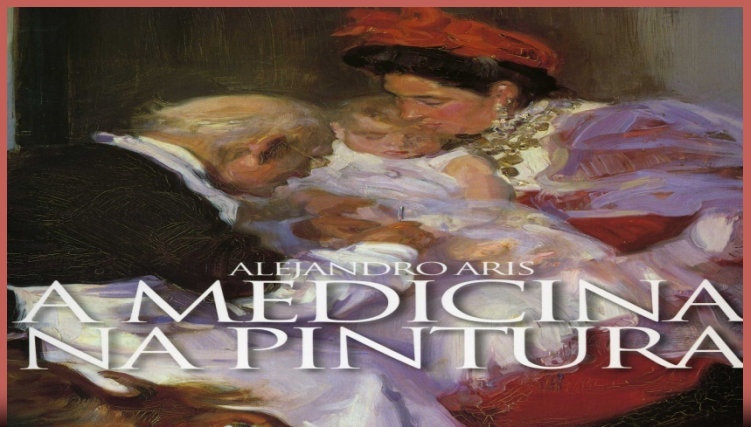
“Breve Resenha Histórica sobre a Evolução da Microbiologia e das Doenças Infecciosas desde a Antiguidade II”

José Poças

Serviço de Doenças Infecciosas
CHS – HSB Setúbal



O PRESENTE

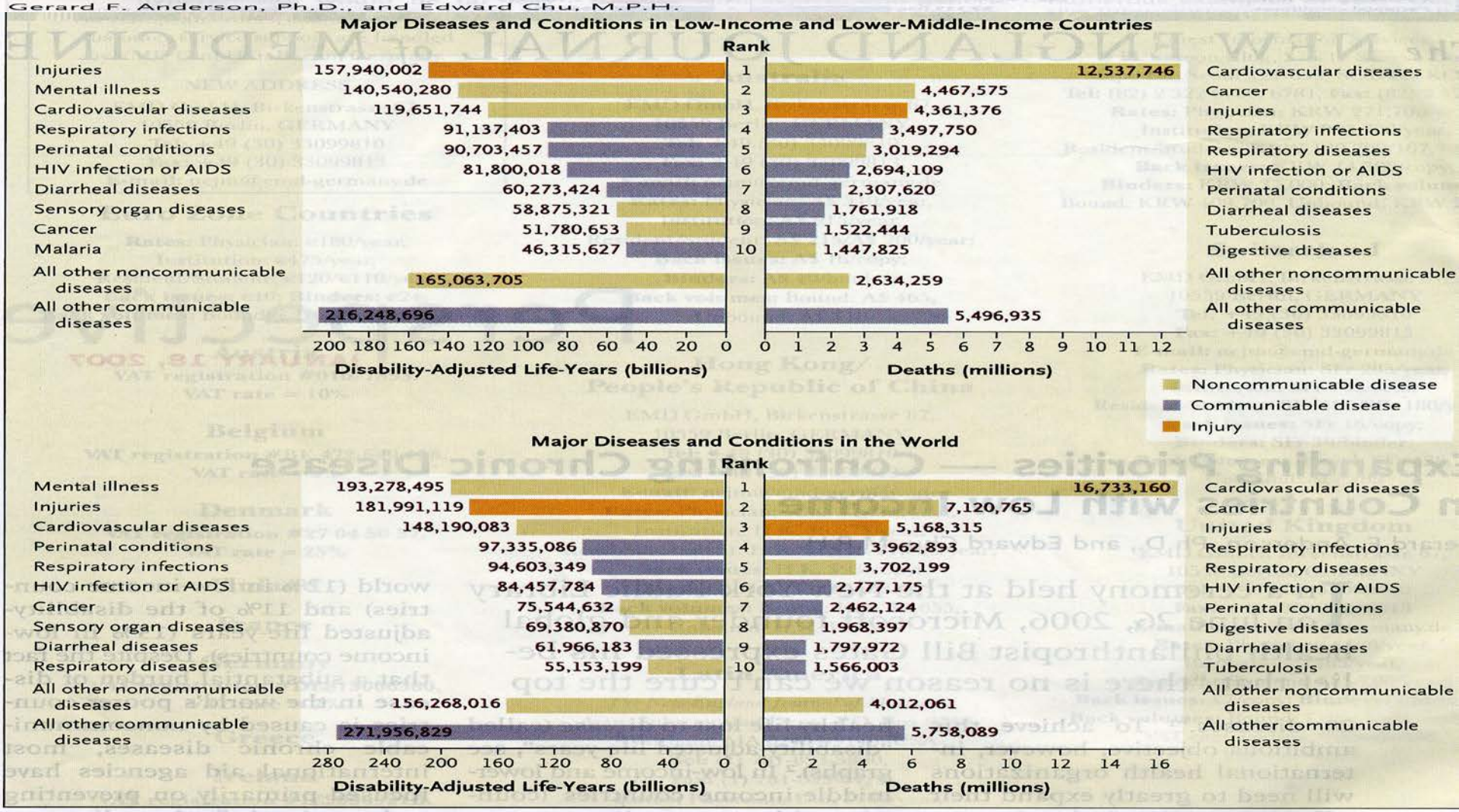
The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JANUARY 18, 2007

Expanding Priorities — Confronting Chronic Disease in Countries with Low Income

Gerard F. Anderson, Ph.D., and Edward Chu, M.P.H.



Years of Healthy Life Lost (Disability-Adjusted Life-Years) and Deaths According to Disease or Condition.

Perinatal conditions include low birthweight, prematurity, birth asphyxia, and birth trauma. Data are from the World Health Organization.[2]

REVIEW ARTICLE

CURRENT CONCEPTS

Control of Neglected Tropical Diseases

Peter J. Hotez, M.D., Ph.D., David H. Molyneux, Ph.D., D.Sc., Alan Fenwick, Ph.D., Jacob Kumaresan, M.B., B.S., Dr.P.H., Sonia Ehrlich Sachs, M.D., Jeffrey D. Sachs, Ph.D., and Lorenzo Savioli, M.D.

Table 1. The Major Neglected Tropical Diseases Ranked by Prevalence.*

Disease	Global Prevalence (millions)	Population at Risk	Regions of Highest Prevalence	Source
Ascariasis	807	4.2 billion	East Asia and Pacific Islands, sub-Saharan Africa, India, South Asia, China, Latin America and Caribbean	Bethony et al.,[6] de Silva et al.[7]
Trichuriasis	604	3.2 billion	Sub-Saharan Africa, East Asia and Pacific Islands, Latin America and Caribbean, India, South Asia	Bethony et al.,[6] de Silva et al.[7]
Hookworm infection	576	3.2 billion	Sub-Saharan Africa, East Asia and Pacific Islands, India, South Asia, Latin America and Caribbean	Bethony et al.,[6] de Silva et al.[7]
Schistosomiasis	207	779 million	Sub-Saharan Africa, Latin America and Caribbean	Steinmann et al.[8]
Lymphatic filariasis	120	1.3 billion	India, South Asia, East Asia and Pacific Islands, sub-Saharan Africa	Ottesen,[9] WHO[10]
Trachoma	84	590 million	Sub-Saharan Africa, Middle East and North Africa	International Trachoma Initiative,[11] Médecins sans Frontières[12]
Onchocerciasis	37	90 million	Sub-Saharan Africa, Latin America and Caribbean	Basáñez et al.[13]
Leishmaniasis	12	350 million	India, South Asia, sub-Saharan Africa, Latin America and Caribbean	Desjeux[14]
Chagas' disease	8–9	25 million	Latin America and Caribbean	WHO[15]
Leprosy	0.4	ND	India, sub-Saharan Africa, Latin America and Caribbean	International Federation of Anti-Leprosy Associations[16]
Human African trypanosomiasis	0.3	60 million	Sub-Saharan Africa	Févre et al.[17]
Dracunculiasis	0.01	ND	Sub-Saharan Africa	Carter Center[18]
Buruli ulcer	ND	ND	Sub-Saharan Africa	Global Buruli Ulcer Initiative[19]

* ND denotes not determined.

