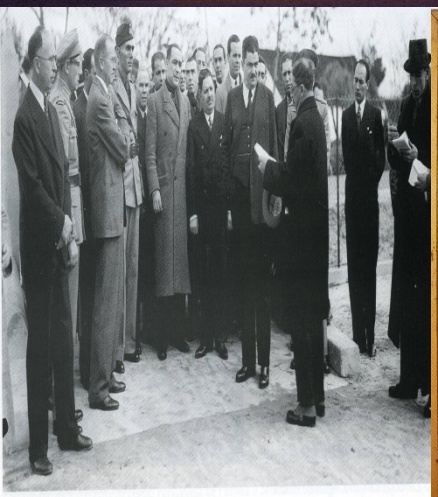








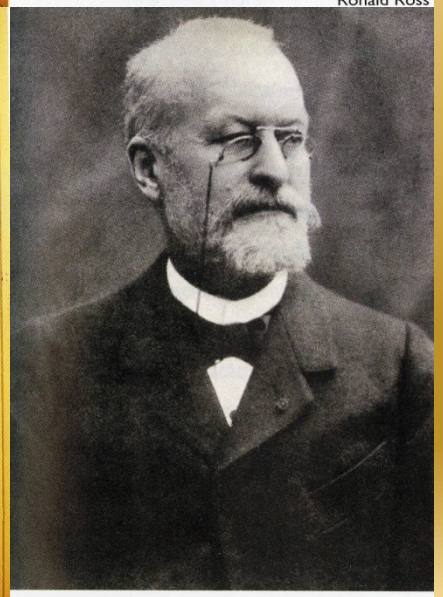




Inauguração do Instituto de Malariologia de Águas de Moura
Fotografia de Américo Ribeiro - Arquivo Municipal de Palmela

Ronald Ross

Curso Internacional de Malariologia para Médicos, 1952
António Levy Mendes (Portugal), Claude Vermeil (França), Guy Houel (Argélia), J. Fernandez Maruto (Espanha), Branimir Richter (Jugoslávia), Luis Contreras Poza (Espanha), Prof. F. Cambournac, Anastassius Marinos (Grécia), L. Saadaz (Irão), George Famellaris (Grécia), Etienne Noel (França), L. Andarelli (Argélia), Vamona Sinari (Portugal), Jean Deniaud (França), Hector Meyus (Bélgica), Luís Meira (Portugal)



Charles Laveran

PESTE

- Primeira Epidemia (1345 – 1380)
  - 60.000.000 mortos (Total)
  - 25.000.000 mortos (Europa)

- 1894
  - *Alexander Yersin*
  - *Shibasaburo Kitasato*
    - Agente
- 1898
  - *Paul-Louis Simond*
    - Vector (Pulga do rato)
- *1896*
  - *Luis Otten*
    - Vacina
- Vitimas Ilustres
  - *Amato Lusitano*
  - *Camara Pestana*

LES GRANDES PESTES

- **541-767 :** peste justinienne, première pandémie. Partie d'Égypte ou d'Éthiopie, elle touche l'ensemble du bassin méditerranéen.

L'empereur Justinien, mosaïque de la basilique de Ravenne, VIe siècle.

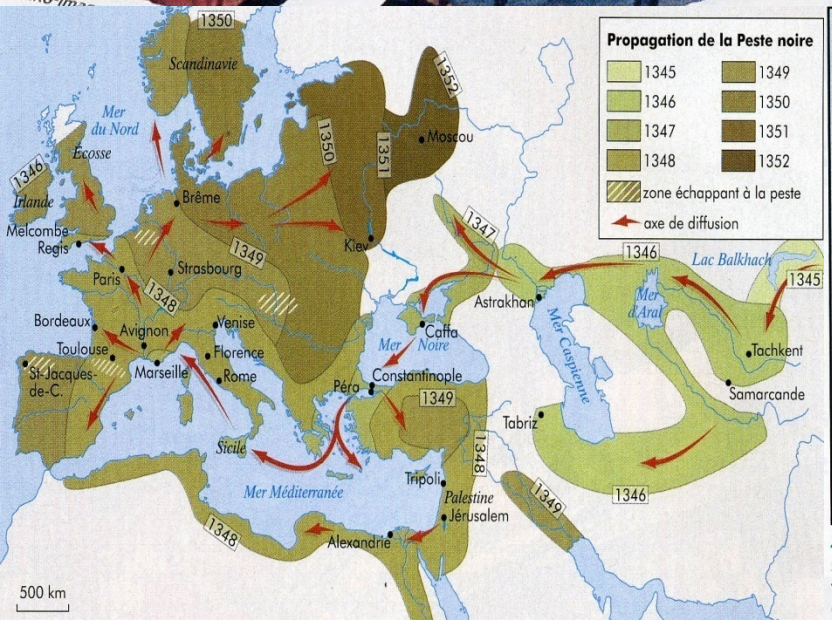
Le bubon de saint Roch

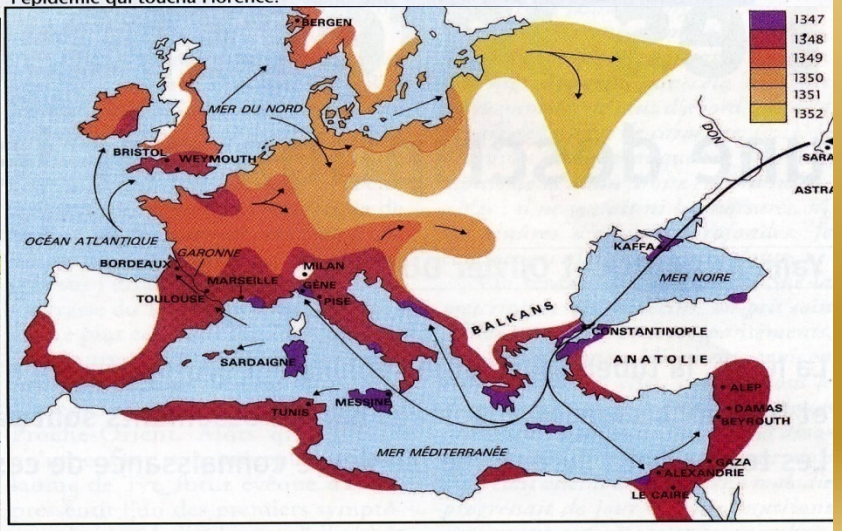
Les tribulations de la peste bubonique

Colin McEVEDY

Pendant plus de 2 000 ans, cette maladie bactérienne, véhiculée par les puces des rats, a décimé l'espèce humaine. Des témoignages historiques permettent de reconstituer le chemin de ce fléau.

2. La Grande Peste emportait les riches comme les pauvres, comme le montre cette enluminure du XVe siècle, au frontispice du Décaméron, œuvre écrite par Boccace après l'épidémie qui toucha Florence.





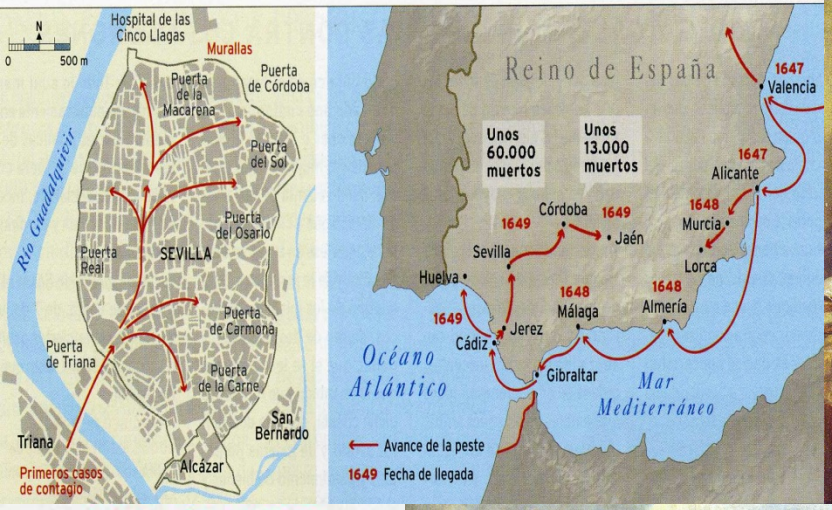
4. La peste noire vint d'Asie centrale et atteignit l'Europe par la route de la soie ; on signala une épidémie à Saraï en 1346 et, de Kaffa, qu'elle atteignit vers 1347, elle fut véhiculée par bateau vers les grands ports de l'Europe et de l'Afrique du Nord. La plus grande partie de l'Europe fut touchée, avant que l'épidémie ne cesse enfin en 1352.

PORTADORAS DE LA MUERTE

MORTANDAD EN SEVILLA

LA IRA DE DIOS

Avance de la peste de 1649

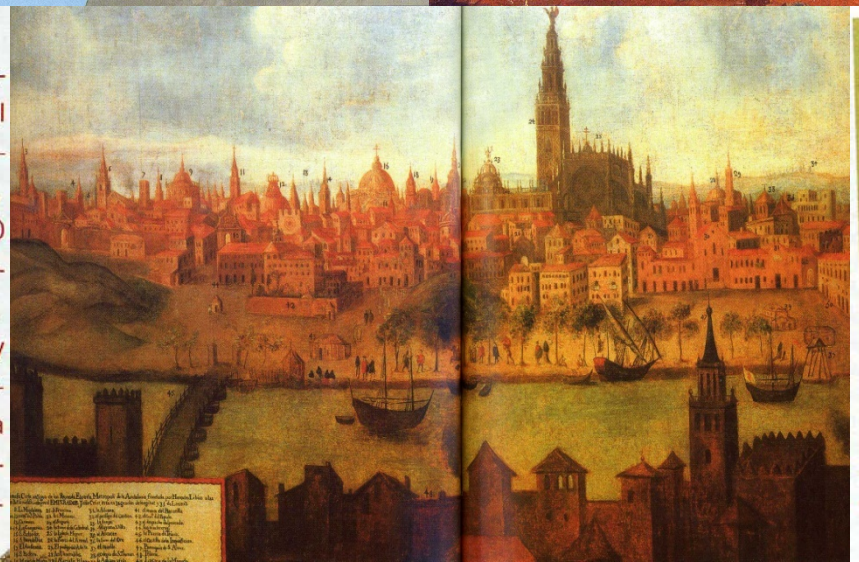


LAS CLAVES

LA RUTA. La peste entró en España por Valencia en 1647. Al año estaba en Málaga y al siguiente llegaba hasta Córdoba.

LAS CIFRAS. Mató a 13.000 de los 45.000 vecinos de Córdoba y casi la mitad de Sevilla.

LA ASISTENCIA. Médicos, y enterradores se vieron desbordados. Hubo quien sepultó a sus muertos en casa para ocultar su exposición a la enfermedad y proteger sus bienes.



COPIOSA
RELACION
DE LOS SVCEDIDO
EN EL TIEMPO QVE DVRO
la Epidemia en la Grande y Augustissima
Ciudad de Seuilla, Año de
1649.

ESCRITA POR VN RELIGIOSO A SU
Reuerendissimo Padre General.

SACALA A LVZ PEDRO LOPEZ DE
San Roman Ladron de Gueuara, Iurado de la
dicha Ciudad, y Familiar del Tribunal
dela Santa Inquisicion.

DEDICALA AL EXCELENTISSIMO SEÑOR
Don Luis Mendez de Haro y Sotomayor, Marques del Carpio, Conde-
Duque de Olinares, Gran Canciller de las Indias, Gentilhombre dela
Camara de su Magestad, y su Caualleriza mayor, Comendador
mayor de Alcantara, y Alcayde de los Reales
Alcaçares de Seuilla, &c.
mi señor.

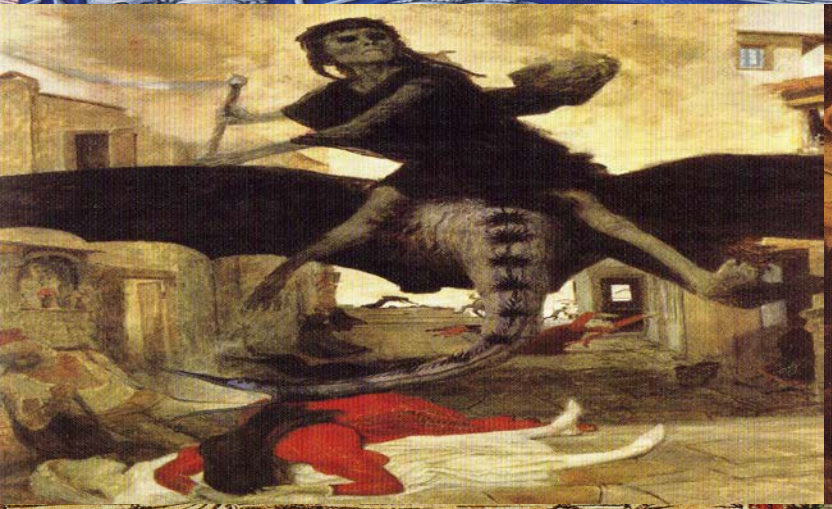
CON LICENCIA.

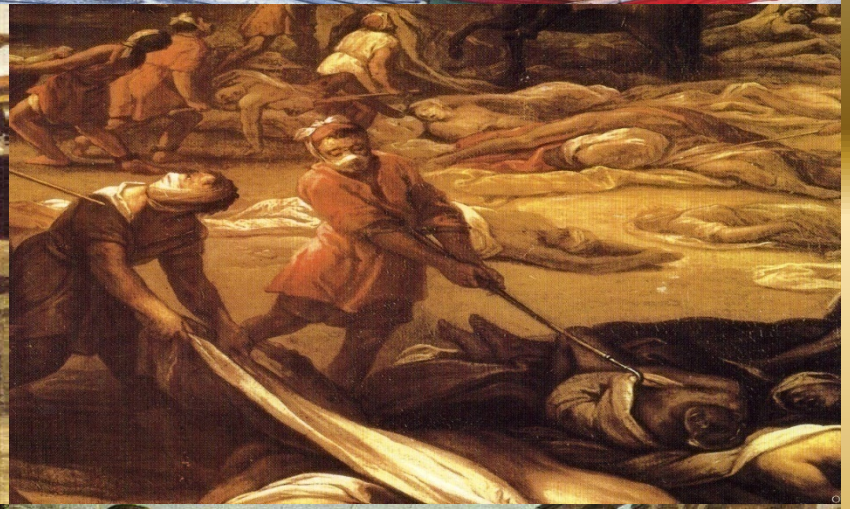
Impresso en Ecija, por Iuan Malpartida de las Alas,
Año de 1649.

CATÁSTROFE DEMOGRÁFICA. Hubo días en que se alcanzaron las 4.000 muertes, según reflejó Pedro López de San Román, en su *Relación*.

LA PESTE NOIRE

Une épidémie mondiale au Moyen Age





Application d'emplâtres, de ventouses et scarification (*Tractabus de Pestilentia*, xve siècle). Ce sont là les traitements privilégiés : les emplâtres (oignons cuits, poudre de crapaud, etc.) comme les ventouses doivent permettre au bubon de mûrir avant que l'on puisse l'inciser.

Stéphane Barry • Doctorant en histoire, rattaché au CAHMC (Bordeaux-III)
Norbert Gualde • Professeur d'immunologie à l'université Bordeaux-II

La plus grande épidémie de l'histoire

C'est peut-être la moitié de la population d'Occident qui a disparu pendant la Peste noire, au milieu du XIVe siècle. Une catastrophe qui soulève des interrogations. Et d'abord, comment l'épidémie a-t-elle pu atteindre une telle ampleur ?

Dante et son maître Vergil devant des pestiférés (manuscrit de *La Divine Comédie*, vers 1400). La présence d'un bubon, ganglion hypertrophié, à l'aine ou à l'aisselle est ce que le médecin recherche en premier, déjà au XIVe siècle, pour diagnostiquer la maladie.

Flagellants de Doornik (Pays-Bas), en 1349 (chronique de l'abbé de Tournai, Gilles Le Muisit, XIVe siècle). Avec la peste, des formes de mysticisme réapparaissent. Ainsi les flagellants, qui utilisent la fustigation en public pour obtenir le pardon des péchés et la fin de la peste. Le pape interdira ces manifestations.

Les Juifs, boucs émissaires

La danse des morts

LA PESTE, UN FLÉAU QUI A TRAVERSÉ LES ÂGES

Les germes d'une nouvelle médecine

Une annexe de Pasteur

Dans son dénuement et sa précarité, la paillotte d'Alexandre Yersin, à Hong-Kong, représente l'archétype du laboratoire colonial. Le disciple de Pasteur y découvre, en 1894, le bacille de la peste.

DESTRUCTION DE LA MAISON D'UN PESTIFÉRÉ, HAWAII, 1900

DE PAR LE ROY.
LE MARQUIS DE BRANCAS,
DES COMTES DE FORCALQUIER, LIEUTENANT General des Armées du Roy & de Provence, Conseiller d'Etat ordinaire, Chevalier de la Toison d'Or, Commandeur de l'Ordre Militaire de Saint Louis, & Commandant pour Sa Majesté en Provence.