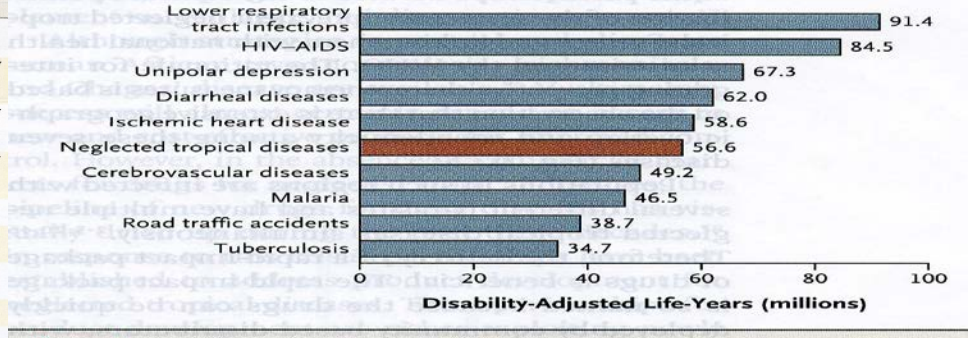


Figure 1. The 10 Leading Causes of Life-Years Lost to Disability and Premature Death.

The number of years lost to disability and premature death (disability-adjusted life-years) for the 13 major neglected tropical diseases were calculated according to a method we described previously.[4] The disability-adjusted life-years for the other conditions are based on data from the World Health Organization.[2,3] The ranking of disease burdens is based on data in Hotez.[5]

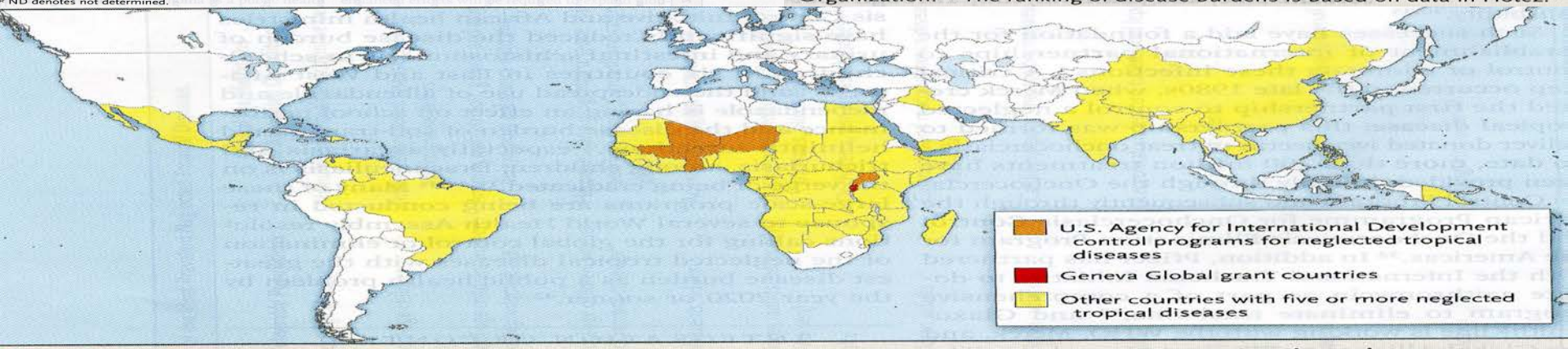
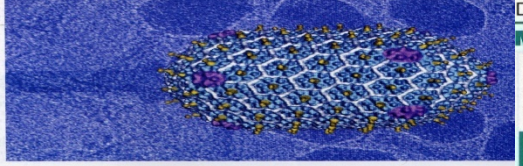


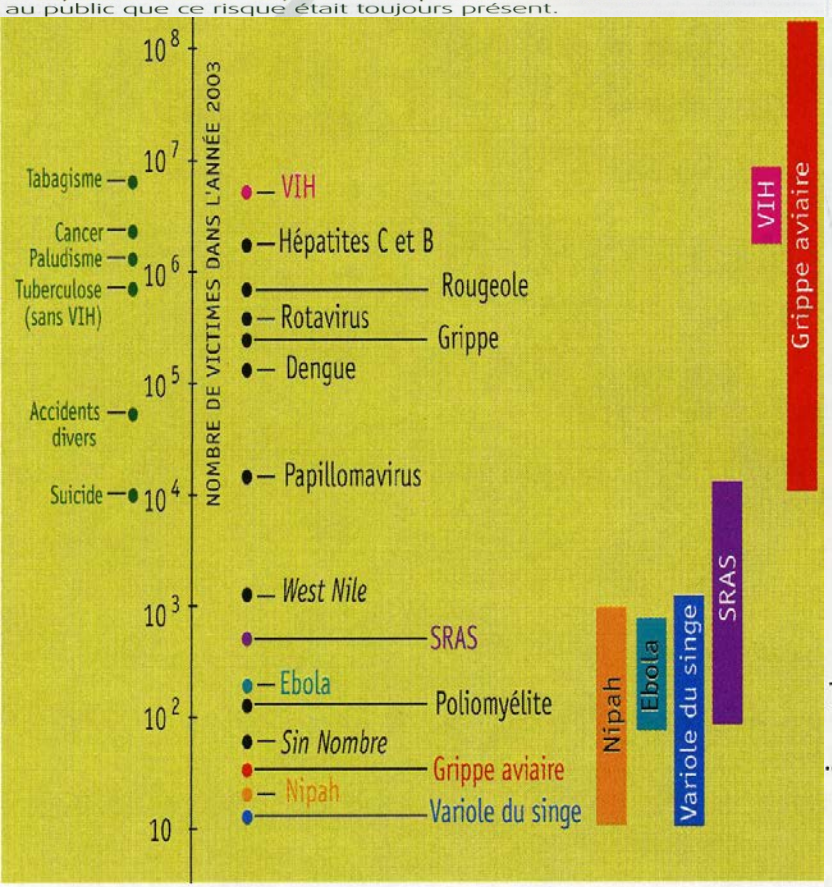
Figure 2. Nations with Five, Six, or Seven Neglected Tropical Diseases to Be Targeted for Integrated Preventive Chemotherapy.

Of the 56 nations to be targeted with a rapid-impact package, shown in yellow, 37 are located in the World Health Organization (WHO) African region, 5 in the WHO Region of the Americas, 5 in the WHO Eastern Mediterranean region, 3 in the WHO South-East Asia region, and 6 in the WHO Western Pacific region. Data regarding the occurrence of lymphatic filariasis, onchocerciasis, schistosomiasis, and the three soil-transmitted helminth infections are derived from the WHO.[44] Data regarding the occurrence of trachoma are derived from the WHO.[45] The five nations shown in orange — Burkina Faso, Ghana, Mali, Niger, and Uganda — will be targeted for integrated control in national programs through the support of the U.S. Agency for International Development Neglected Tropical Disease Control Program beginning this year. The two nations shown in red — Rwanda and Burundi — will be targeted for integrated control in national programs through the support of Geneva Global beginning this year.



Les nouveaux risques infectieux

Ces dernières années ont ressuscité la peur des maladies infectieuses. Celle-ci a été parfois excessive et disproportionnée, mais, dans tous les cas, elle a fait prendre conscience au public que ce risque était toujours présent.

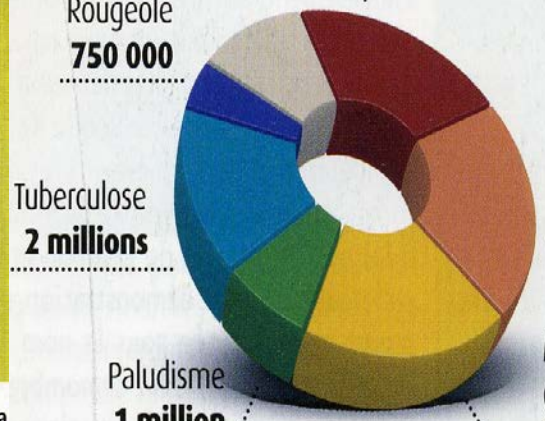


3. Les virus les plus meurtriers sont classés selon le nombre de victimes qu'ils ont occasionné en 2003 *(au centre)*. Le SIDA est la plus importante des maladies virales à ce jour, mais elle n'atteint pas le funeste record du tabagisme mondial. Toutefois, si des virus mutent certains pourront devenir plus meurtriers *(à droite)*. Ainsi, la grippe aviaire est responsable de quelques décès aujourd'hui, mais si le virus mute en une souche transmissible d'homme à homme, elle pourrait dépasser le SIDA et devenir la première pandémie du XXIe siècle.