« Ordonnance publiée et affichée dans toutes les villes, bourgs, villages et lieux de cette province, à ce que personne n'en prétende cause d'ignorance », signée par le marquis de Brancas, en date du 16 mai 1722. Afin d'éviter la contagion de la peste, il fut interdit à toute personne de sortir de Marseille sous peine de mort et ordonné aux villes et villages alentour de « tirer sur ceux qui voudraient passer par ruse ou par violence ». (Coll. Bautzmann)

Table 5
Plague pandemics

Plague pandemic	Year	Location	Vector	Historical significance
Plague of Athens	430–426 BC	Athens	Unknown. No antecedent rat deaths described	Decimated military/civilian population of Athens. Pericles died of plague. Spartans victorious over Athens. End of Greece's Golden Age. Western civilization changed forever. Cause: Possibly plague versus measles
Antonine plague	166–270 AD	Pelusium, Egypt, to Roman Empire, (Mediterranean Europe/Asia Minor)	Unknown. No antecedent rat deaths described	Decisively weakened the Roman army resulting in subsequent Barbarian invasions and eventual fall of the Western Roman Empire. Cause: Probably plague versus smallpox
Justinian Plague (1st pandemic)	542–590 AD	Africa to Byzantium	Unknown. No antecedent rat deaths described	Reduced population of Roman Empire by one third resulting in subsequent Barbarian invasions and final collapse of the eastern Roman Empire (Byzantium). Cause: Definitely bubonic plague
"Black Death" of Europe (2nd pandemic)	Early 1300s–late 1600s	Began in China and spread via caravan trade routes to the Middle East. Reached Messina in 1347 and ravaged Europe for centuries	Rats	Decimated European population by one third to one half. Mortality varied by location from 25–70%
Modern era (3rd pandemic)	1894–early 1900s	Began in China and spread via ships to ports worldwide	Rats, rodents	Plague introduced in North America, Latin America, Australia, Philippines, Japan, and Southern Africa resulting in the establishment of endemic plague in the Americas and Africa

Data from Refs. [1,4,7–10,14,15,20,25].

Table 6
Selected plague epidemics/outbreaks

Year	Location	Clinical presentations	Vector	Effects
1910–1911	Manchuria	Pneumonic plague. No cases of bubonic plague	Marmots	43,942 plague deaths (100% mortality)
1924	Los Angeles	Pneumonic plague. No cases of bubonic plague	Rats	30 plague deaths (100% mortality)
1994	India	876 cases of bubonic plague	Rats	54 plague deaths
1995–1996	Madagascar	Bubonic plague endemic in Madagascar since 1898	Rats, shrews	60 plague deaths

Data from Refs. [1,4,26–28].

Table 7
Plague biological warfare

Years	Location	Attackers/defenders	Methods	Effects
300 BC–1100 AD	Ancient Greco-Roma-Persian world	Greeks, Romans, local enemies	Plague-infected corpses catapulted[a] into walled fortifications	Possible local spread of plague/unknown effects
1346 AD	Caffa (Crimea)	Tartars/Genoese	Plague-infected corpses catapulted[a] into walled fortifications	Effect of plague decisive. Defenders return to Sicily with plague. Subsequent spread of plague from Sicily to Europe beginning the Great Plague of 1348
1710 AD	Keval	Russians/Swedes	Plague-infected corpses catapulted[a] into walled fortifications	Possible local spread of plague/unknown effects
1915	St. Petersburg	Germans/Russians	Ground delivered—plague-contaminated food/objects	Unproven allegations/unknown effects
1940–1942	Chuhsien/Chinese cities	Japanese/Chinese	Air delivered—rice contaminated with infected fleas	Thousands infected with bubonic plague; ~700 plague-related deaths

[a] Catapults were incapable of hurling corpses over walls. Trebouchets were used to catapult corpses over walls (a trebouchet could hurl 300 lb 300 yards).
Data from Refs. [1,2,4,29,30,33–35].

Didier Raoult · Michel Drancourt *Editors*

Paleomicrobiology

Past Human Infections

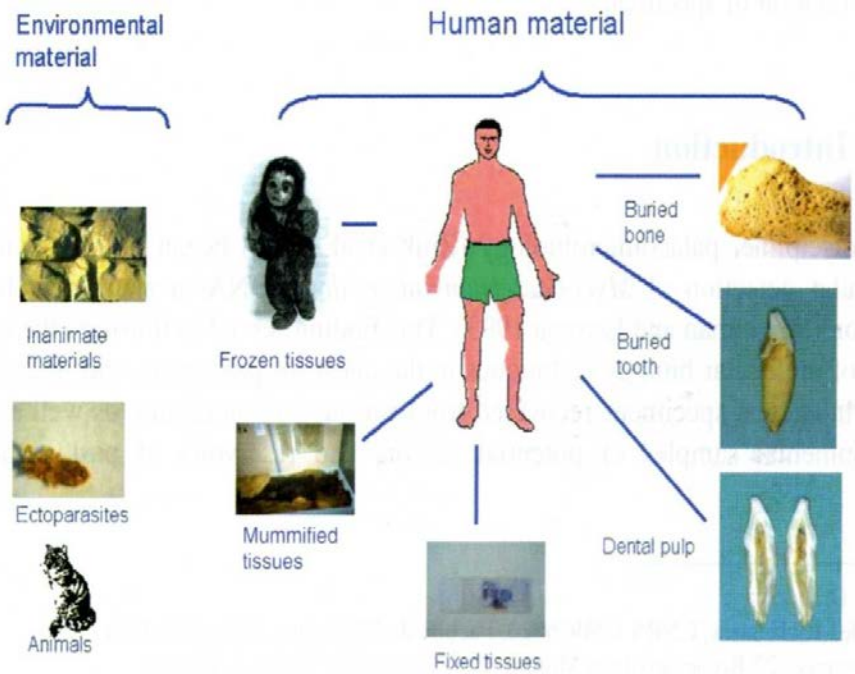


Fig. 4.1 Suitable source materials for amplification and sequencing of ancient microbe DNA

Table 1.1 Differential diagnosis of athenian plague (Adapted from Cunha 2004b and Cunha and Cunha 2006)

Clinical description by Thucydides	Time of appearance	Bubonic plague	Typhoid fever	Smallpox	Measles	Epidemic typhus[a]
Rapid onset	Early	•		•	•	•
Fever	Early	•	•	•	•	•
Red eyes	Early			•	•	•
Runny nose and sneezing	Early	•			•	•
Red throat and hoarseness	Early				•	•
Foul breath	Early				•	•
Retching and convulsions	Middle					•
Livid red rash	Middle	•		•	•	•
Blisters and sores	Middle				•	•
Sensation of "intense internal heat"	Middle			•	•	•
Insomnia	Late	•		•		
Diarrhoea	Late		•		•	•
Tracheal/laryngeal ulcers	Late					•
Red throat and hoarseness	Late			•	•	•
Death by haemorrhage	Late					•

[a]Most likely etiology based on clinical/historical analysis

Table 1.2 Differential diagnosis of antonine plague

Clinical description by Galen	Time of Appearance	Bubonic plague	Typhoid fever	Measles	Epidemic typhus	Smallpox[a]
Rapid onset	Early	•		•	•	•
Fever	Early	•	•	•	•	•
Foul breath	Middle			•	•	•
Livid red rash	Middle			•	•	•
Blisters and sores	Middle				•	•
Sensation of "intense internal heat"	Middle			•	•	•
Insomnia	Late	•		•		
Diarrhoea	Late		•		•	•
Tracheal/laryngeal ulcers	Late					•
Red throat and hoarseness	Late			•	•	•
Death by haemorrhage	Late					•

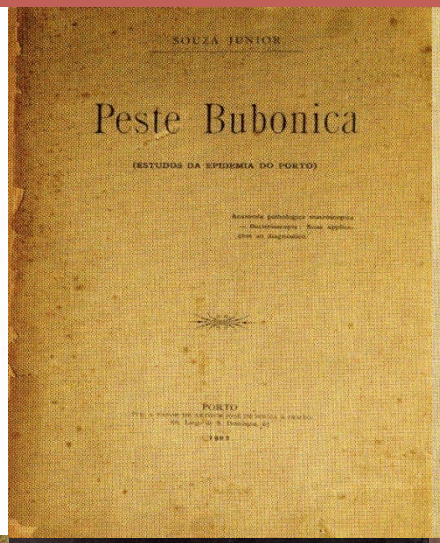
[a]Most likely etiology based on clinical/historical analysis

Table 1.3 Differential diagnosis of justiniac plague

Clinical description by Procopius	Time of appearance	Typhoid fever	Measles	Epidemic Typhus	Smallpox	Bubonic plague[a]
Rapid onset	Early		•	•	•	•
Slight fever	Early	•	•	•	•	•
Coma	Middle					•
Buboes	Middle					•
Delirium	Middle			•		•
Haematoemesis	Middle					•
Insomnia	Middle		•			•
Diarrhoea	Middle	•		•	•	
Red throat and hoarseness	Middle		•	•	•	•
Death by haemorrhage	Late				•	