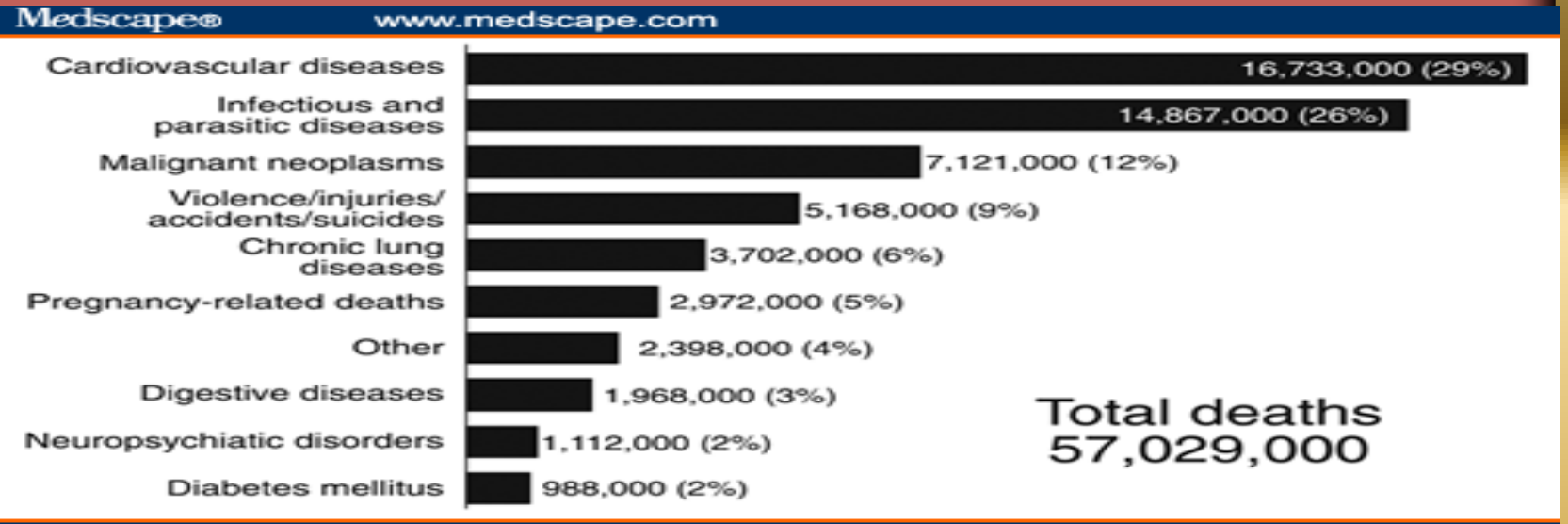
Les épidémies qui nous guettent

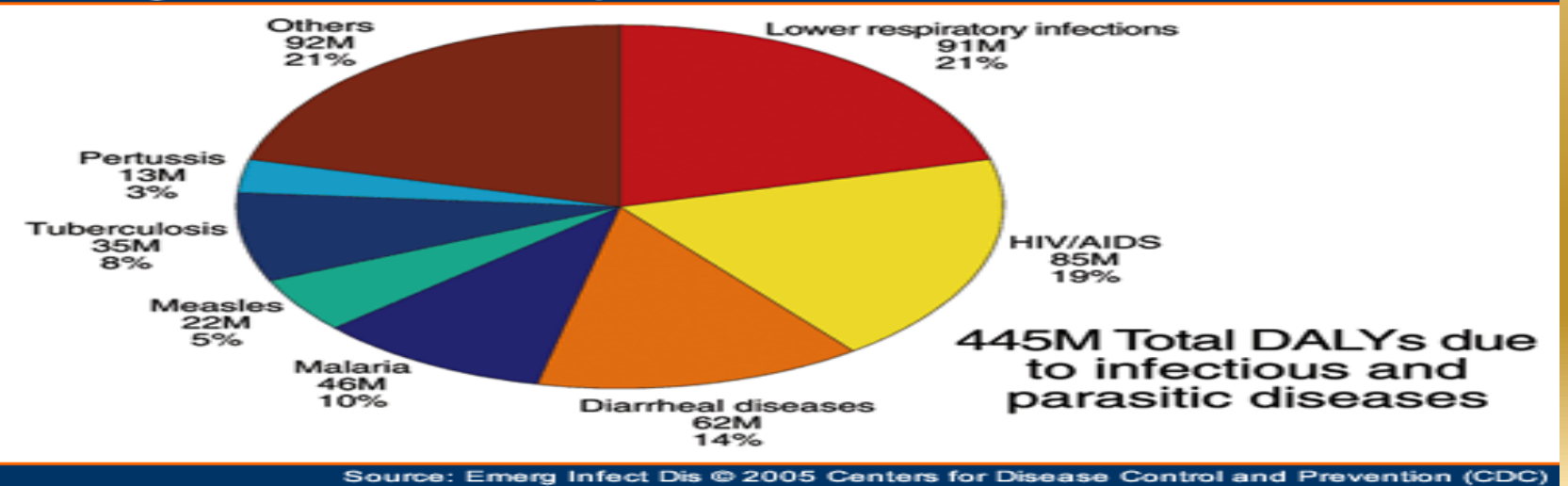
Les maladies infectieuses les plus meurtrières

90 % des décès par infection dans le monde sont dus à six grands types de maladies seulement.
(Nombre de morts par an)



Source : OMS, ONUSIDA, Institut Pasteur, 2005


Medscape®
www.medscape.com
Cardiovascular diseases
16,733,000 (29%)
Infectious and parasitic diseases
14,867,000 (26%)
Malignant neoplasms
7,121,000 (12%)
Violence/injuries/ accidents/suicides
5,168,000 (9%)
Chronic lung diseases
3,702,000 (6%)
Pregnancy-related deaths
2,972,000 (5%)
Other
2,398,000 (4%)
Digestive diseases
1,968,000 (3%)
Neuropsychiatic disorders
1,112,000 (2%)
Diabetes mellitus
988,000 (2%)
Total deaths
57,029,000
Source: Emerg Infect Dis © 2005 Centers for Disease Control and Prevention (CDC)


Medscape®
www.medscape.com
Others
92M
21%
Lower respiratory infections
91M
21%
Pertussis
13M
3%
Tuberculosis
35M
8%
HIV/AIDS
85M
19%
Measles
22M
5%
Malaria
46M
10%
Diarrheal diseases
62M
14%
445M Total DALYs due to infectious and parasitic diseases
Source: Emerg Infect Dis © 2005 Centers for Disease Control and Prevention (CDC)

CHALLENGES FOR HUMANITY

War on Disease

Just a few years ago medicine seemed to be winning the fight against disease. But now old adversaries are coming back and new infections are emerging, exposing us all to serious, sometimes unexpected, threats.

By Rick Weiss
Photographs by Karen Kasmauski

STALKING THE WORLD'S EPIDEMICS

THE DISEASE DETECTIVES

By PETER JARET
Photographs by MATTHEW NAYTHONS and STUART FRANKLIN MAGNUM

Searching for clues to Lyme disease, researcher Sam Telford drags a blanket to snare infected ticks on Nantucket Island.

Global Enemies

Six maladies alone account for 90 percent of the deaths from infectious diseases worldwide. Spread in different ways and influenced by different factors, they continue to resist control. Aggravating social, economic, and political instability, these diseases have increasingly become global security threats. Large, densely populated cities in developing countries, where most of the world's people now live, are especially vulnerable.

Influenza

Prone to mutate, influenza viruses continually appear in different forms, requiring the production of a new vaccine each flu season. In some years the symptoms are mild; in others they can be lethal. Three episodes were especially virulent: the influenza pandemic in 1918-19, the Asian flu in 1957-58, and the Hong Kong flu in 1968-69.

HIV / AIDS

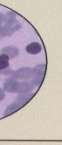
Passed on through bodily fluids, human immunodeficiency virus, or HIV, almost invariably leaves the body defenseless against the infections that define full-blown acquired immunodeficiency syndrome, or AIDS. Sub-Saharan Africa, with one-tenth of the world's population, has more than 70 percent of all HIV cases.

Diarrheal Diseases

Waterborne bacteria, viruses, and parasites produce about four billion cases of diarrhea a year. Those at highest risk include the 1.1 billion people lacking access to safe drinking water and the 2.4 billion without adequate sanitation facilities. Cholera, an acute diarrheal disease, claims more than 5,000 lives a year.

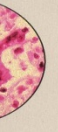
Tuberculosis

Propelled by a cough or sneeze from an infected person, tuberculosis bacteria can begin to grow in the lungs and throat of anyone who breathes them in. Drugs discovered in the 1940s beat back the disease, but the bacteria have recently begun to develop resistance, and tuberculosis has reappeared with a vengeance.



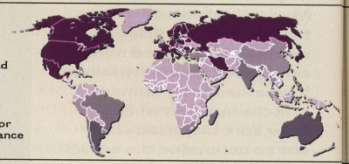
Malaria

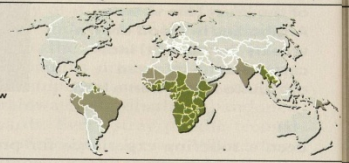
Caused by microscopic parasites transmitted by the bites of infected mosquitoes, malaria attacks red blood cells. Global warming has expanded the range of malaria-carrying mosquitoes, putting more than 40 percent of the world's population at risk. In addition, warmer weather makes mosquitoes breed faster and bite more often.

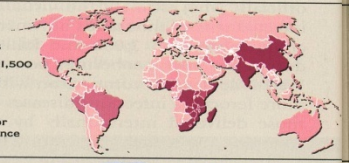


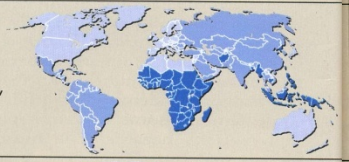
Measles

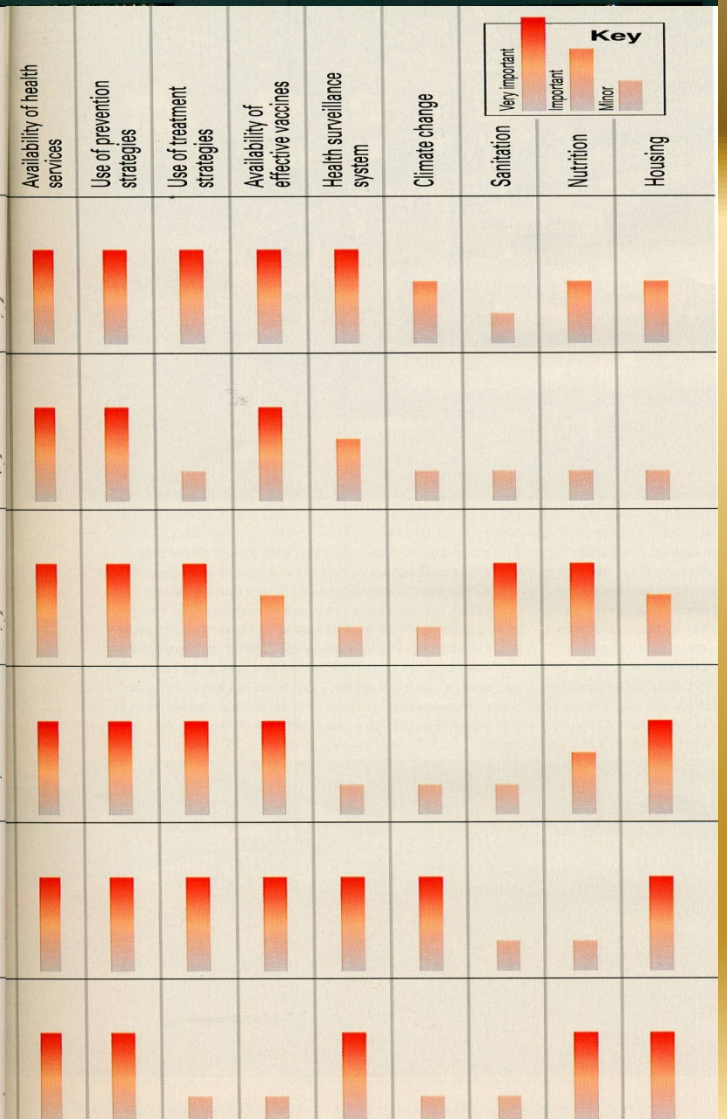
A highly contagious viral disease that can lead to pneumonia or encephalitis, measles was an inevitable rite of childhood until an effective vaccine became available in 1963. Still striking more than 30 million a year and killing some 900,000, it is the world's leading cause of vaccine-preventable death in children.











Dossier

MALADIES ÉMERGENTES

Le classement des germes tueurs

Dangerosité globale (en Europe)	Microbes et maladies	Critères de dangerosité			Réponses médicales	
		risque de contage en Europe	virulence	lésions des organes vitaux	vaccin	médicament
⚜	Virus de la grippe *	⚜⚜⚜	⚜⚜⚜	⚜⚜⚜	💉	💊
	Virus du sida	⚜⚜	⚜⚜⚜	⚜⚜⚜	—	💊
	Virus de l'hépatite B	⚜⚜	⚜⚜	⚜⚜⚜	💉💉💉	—
	Virus de la rage	⚜	⚜⚜⚜	⚜⚜⚜	💉💉	—
	Virus de la poliomyélite	⚜⚜⚜	⚜⚜	⚜⚜	💉💉	—
	Bacille de Koch (tuberculose)	⚜⚜⚜	⚜	⚜⚜⚜	💉💉	💊
	Bacille de la diphtérie	⚜	⚜⚜⚜	⚜⚜⚜	💉💉	💊
	Plasmodium (paludisme)	⚜	⚜⚜	⚜⚜	—	💊
	Bacille du choléra	0	⚜⚜⚜	⚜⚜⚜	—	💊
0	Virus Ebola (fièvre hémorragique)	0	⚜⚜⚜	⚜⚜⚜	—	—

— pas de vaccin, pas de médicament 💉 vaccin moyennement efficace 💉💉 vaccin efficace 💉💉💉 vaccin très efficace