[a]Most likely etiology based on clinical/historical analysis

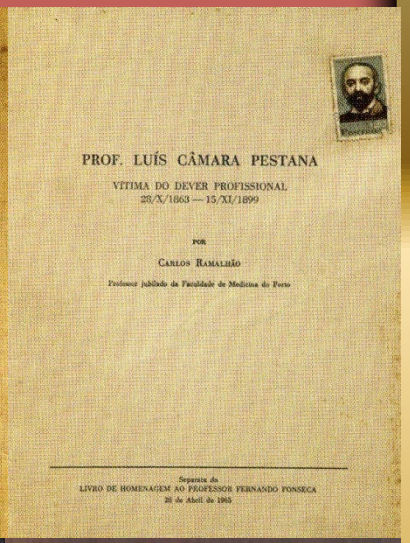
A Peste Bubónica no Porto


SOUZA JUNIOR

Peste Bubonica

(ESTUDOS DA EPIDEMIA DO PORTO)

PORTO


PROF. LUÍS CÂMARA PESTANA

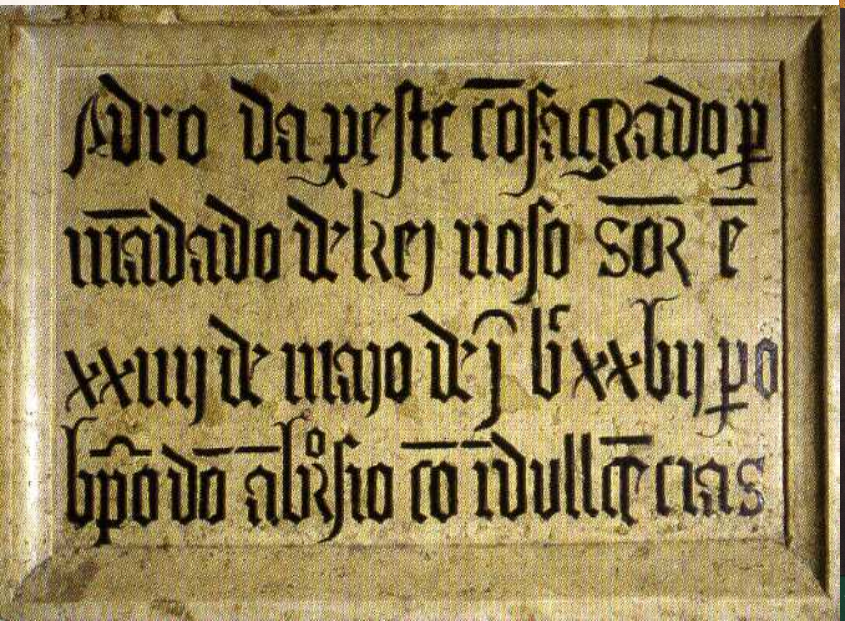
VÍTIMA DO DEVER PROFISSIONAL
20/X/1863 — 15/XI/1899

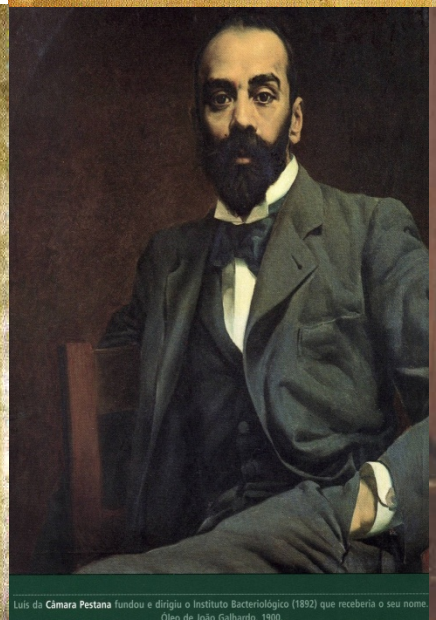
POR

CARLOS RAMALHÃO

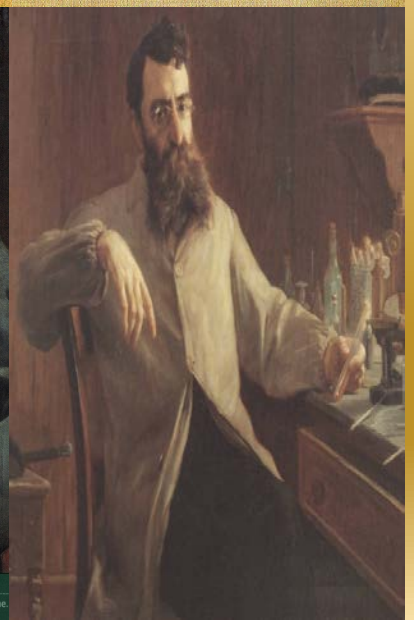
Professor jubilado da Faculdade de Medicina do Porto

Separata do
LIVRO DE HOMENAGEM AO PROFESSOR FERNANDO PONSECA
26 de Abril de 1965





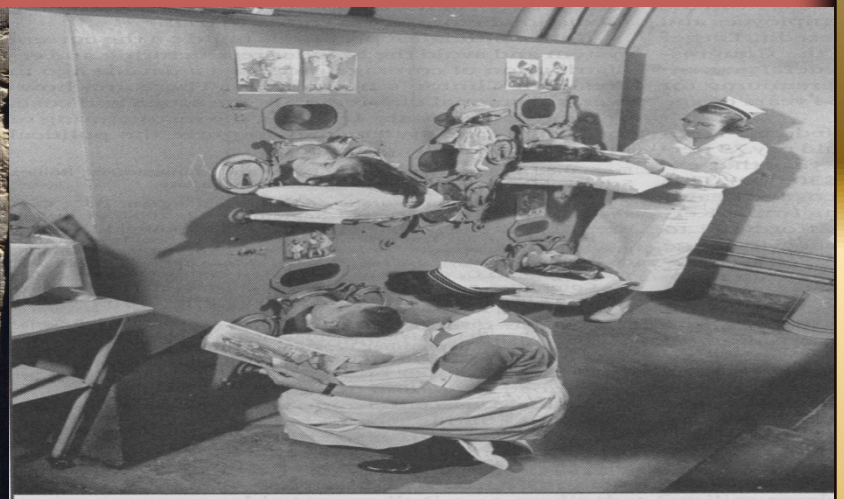
Luis da **Câmara Pestana** fundou e dirigiu o Instituto Bacteriológico (1892) que receberia o seu nome.
Óleo de João Galhardo, 1900



POLIOMIELITE

- **1840**
  - ***Heinrich Heine***
    - **Primeira Referência**
- **1890**
  - ***Oskar Medin***
    - **Primeira Descrição**
- **1908**
  - ***Karl Landsteiner e Erwin Popper***
    - **Transmissibilidade**
- **1953 - 1962**
  - ***Jonas Salk e Albert Sabin***
    - **Vacina (OPV) e (IPV)**

POLIOMIELITE

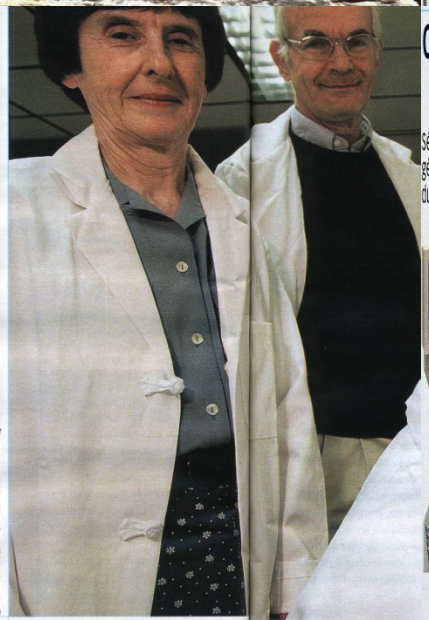


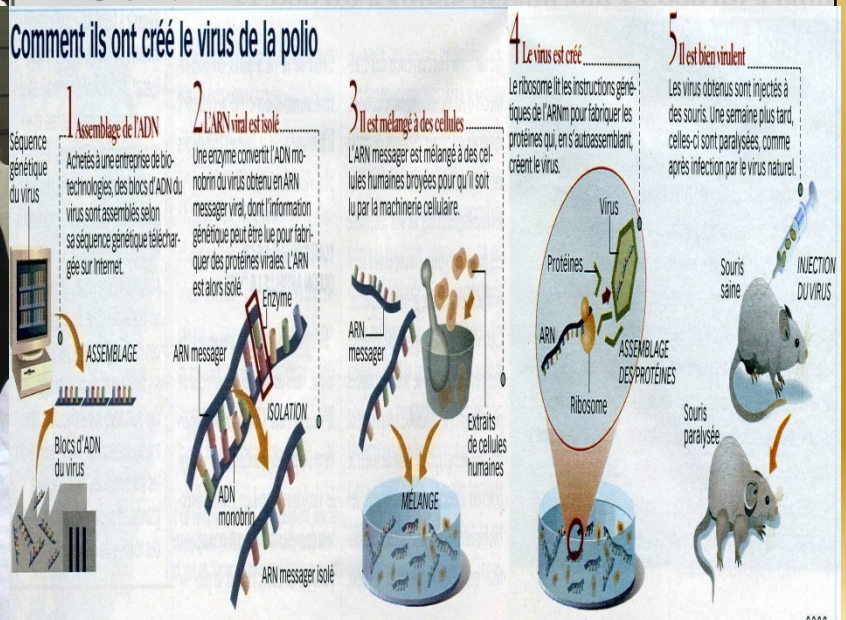
Nurses Tending Young Patients with Poliomyelitis in an Iron Lung, 1938.
Photograph by Hansel Mieth, Time Life Pictures, Getty Images.

Ils cherchent à **créer la vie** à partir de "rien"

En réussissant à fabriquer le génome du virus de la polio par simple assemblage, des biologistes américains viennent de prendre date : la vie pourrait être créée à partir de l'inerte. Toutefois, les avis divergent.

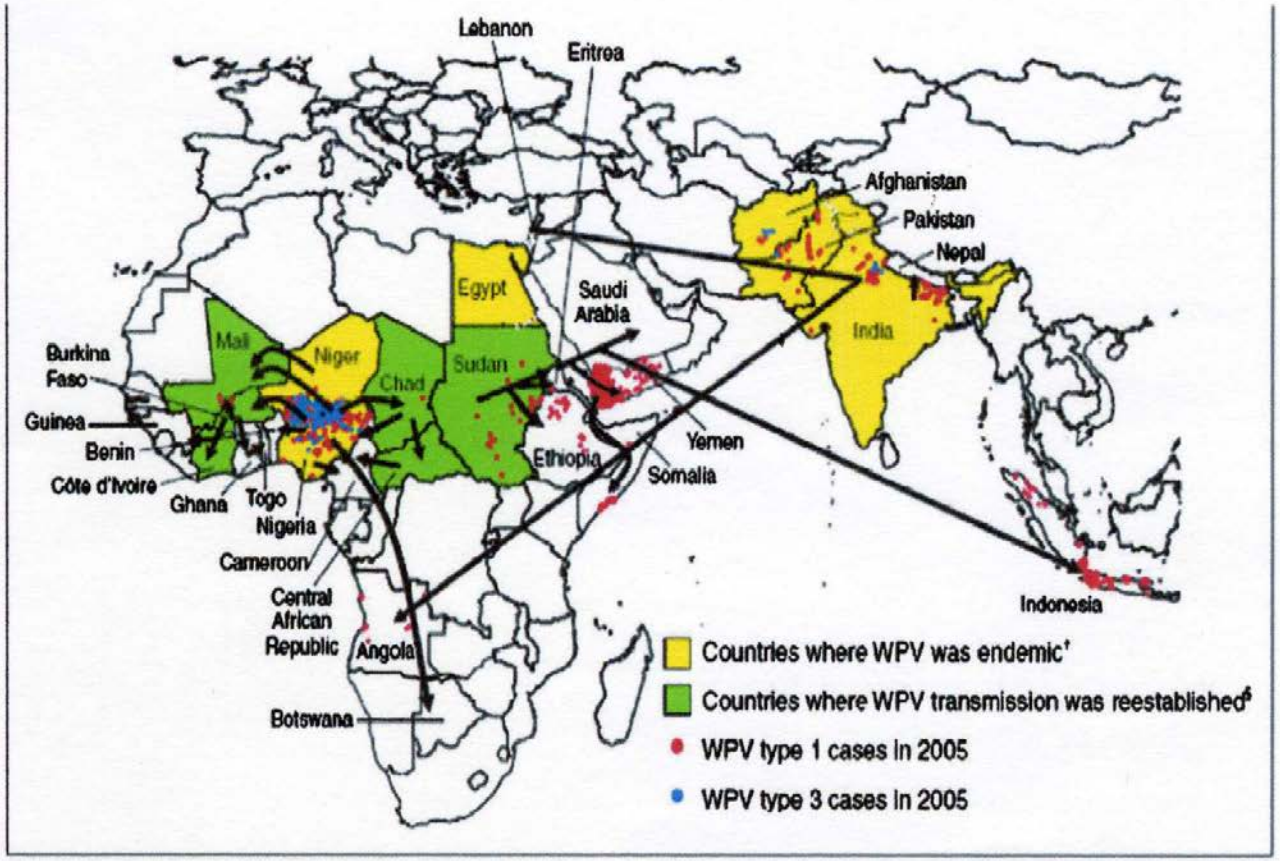
Par Kheira Bettayeb





The Role of the Traveler in Emerging Infections and Magnitude of Travel

Lin H. Chen, MD, FACP[a,*], Mary Elizabeth Wilson, MD, FACP, FIDSA[b]



*Routes (not all importation events) indicated by arrows.
†As of February 1, 2006, Niger and Egypt were considered no longer endemic for WPV because neither country had indigenous transmission during the preceding 12 months.
§Countries were considered to have reestablished transmission if WPV was detected for >1 year after importation. The majority of these countries have not experienced WPV type 1 transmission since July 2005.

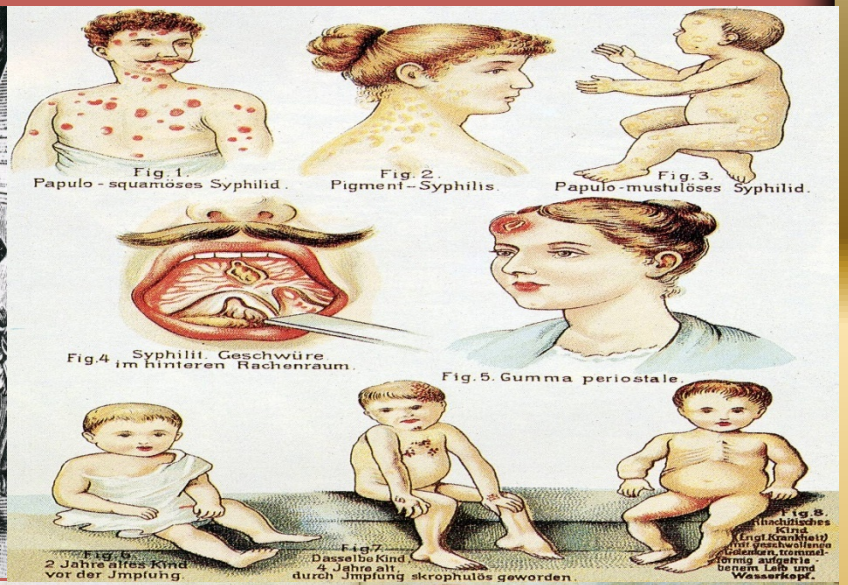
Fig. 3. Wild poliovirus (WPV) cases in 2005 and importation routes during 2002–2005 worldwide. (*From* CDC. Resurgence of wild poliovirus type 1 transmission and consequences of importation—21 countries, 2002–2005. Morbidity Mortality Weekly Report 2006;55(6):145–50; with permission.)

SÍFILIS

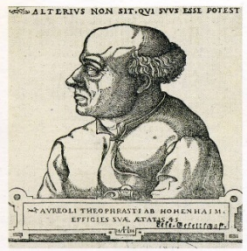
- *Vítimas Ilustres*
  - *Henrique VIII*
  - *Ivan (O terrível)*
  - *Napoleão Bonaparte*
  - *Ludvig van Beethovan*
  - *Franz Schubert*
  - *Al Capone*
  - *Florence Nigthingale*
  - *Arthur Schopenhauer*
  - *Ignaz Semmelweis*
  - *Cherles Baudelaire*
  - *Gustave Flaubert*
  - *Edouard Manet*
  - *Friedrich Nitzeche*
  - *Paul Gaugin*
  - *Guy de Maupassant*
  - *Nicolai Paganini*
  - *Gaetano Donizetti*
  - *Mikhail Glinka*
  - *Robert Schuman*
  - *Bedrich Smetana*

- **1529**
  - *Paracelso*
    - *Mercúrio*
- **1530**
  - *Girolamo Fracastoro*
    - **Doença venéra**
      - **"Contagium vivum ou contagium animatum"**
- **1905**
  - *Fritz Schaudinn*
    - **Isola o Agente**
- **1908**
  - *Paul Ehrlich*
  - *Sahashito Hata*
    - **"Salvarsan" (Composto Arsenical)**
- **1917**
  - *Julius Wagner Ritter von Jauregg*
    - **Malarioterapia da forma cerebral**
- ***"… uma noite com Vénus leva a uma vida inteira com Mercúrio …"***

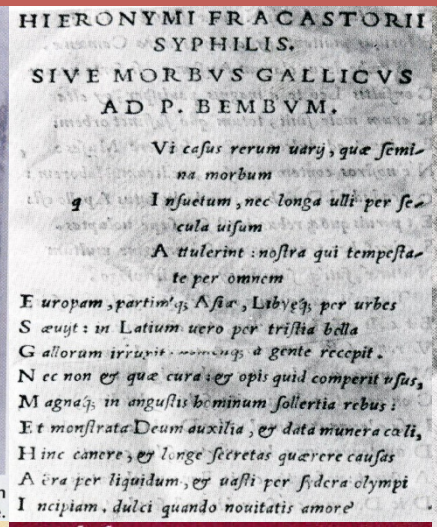
SÍFILIS



Theophrastus Bombastus von Hohenheim - mais conhecido como Paracelso - aprendeu a tratar a sífilis com mercúrio quando estudava em Ferrara. Ele via no azoth - nome do mercúrio entre os alquimistas - uma substância primordial, um símbolo da criação de todas as coisas. Muitos retratos o mostram segurando uma espada com azoth no pomo. Paracelso fez um estudo minucioso da sífilis e publicou os seus achados e observações médicas nos livros ''Vom Holz Guajaco gründlicher Heilung'' (Nuremberg, 1529) e ''Von der frantzösischen Krankheit drey Bücher'' (Nuremberg, 1529).