Conflict and Emerging Infectious Diseases

Michelle Gayer,* Dominique Legros,* Pierre Formenty,* and Maire A. Connolly*

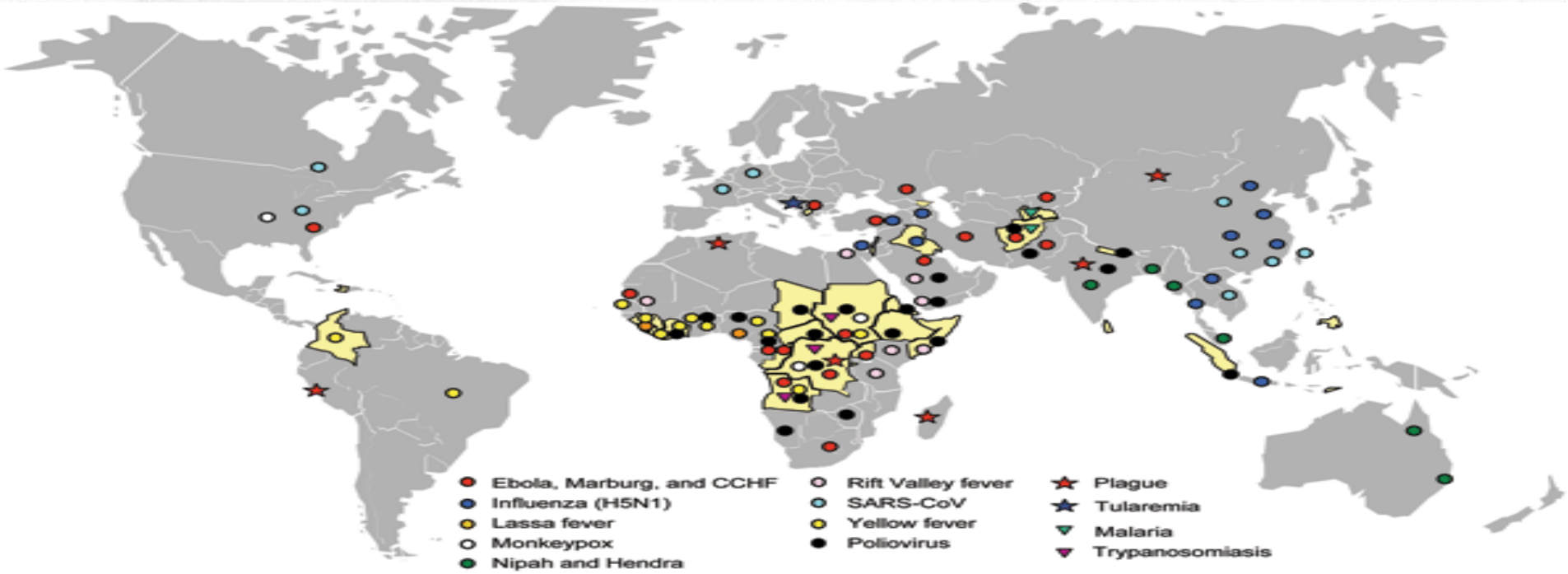


Figure. Geographic distribution of recent emerging or reemerging infectious disease outbreaks and countries affected by conflict, 1990–2006. Countries in yellow were affected by conflict during this period (source: Office for the Coordination of Humanitarian Affairs, World Health Organization, www.reliefweb.int/ocha_ol/onlinehp.html). Symbols indicate outbreaks of emerging or reemerging infectious diseases during this period (source: Epidemic and Pandemic Alert and Response, World Health Organization, www.who.int/csr/en). Circles indicate diseases of viral origin, stars indicate diseases of bacterial origin, and triangles indicate diseases of parasitic origin. CCHF, Crimean-Congo hemorrhagic fever; SARS-CoV, severe acute respiratory syndrome coronavirus.

ELSEVIER SAUNDERS

Infect Dis Clin N Am 18 (2004) 171–188

INFECTIOUS DISEASE CLINICS OF NORTH AMERICA

History of human parasitic diseases

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Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

Table 1
Parasitic diseases

Disease	Parasite	Numbers infected
Malaria	*Plasmodium* spp	300–500,000,000
Amoebiasis	*Entamoeba histolytica*	48,000,000
Sleeping sickness	*Trypanosoma brucei gambiense* and *T b rhodesiense*	300,000
Chagas' disease	*Trypanosoma cruzi*	18,000,000
Schistosomiasis	*Schistosoma* spp	200,000,000
Hookworm	*Ancylostoma duodenale* and *Necator americanus*	150,000,000
Lymphatic filariasis	*Wuchereria* spp *Brugia* spp	120,000,000
Loiasis	*Loa loa*	No accurate figures
Onchocerciasis	*Onchocerca volvulus*	18,000,000
Guinea worm disease	*Dracunculus medinensis*	80,000
Larval cestodiasis	*Taenia* spp *Echinococcus granulosus*	No accurate figures

AT WORK IN THE COMBAT ZONE

Dossier

MALADIES ÉMERGENTES

Que peut la science face aux VIRUS

MALADIES ÉMERGENTES

1975 - 1995 : 25 nouveaux agents infectieux

Microbes sans frontières

Depuis vingt ans, au moins 25 nouveaux agents infectieux ont fait leur apparition aux quatre coins de la planète. Sciences et Avenir *raconte l'histoire de douze de ces nouveaux microbes.**

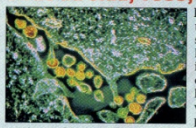
Hantavirus, 1993, Etats-Unis.

En mai, l'alerte est donnée: deux membres d'un jeune couple sont mystérieusement foudroyés par une insuffisance respiratoire aiguë *(voir Sciences et Avenir n°564, février 1994)*. Le Centre de contrôle des maladies d'Atlanta constate une petite épidémie limitée, dans un premier temps, au territoire des Navajos puis plus étendue (Nouveau-Mexique, Nevada, Colorado). Le coupable est identifié: un virus, inconnu jusqu'alors, d'un genre lui-même déjà identifié, les hantavirus. Cette nouvelle souche virale est le fruit de changements écologiques: un hiver et un printemps inhabituellement doux et humides ayant conduit à une production abondante de pignons de pins dont se nourrissent les souris, hôtes du virus. Ces rongeurs ont alors pullulé au printemps et en été, d'où une possibilité de contamination accrue pour l'homme.

Legionella pneumophilia, 1976, Etats-Unis.

Une pneumonie d'allure inhabituelle frappe des participants de l'assemblée de l'American Legion (anciens combattants) de Pennsylvanie, dans un grand hôtel de Philadelphie. L'enquête du Centre de contrôle des maladies d'Atlanta établit que le microbe responsable est une bactérie jusqu'alors inconnue, mais en fait déjà présente et inoffensive. La cause de la «maladie des légionnaires» est l'intervention d'un facteur écologique nouveau et non pas une mutation du germe donnant naissance à une souche bactérienne particulièrement virulente. Les Legionella sont devenues dangereuses en raison de leur multiplication dans l'eau stagnante des climatiseurs et de leur dissémination dans des aérosols.

Virus du sida, 1983, mondial.



Bien que non démontrée, l'origine du sida est très probablement une infection touchant des singes d'Afrique centrale. La transmission à l'homme a dû avoir lieu dans une zone rurale isolée. Puis, par voie sexuelle ou sanguine, débuta la contamination interhumaine. A l'occasion de migrations de la campagne à la ville, les premiers citadins furent atteints par le VIH1 qui diffusa alors d'est en ouest du continent africain *via* la route reliant Kinshasa (Zaïre) à Mombassa (Kenya), et simultanément aux Etats-Unis *via* les transports aériens. Cette dernière étape fut cruciale pour le développement de la pandémie planétaire, favorisée par les comportements humain (sexualité libérée, toxicomanie intraveineuse) et les pratiques médicales (transfusion sanguine, transplantation d'organes).

Bactérie de la maladie de Lyme, 1982, Europe et Etats-Unis.

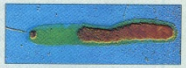
Borrelia burgdorferi, l'agent de la maladie de Lyme (une arthrite récidivante associée à une éruption cutanée) est apparu à la faveur de la reforestation autour de certains habitats (notamment les lotissements de maisons individuelles) qui favorisent la pullulation des tiques vecteurs et celle des cerfs (second réservoir animal). Les incessants mouvements de population dans ces zones mettent de nombreuses personnes en contact avec des vecteurs.

Virus Guanarito, 1991, Venezuela.

Quinze cas de cette fièvre hémorragique surviennent dans une communauté rurale qui a entrepris de défricher une forêt, soulevant des poussières infectées par les urines ou les excréments de l'animal réservoir du virus, un rongeur, *Sigmodon alstoni*. Contamination par voie respiratoire.

Choléra, 1991, Amérique du Sud.

L'entrée de la maladie en Amérique du Sud, pour la première fois du siècle, survient à partir d'eau contaminée transportée au fond de la cale d'un cargo en provenance d'Asie. Ce variant du *Vibrio choleræ*, étiqueté 0139, doit son développement à la misère, au manque d'hygiène et à la moindre chloration des eaux d'alimentation.



Virus de l'hépatite C, 1989, mondial.

Sa diffusion subite est liée à l'utilisation de produits sanguins et tissulaires (transfusions, greffes d'organes) ou de seringues contaminées *(voir* Sciences et Avenir, *n° 576, février 1995)*. Ce microbe témoigne des difficultés extrêmes rencontrées par les virologues: alors que les outils modernes de la biologie moléculaire ont permis de connaître son identité génétique, il n'a pas pu encore être photographié.

Prion, 1982, Grande-Bretagne et France.

Entre 1986 et 1994, 138444 bovins succombent à la «maladie de la vache folle» en Grande-Bretagne. La source de la contamination par le prion, un agent transmissible non conventionnel (ni viral ni bactérien) identifié en 1982, se trouvait dans l'alimentation animale qui, depuis l'introduction de nouveaux procédés de fabrication, contenait des déchets de boucherie à base de cervelles de moutons atteints de la «scrapie» (une autre maladie due au prion). La transmission de la maladie de la vache folle par voie orale aux humains apparaît improbable. Toutefois l'homme peut, comme l'animal, être infecté par le prion. En témoigne une deuxième épidémie révélée en France en 1992: la maladie de Creutzfeldt-Jakob. Elle touche certains enfants atteints de nanisme hypophysaire, traités par l'hormone de croissance extraite d'hypophyses prélevées sur des cadavres.

Virus de la dengue hémorragique, 1977, Asie.

L'urbanisation sauvage du continent asiatique entraîne une prolifération des réservoirs d'eau ouverts, des bouteilles en plastique ou des pneus pleins d'eau qui abritent, par conséquent, une population de moustiques *(asian tiger mosquito)* en augmentation. Or cet insecte est le vecteur de l'infection. L'importation aux Etats-Unis de pneus à rechaper a favorisé, en 1985 puis 1993, la diffusion de la dengue hémorragique dans certaines cités américaines.