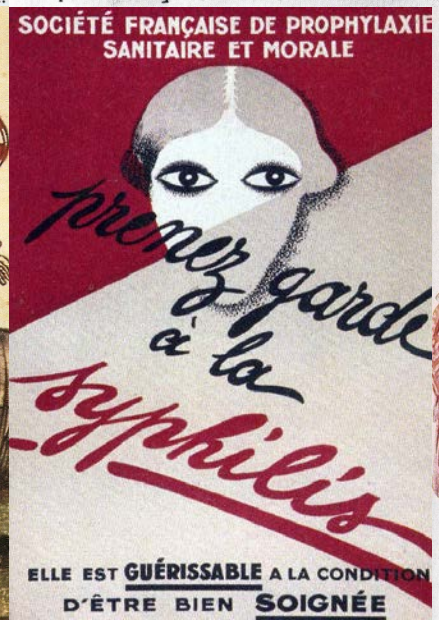
SÍFILIS

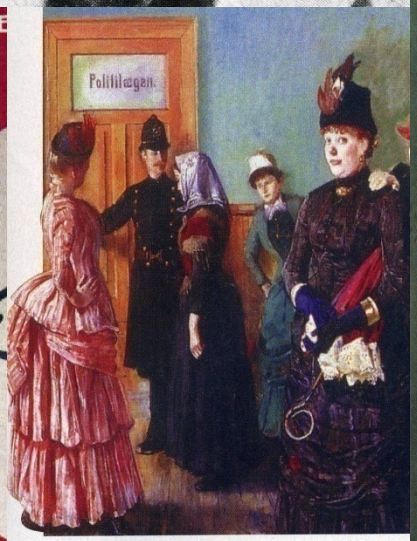

HIERONYMI FRACASTORII
SYPHILIS.
SIVE MORBVS GALLICVS
AD P. BEMBVM.

Vi casus rerum uarij, quæ semina morbum
Insuetum, nec longa ulli per secula uisum
Attulerint: nostra qui tempestate per omnem
Europam, partimq; Asiæ, Libyeq; per urbes
Sæuit: in Latium uero per tristia bella
Galloram irruit: mutatq; à gente recepit.
Nec non & quæ cura: & opis quid comperit usus,
Magnaq; in angustis hominum sollertia rebus:
Et monstrata Deum auxilia, & data munera cœli,
Hinc canere, & longe secretas quærere causas
Aëra per liquidum, & uasti per sidera olympi
Incipiam, dulci quando nouitatis amore

2. Le médecin italien Fracastor *(à gauche)* est le premier à décrire la syphilis dans un poème médical et à expliciter les modes de contagion, comme l'illustre la figure à droite.

3. La syphilis provoque des lésions cutanées. Le moulage de cette femme syphilitique pourrait représenter celui de Véronique, personnage de Balzac, atteinte de syphilis cutanée.





La lutte contre le péril vénérien

En France comme en Norvège (ci-dessus vers 1887), les prostituées sont soumises à un strict suivi médical

TIFO

- 1083
  - 1ª Descrição
    - Mosteiro de La Cava
- 1570
  - *Francisco Bravo* (México)
    - *“Opera Medicinalia” (Tebardilho Pintado)*
- Surtos
  - Rússia (1918 – 1922)
    - 30.000.000 casos
    - 3.000.000 mortos
- 1909
  - *Charles Nicolle*
    - Vector
- *Rocha Lima* (1879 – 1956)
  - DD das Ricketsioses
    - Endémico / Epidémico
- 1948
  - *Paul Muller*
    - Prémio Nobel
      - DDT
- Vítimas Ilustres
  - *Lenine*
  - *Howard Rcketts*
  - *Stanislaus von Prowazek*

Judeus queimados vivos numa fogueira, acusados de envenenarem a água, causando a peste... (gravura em Madeira: Hartman Schedel, 1493, Alemanha).

Gott hilf gnädig!
Kurtzer bericht
von der
allgemainen anstekenden
Lagersucht/
das ist/
von dem
giftigen und hitzigen haubt-hals-
brust-magen-und bauch-wehe/
mit und one ficten/
aus
aigner erfahrung/ und dem grund
der feärkünstlerischen lehrsätzen
aufgefeiret
durch
Hainrich Skreta von Zavorzitz
der arzney Doktorn.
Schafhausen
in verlag Onofrions von Waldkirch/
gedruckt bei Alexander Riebing.
M DC LXXVI.

Heinrich Skreta published a detailed account of

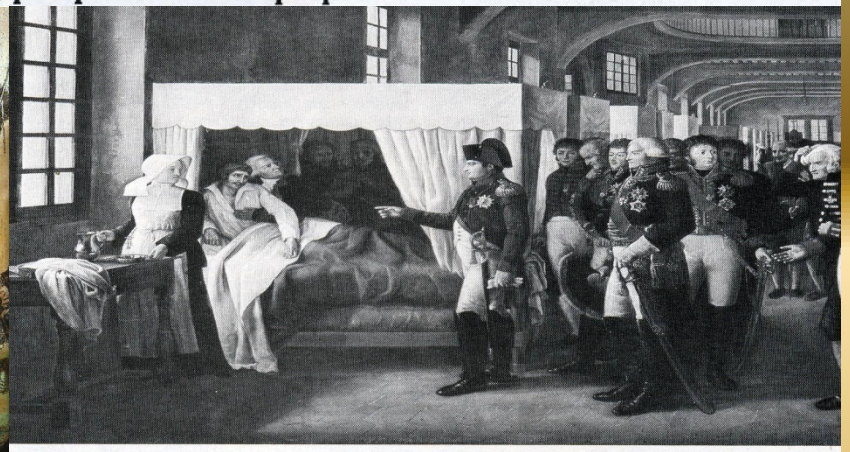
T. H. Ricketts (1871 - 1910)

Les soldats de Napoléon vaincus par le typhus

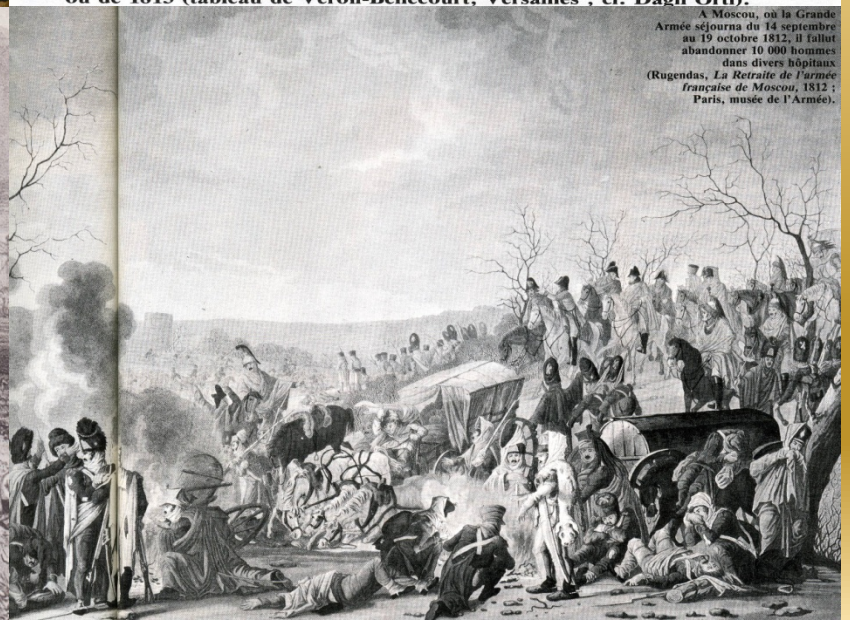
par Yves-Marie Bercé

Le typhus, maladie de la saleté, de la promiscuité et de la misère, a été pendant des siècles le complément inévitable des malheurs de la guerre. Les soldats de Napoléon ont été vaincus, en Russie, plus par la maladie que par le sort des armes.

Tournant le dos à la légende héroïque, Raffet (1804-1860) montre ici une scène de typhus à Mayence pendant l'automne 1813. Les malades, jonchant les rues, cherchaient à échapper à l'horreur de l'entassement des cadavres dans les maisons (BN ; cl. H. Josse).



Napoléon visite l'infirmerie des Invalides le 11 février 1808. Dans la salle, une vingtaine de lits individuels, avec baldaquins et draps blancs. Les sœurs de Saint-Vincent-de-Paul, revenues depuis 1800, s'occupent des malades. On est bien loin des improvisations d'hôpitaux pendant les épidémies de 1807 ou de 1813 (tableau de Véron-Bellecourt, Versailles ; cl. Dagli Orti).

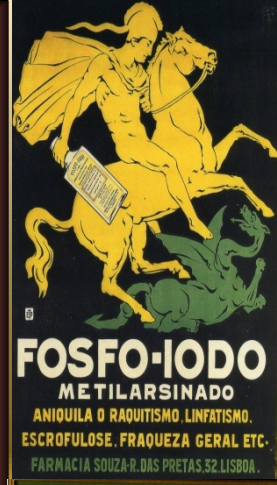


A Moscou, où la Grande Armée séjourna du 14 septembre au 19 octobre 1812, il fallut abandonner 10 000 hommes dans divers hôpitaux (Rugendas, *La Retraite de l'armée française de Moscou*, 1812 ; Paris, musée de l'Armée).

TUBERCULOSE

- Vítimas Ilustres
  - *Amades Modigliani*
  - *Albert Camus*
  - *Karl Marx*
  - *Franz Kafka*
  - *Moliére*
  - *George Orwell*
  - *Friedrich Schiller*
  - *Paul Eherlich*
  - *Paul Langerhans*
  - *Henry Purcell*
  - *Giovani Pergolesi*
  - *Carl Bach*
  - *Luigi Bocherini*
  - *Nicolai Paganini*
  - *Carl Maria von Weber*
  - *Imperador José II*
  - *Calvino*

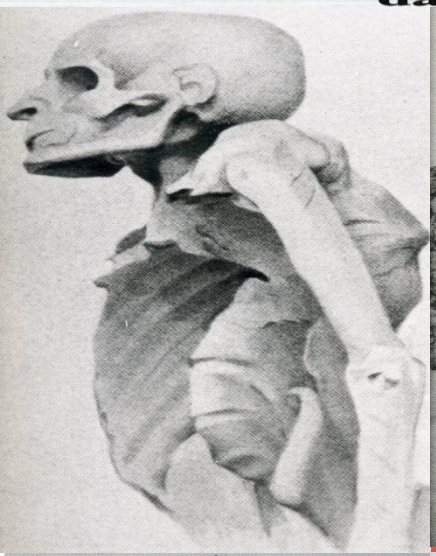
- 3000 ac
  - China
    - Primeira Descrição
- Grécia / Roma Antigas (485 ac – 79 dc)
  - Referências
    - *Heródoto*
    - *Hipocrates*
    - *Plínio (O Velho / O Novo)*
- Árabes
  - *Avicena* (980 – 1037 dc)
- Sylvius Deleboe (1614 – 1672)
  - Tuberculos
- 1865
  - *Jean Villemin*
    - Transmissibilidade
- 1921
  - Aplicação do BCG
- 1952
  - *Selman Waksman*
    - Prémio Nobel
      - Estreptomicina



Guerre à la tuberculose !

par Roger-Henri Guerrand

85 000 morts en 1920. 42 000 en 1945...
Face à la tuberculose, une véritable « guerre » est déclenchée.
La lutte contre le bacille
de Koch remplace celle contre le « boche »
dans l'opinion publique française.



MALADIES ET ÉPIDÉMIES

1. LA TUBERCULOSE OSSEUSE crée des difformités de la colonne vertébrale, notamment les gibbosités des bossus. Ces anomalies osseuses permettent le suivi de cette maladie dans les populations anciennes.

Convalescents, en 1920, à Arcachon — première ville sanatorium française (cl. G. Mouls/IFA).

Fig. 36 – Laënnec – desenhado e litografado pelo próprio em 1820, quatro anos antes de morrer tuberculoso.

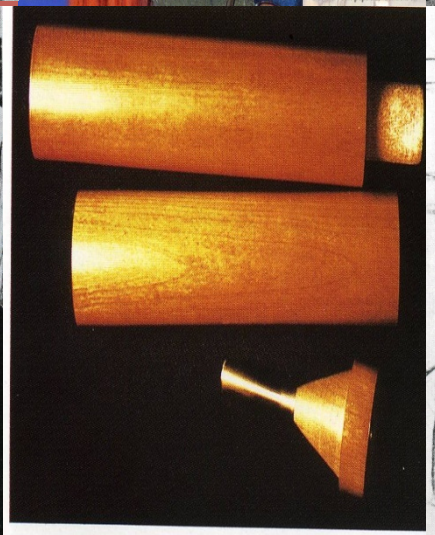
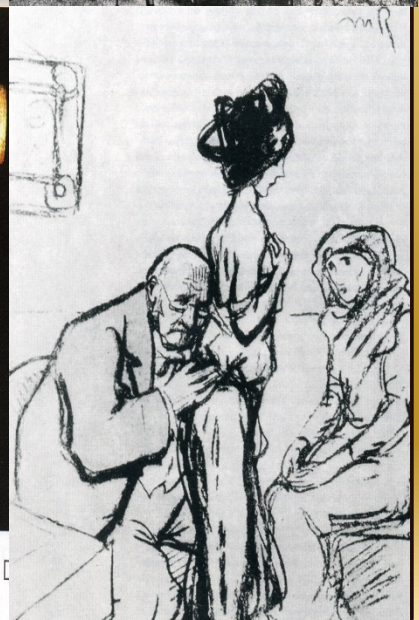


Fig. 37 – Estetoscópio do tipo de Laënnec. Colecção do D
Philip Reichert, Nova Iorque.



O PORTO E A TUBERCULOSE
HISTÓRIA DE 100 ANOS DE LUTA

ANTÓNIO RAMALHO DE ALMEIDA

FRONTEIRA DO CAOS

Tuberkulose-Merkblatt.

Für den Hauptverein für Volkswohlfahrt in Hannover

verfaßt von Kreisarzt Dr. Karl Dohrn in Hannover.

Verteilt durch die Fürsorgestelle in

Hier siehst du den rotgefärbten, stäbchenförmigen Tuberkelbazillus, den Erreger der Tuberkulose.

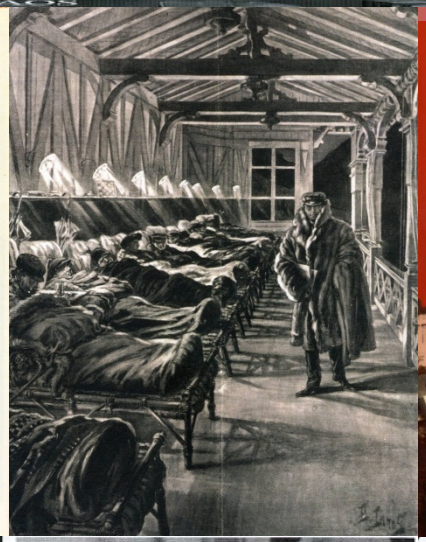
In einem Schleimtröpfchen, das ein Lungenkranker ausbustet, sind oft Tausende dieser Krankheitskeime vorhanden. Darum **spucke nicht auf den Boden.**

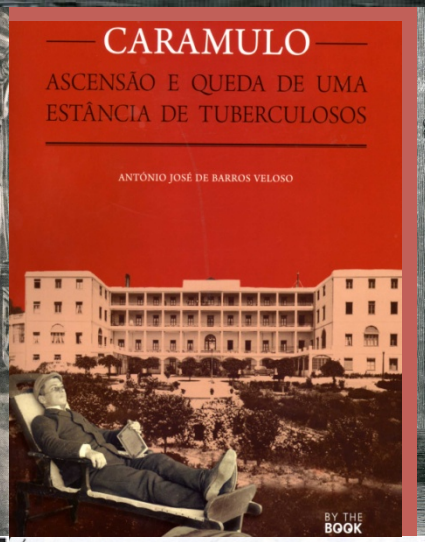
Atmest du nämlich den mit Krankheitskeimen durchsetzten Staub ein, so kannst du selbst erkranken, besonders aber die Kinder, die auf dem **Boden** spielen.

Noch gefährlicher ist es, wenn ein Lungenkranker dich anhustet, ohne die Hand vor den Mund zu halten. (Auch Schnupfen und Diphterie werden dir so zugetragen.) Darum **Taschentuch vor den Mund beim Husten.**

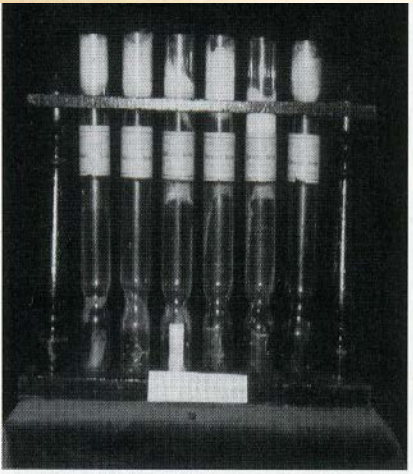
Willst du wissen, wie du dich vor Tuberkulose schützen kannst, so merk dir folgendes: zunächst achte darauf, daß der

Krankheitskeim nicht sorglos durch Spucken und Husten verstreut wird. Das bist du dir und deinem Nächsten schuldig!