Virus de la fièvre de la vallée du Rift, 1977, Egypte.

Six ans après la mise en eau du barrage d'Assouan, 600 personnes sont mortes de cette fièvre hémorragique transmise par les moustiques. En dehors de telles épidémies, le virus «dormirait» dans des œufs de moustique, très résistants à la sécheresse. Les inondations favorisent la pullulation des moustiques tandis que la contagion est renforcée par les concentrations humaines et animales. Ces deux facteurs sont à l'origine du retour de la fièvre de la vallée du Rift, déjà observée en 1930 au Kenya.

Morbillivirus équin, 1994, Australie.

Un homme et 14 chevaux décèdent en septembre 1994, non loin de Brisbane, d'une maladie respiratoire suraiguë. En quelques jours, le Laboratoire australien de santé animale du CSIRO, le plus grand centre de recherche scientifique national, écarte tout empoisonnement ou toute infection déjà connue et identifie le nouveau tueur, un morbillivirus équin, de la même famille que le virus de la rougeole.

Virus Ebola, 1976, Zaïre.

Autour de l'hôpital de Yambuku au bord de la rivière Ebola, 280 personnes sont mortes de cette fièvre hémorragique. Origine accidentelle hospitalière: 85 personnes avaient reçu une injection dans le centre de soins local. Le premier cas fut un instituteur hospitalisé pour un supposé paludisme. Il reçut une injection de quinine. Comme l'hôpital ne disposait que de cinq seringues qui n'étaient pas stérilisées après chaque usage, l'épidémie s'est propagée. Quatre autres émergences du virus Ebola ont ensuite été relevées: au Soudan (1976), à Reston, aux Etats-Unis (1989), en Côte-d'Ivoire (1995), et actuellement de nouveau au Zaïre (avec la même souche qu'en 1976). Le réservoir animal du virus reste indéterminé.

*Dans l'ordre, nom de l'agent pathogène, date de son identification, pays, circonstances d'apparition

L'émergence virale permanente

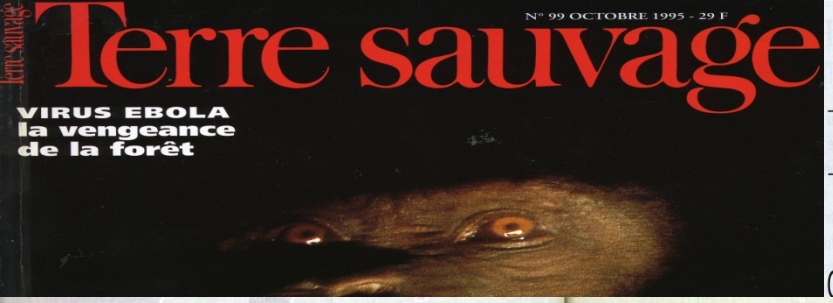
Antoine GESSAIN et Jean-Claude MANUGUERRA

Mutations de virus et réservoirs animaux contribuent à l'apparition de nouvelles souches pathogènes pour l'homme. Mode de vie, changements environnementaux et transports intercontinentaux favorisent ensuite la survenue de pandémies.

Quelques exemples de maladies virales émergentes (ou réémergentes) apparues entre 1994 et 2007

1 - Fièvre Crimée-Congo
2 - Dengue hémorragique
3 - Fièvre Ebola
4 - Entérovirus 71
5 - Hendra
6 - Orthopoxvirose simienne
7 - Grippe A (H5N1)
8 - Grippe A (H9N2)
9 - Fièvre Lassa
10 - Nipah
11 - Fièvre d'Omsk
12 - Fièvre O'nyong-nyong
13 - Poliomyélite
14 - Virose Reston
15 - Fièvre de la vallée du Rift
16 - Virose Ross River
17 - Encéphalite équine vénézuélienne
18 - Fièvre West Nile
19 - Fièvre jaune
20 - *Sin Nombre*
21 - Chikungunya
22 - SRAS

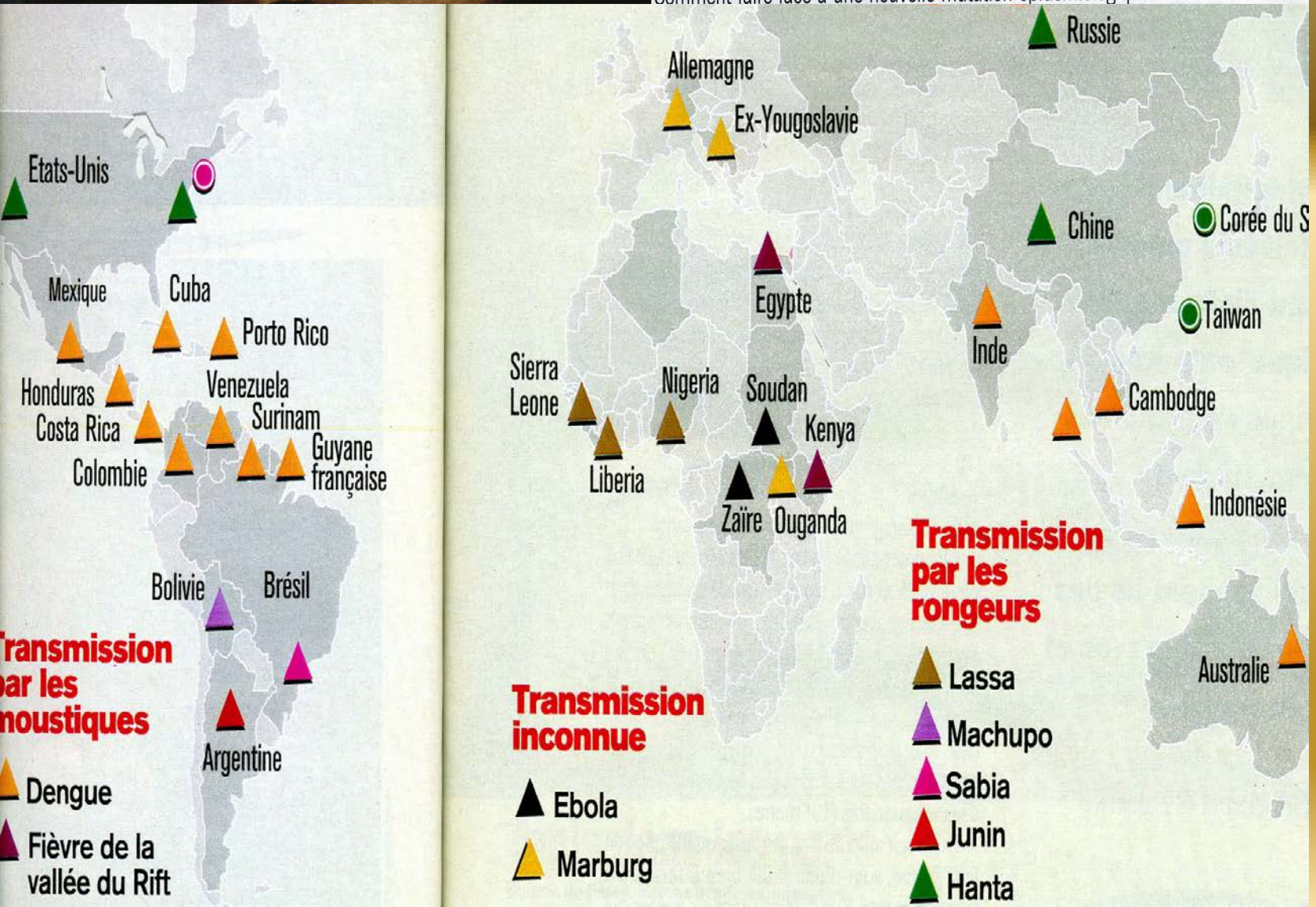
1. RÉPARTITION DES VIRUS ÉMERGENTS dans le monde entre 1994 et 2007. Les zones tropicales sont propices à l'apparition de nouveaux virus, car de nombreux facteurs d'émergence y sont regroupés : la déforestation, le rapprochement des population de réservoirs infectieux animaliers, la vétusté des infrastruc tures sanitaires, etc.



DES RÉSEAUX PLANÉTAIRES POUR LES MICROBES

George J. Armelagos

Comment faire face à une nouvelle mutation épidémiologique ?

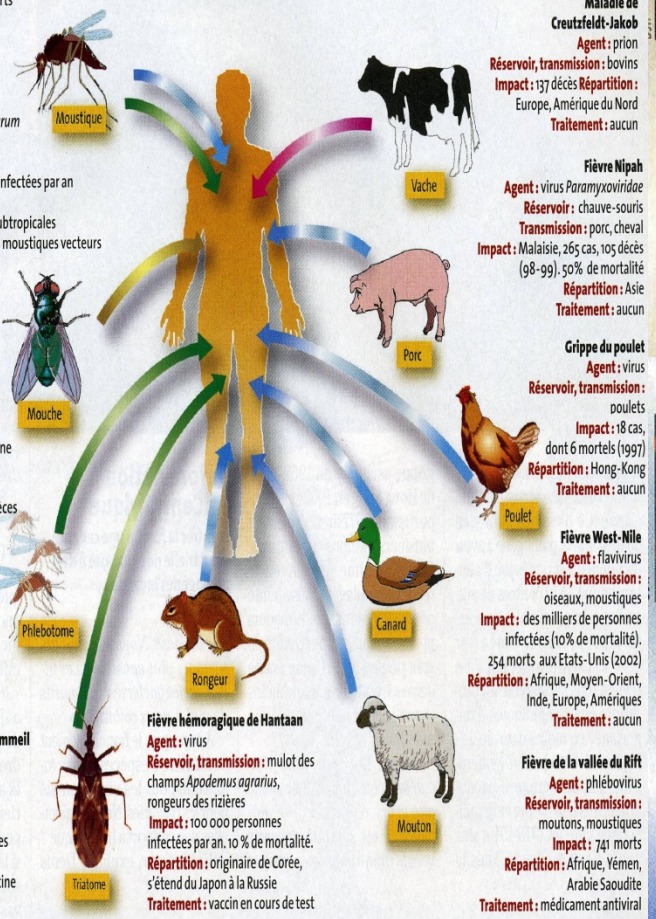


La barrière des espèces s'est effondrée !

Sida, grippe, pneumopathie atypique... les agents pathogènes passent des animaux à l'homme. Responsables : la promiscuité, l'élevage intensif ou encore la déforestation.

Des relations à risques

Nos amies les bêtes sont vecteurs de maladies. Tour d'horizon des zoonoses qui nous infectent et de leurs réservoirs.



Dengue
Agent : flavivirus
Réservoir : homme, singe
Transmission : *Aedes aegypti*
Impact : 100 millions de personnes infectées chaque année, 20 000 morts
Répartition : mondiale
Traitement : aucun. Contrôle des moustiques vecteurs

Paludisme
Agent : parasite *Plasmodium falciparum*
Réservoir : homme
Transmission : anophèle
Impact : 300 millions de personnes infectées par an et plus d'un million de morts
Répartition : régions tropicales et subtropicales
Traitement : préventif. Contrôle des moustiques vecteurs

Shigellose (dysenterie)
Agent : entérobactérie *Shigella*
Réservoir : homme, primates non humains, chien (plus rare)
Transmission : mouche
Impact : 600 000 à un million de morts par an
Répartition : zones tropicales
Traitement : antibiothérapie. Hygiène

Leishmaniose
Agent : parasite *Leishmania*, 20 espèces
Réservoir : homme, chien, rongeurs
Transmission : phlébotome
Impact : 1,5 à 2 millions de personnes infectées par an
Répartition : Afrique, Asie, Amériques, Méditerranée
Traitement : sels organiques d'antimoine. Anti-moustiques

Maladie de Chagas / Maladie du sommeil
Agent : parasite *Trypanosoma*
Transmission : triatome (insecte hématophage)
Réservoir : homme
Impact : 16 à 18 millions de personnes sont infectées par an
Répartition : Afrique / Amérique latine
Traitement : aucun

Fièvre hémoragique de Hantaan
Agent : virus
Réservoir, transmission : mulot des champs *Apodemus agrarius*, rongeurs des rizières
Impact : 100 000 personnes infectées par an. 10 % de mortalité.
Répartition : originaire de Corée, s'étend du Japon à la Russie
Traitement : vaccin en cours de test

Maladie de Creutzfeldt-Jakob
Agent : prion
Réservoir, transmission : bovins
Impact : 137 décès **Répartition :** Europe, Amérique du Nord
Traitement : aucun

Fièvre Nipah
Agent : virus *Paramyxoviridae*
Réservoir : chauve-souris
Transmission : porc, cheval
Impact : Malaisie, 265 cas, 105 décès (98-99). 50% de mortalité
Répartition : Asie
Traitement : aucun

Grippe du poulet
Agent : virus
Réservoir, transmission : poulets
Impact : 18 cas, dont 6 mortels (1997)
Répartition : Hong-Kong
Traitement : aucun

Fièvre West-Nile
Agent : flavivirus
Réservoir, transmission : oiseaux, moustiques
Impact : des milliers de personnes infectées (10% de mortalité). 254 morts aux Etats-Unis (2002)
Répartition : Afrique, Moyen-Orient, Inde, Europe, Amériques
Traitement : aucun

Fièvre de la vallée du Rift
Agent : phlébovirus
Réservoir, transmission : moutons, moustiques
Impact : 741 morts
Répartition : Afrique, Yémen, Arabie Saoudite
Traitement : médicament antiviral

Les agents infectieux ne se ressemblent guère. Ne pas les confondre !

UN RECENSEMENT PLANÉTAIRE DES MICROBES

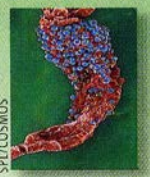
William B. Whitman et William J. Wiebe

Plus nombreux que les étoiles, ils constituent la moitié de la biomasse terrestre

Les bactéries

Ces organismes unicellulaires autonomes de 0,2 µm à 50 µm peuvent survivre hors d'un milieu vivant. Certaines (tétanos, charbon...) résistent même dans un sol sec sous forme de spores. Leur multiplication dans un organisme entrave son fonctionnement. Les bactéries peuvent engendrer une suppuration localisée (gastro-entérite) ou générale (septicémie), ou produire des substances toxiques (tétanos). Elles cèdent aux antiseptiques (alcool, savon) et à la chaleur et sont sensibles le plus souvent aux antibiotiques.

Les parasites



SPL/COSMOS

Ce sont des organismes vivants uni ou pluricellulaires, dont la taille varie de quelques dizaines de micromètres (plasmodium, trypanosome...) à plusieurs mètres (ténia). Ils colonisent un ou plusieurs hôtes sous forme larvaire ou adulte pour se nourrir et se reproduire, engendrant une série de troubles plus ou moins sérieux. Il existe des traitements préventifs pour certains (paludisme), pas toujours efficaces. La parasitose s'évite surtout en améliorant l'hygiène et en luttant contre les insectes piqueurs.

Les virus

Il s'agit de micro-organismes intracellulaires 130 fois plus petit qu'une grosse bactérie, sans matériel autre qu'un acide nucléique (ADN ou ARN). Sont-ils vivants ? Difficile à dire, car le virus ne respire pas, n'a pas de mouvement propre, ne grandit et ne se reproduit pas seul. Il colonise une cellule dont il détourne la machinerie pour se multiplier. Certains (sida...) sont sensibles à la chaleur, à la déshydratation et aux antiseptiques, d'autres (hépatite...) résistent aux températures élevées et aux désinfectants usuels.

Les prions

Ces protéines mystérieuses au comportement aberrant sont responsables de la maladie de Creutzfeldt-Jakob chez l'homme et rendent fous les vaches et les moutons. Ces agents infectieux, qui échappent pour le moment à toute investigation (on ne sait rien de leur aspect), altèrent les protéines voisines saines d'une cellule, par simple contact. Insensibles aux antiseptiques usuels et à la chaleur, ils provoquent une détérioration des cellules du cerveau, jusqu'à lui conférer un aspect spongieux.

GLOBAL 2005 HEALTH

The Paths Of Infection

Amid ancient armies, in sailing ships and on jet planes, epidemics have always shadowed humans. Are we ready for the next big one?