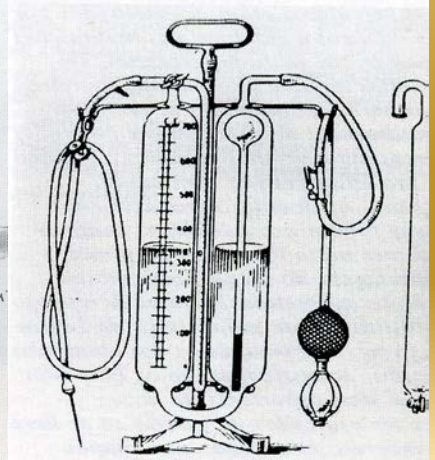


Dispositivo idealizado por Carlo Forlan em 1897 para a produção de pneumotó artificial. Seguiram-se a este modelo desenvolvidos por Murphy (1910), Kr (1917) e Morelli e Davidson (1931).



Original BCG culture on glycerinated - potato - medium in special constricted (Roux) tubes.

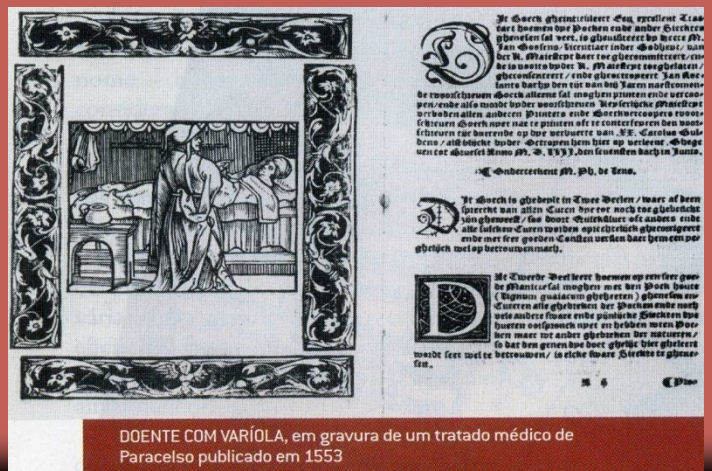
Camille Guérin (left) and Albert Calmette (right) in their laboratory in Lille.



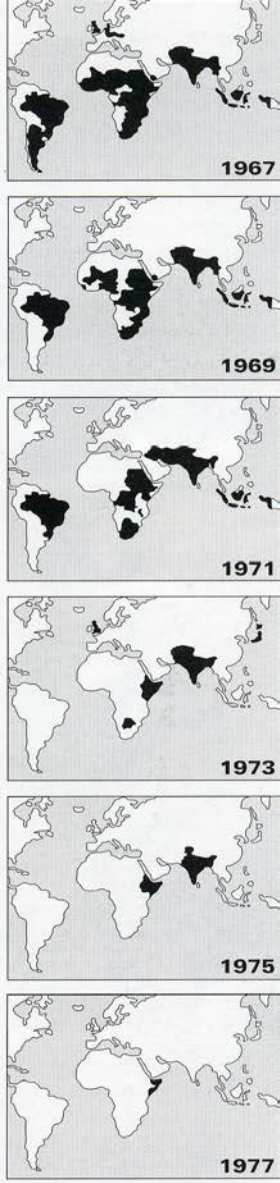
VARÍOLA

- **1500 ac - 1160 ac**
  - **Primeiras descrições**
    - **Índia**
    - **China**
    - **Egipto (*Ramsés V*)**
- ***Galeno* (130 – 200 dc)**
  - **1ª Descrição da Doença**
  - ***Vitimou Marco Aurélio***
  - **Peste Antonina: 5.000.000 mortos**
- **1518**
  - **Ameríndios**
    - **População < 10%**
- **1796**
  - ***Edward Jenner***
    - **Escarificação com *"cow pox"***
  - *(Jacob de Castro Sarmento, 1720, Universidade de Aberdeeen e Hospital Beath Holim de Londres)*

- **Séc XVIII – XIX**
  - **Europa: 400.000 mortos / ano**
- **1906**
  - ***Enrique Pachen***
    - **Identificação do agente**
- **1910**
  - **Vacina *"humanizada"***
- **1967**
  - **10 a 15.000.000 casos**
- **1977**
  - **Somália**
    - **Último caso de doença por estírpe selvagem**
- **1984**
  - **Abandono da prática da vacinação**
- **Vítimas Ilustres**
  - ***Luís XV***



DOENTE COM VARÍOLA, em gravura de um tratado médico de Paracelso publicado em 1553



In 1967 the World Health Organization embarked upon a ten-year global smallpox eradication programme, with mass vaccination and selective control.

La croisade antivariolique

par Pierre Darmon

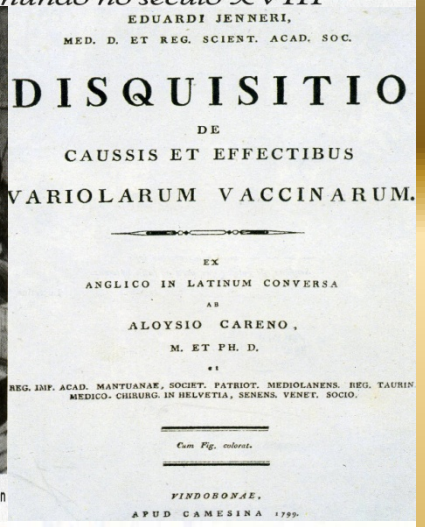
Il a fallu un siècle pour vaincre les craintes des Français devant une vaccination antivariolique qui n'était d'ailleurs pas sans risques.

Da variolização à vacina

A partir de uma doença comum em vacas, o médico Edward Jenner descobriu uma forma de inocular humanos e combater a varíola, que matou 40 milhões de pessoas em todo o mundo no século XVIII

ETRATO DE LADY MARY
Vortley Montagu,
ntrodutora na Inglaterra
a técnica asiática
e variolização (por
noculação subcutânea
o líquido extraído das
esículas variólicas)

ILUSTRAÇÃO DO MÉTODO DE OBTENÇÃO da vacina antivariólica a partir das vesículas do abdômen de uma vaca (1872)



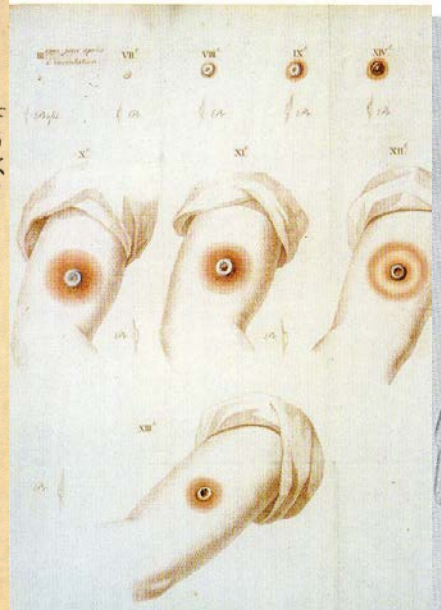
EDUARDI JENNERI,
MED. D. ET REG. SCIENT. ACAD. SOC.

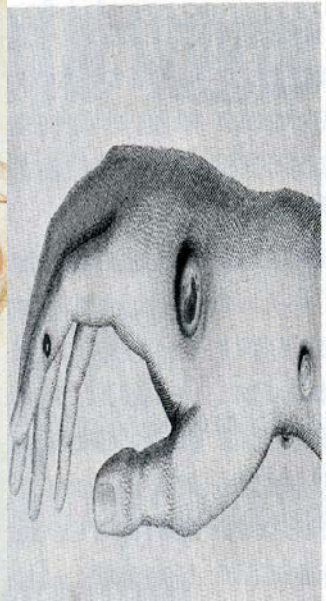
DISQUISITIO
DE
CAUSSIS ET EFFECTIBUS
VARIOLARUM VACCINARUM.

EX
ANGLICO IN LATINUM CONVERSA
AB
ALOYSIO CARENO,
M. ET PH. D.
ET
REG. IMP. ACAD. MANTUANAE, SOCIET. PATRIOT. MEDIOLANENS. REG. TAURIN.
MEDICO-CHIRURG. IN HELVETIA, SENENS. VENET. SOCIO.

Cum Fig. colorat.

VINDOBONAE,
APUD CAMESINA 1799.





Une main avec pustule variolique : Edward Jenner découvre après plusieurs années d'observations et de recherches le moyen d'immuniser l'homme contre la variole par inoculation de la vaccine (cl. Edimédia).