HISTORY'S BIG KILLERS

Infectious diseases tend to emerge and cause widespread deaths when populations mix through migrations, wars or urbanization

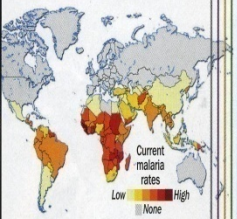
TUBERCULOSIS

1.75 MILLION DEATHS (2003)

Cause Airborne *Mycobacterium tuberculosis*, first identified in 1882, has infected humans since ancient times

Treatment Can be cured with a combination of antibiotics. A vaccine can be given to children in affected areas

Outlook AIDS and multi-drug-resistant strains have triggered a resurgence



MALARIA

1-3 MILLION DEATHS A YEAR

Cause A one-celled parasite called plasmodium that is transmitted by female anopheles mosquitoes

Treatment Conventional drugs are becoming less effective. New treatments based on artemisinin are in short supply

Outlook About 40% of the world's population is at risk

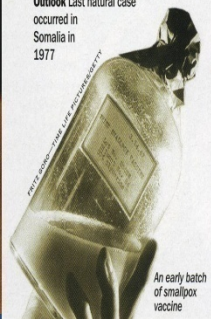
SMALLPOX

NO CURRENT FATALITIES

Cause The variola virus, thought to have evolved from an animal poxvirus in central Africa thousands of years ago

Treatment None available, but there is an effective vaccine

Outlook Last natural case occurred in Somalia in 1977



An early batch of smallpox vaccine

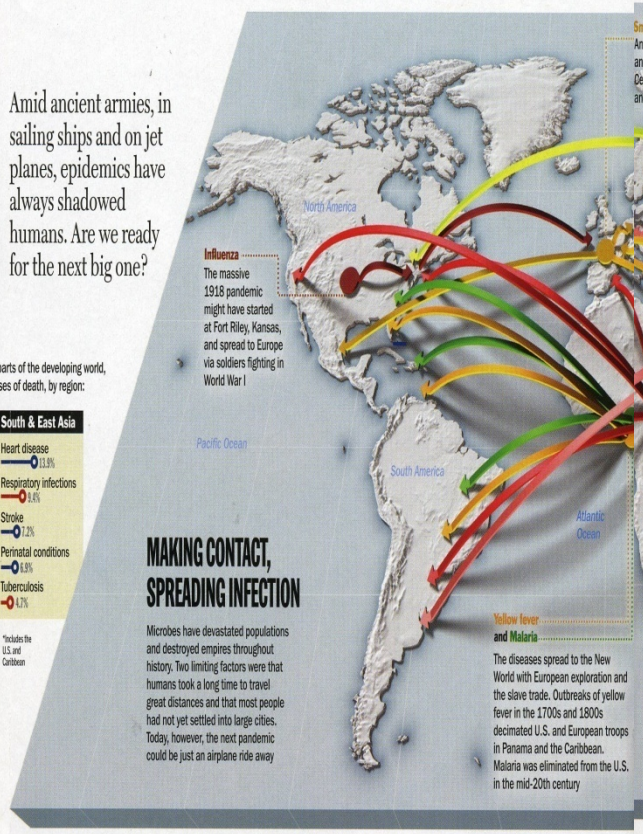
WHERE YOU LIVE, HOW YOU DIE

In much of the world, heart disease is the leading cause of death. But in parts of the developing world, particularly Africa, **infectious diseases** claim more lives. The top five causes of death, by region:

U.S.	The Americas*	Europe	South & East Asia
Heart disease 28.5%	Heart disease 15.3%	Heart disease 24.7%	Heart disease 13.8%
Cancer 22.8%	Stroke 7.8%	Stroke 15.1%	Respiratory infections 9.4%
Stroke 6.7%	Diabetes 4.2%	Throat, lung cancer 3.8%	Stroke 7.2%
Respiratory diseases 5.0%	Pulmonary disease 4.0%	Respiratory infections 2.8%	Perinatal conditions 4.9%
Accidents 4.3%	Throat, lung cancer 3.8%	Pulmonary disease 2.7%	Tuberculosis 4.7%

Middle East	China & Pacific Rim	Africa
Heart disease 12.9%	Stroke 16.4%	HIV/AIDS 20.4%
Respiratory infections 8.8%	Pulmonary disease 11.5%	Malaria 10.1%
Perinatal conditions 7.3%	Heart disease 8.3%	Respiratory infections 8.8%
Diarrheal diseases 6.0%	Stomach cancer 4.2%	Diarrheal diseases 6.5%
Stroke 5.4%	Respiratory infections 4.1%	Perinatal conditions 5.1%

*Includes the U.S. and Caribbean



Influenza The massive 1918 pandemic might have started at Fort Riley, Kansas, and spread to Europe via soldiers fighting in World War I

Smallpox An ancient disease, it emerged from India or Egypt and was taken to Europe, perhaps by Roman legions. Centuries later, Europeans carried it to the New World and Australia, with devastating consequences

Plague An old disease that re-emerged in Asia in the mid-14th century and spread along trade routes, ravaging China and Europe

SARS The recent SARS outbreak demonstrated how quickly diseases can spread via air travel. The virus from China killed dozens in Canada before it was contained

Cholera Originally endemic to the Ganges River area of India, the disease spread via trade routes to all parts of the world. Documented as early as the 16th century, pandemics began in the early 1800s

Yellow fever and Malaria The diseases spread to the New World with European exploration and the slave trade. Outbreaks of yellow fever in the 1700s and 1800s decimated U.S. and European troops in Panama and the Caribbean. Malaria was eliminated from the U.S. in the mid-20th century

AIDS HIV is believed to have moved from primates to humans in central Africa in the middle of the 20th century. The path of the virus to the rest of the world is not known. The first officially designated cases were in the U.S.

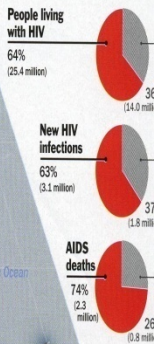
MAKING CONTACT, SPREADING INFECTION

Microbes have devastated populations and destroyed empires throughout history. Two limiting factors were that humans took a long time to travel great distances and that most people had not yet settled into large cities. Today, however, the next pandemic could be just an airplane ride away

AFRICA'S AIDS CRISIS

Sub-Saharan Africa has 10% of the world's population but 64% of all HIV cases. The next generation will be even worse off: more than 80% of the HIV-positive children in the world live in the region. The records for 2004:

Sub-Saharan Africa | Rest of the world



TIME Graphic by Jackson Dykman and Joe Lertola. Reported by Sora Song, Kristina Dell and Missy Adams

Sources: World Health Organization; Centers for Disease Control and Prevention; Joint United Nations Program on HIV/AIDS; National Institute of Allergy and Infectious Diseases/NIH; Tuberculosis Research Center, Chennai, India; United Nations Population Fund; Data.org; Saving Lives Millions at a Time, by the Johns Hopkins Bloomberg School of Public Health (Johns Hopkins University Press; 2004); The Coming Plague, by Laurie Garrett (Farrar, Straus & Giroux; 1994); The Forgotten Plague, by Frank Ryan, M.D. (Little, Brown & Co.; 1993); Scourge: The Once and Future Threat of Smallpox, by Jonathan Tucker (Atlantic Monthly Press; 2001); Harvard University; Encyclopaedia Britannica

THE ANCIENT WORLD

200 BC — *The Plague of Athens, perhaps typhus, ends the Golden Age of Greece*

100 BC — *Roman troops returning from the Middle East bring a plague that kills 4 million to 7 million in Europe*

AGE OF EXPLORATION

AD 1300 — *The Black Death arises in central Asia before spreading to Europe*

By 1350, the Black Death has killed 20 million to 30 million Europeans, a third of the total population

European contact with New World populations

Smallpox, brought by conquistadores, kills nearly half the Aztec population

First documented flu pandemic sweeps into Europe

TB causes 1 in every 5 deaths in London

Smallpox epidemic in Boston leads to early inoculations in the New World

AGE OF INDUSTRIALIZATION

Yellow fever kills 10% of Philadelphia's population

Cholera kills 500,000 people in New York City

Flu pandemic kills 20 million to 40 million people worldwide

30,000 in Ethiopia killed by yellow fever

AGE OF TECHNOLOGY

Smallpox declared eradicated

First reported AIDS case

1400 — 1500 — 1600 — 1700 — 1800 — 1900 — 2000

MEASLES

500,000 DEATHS (2003)

Cause One of the most contagious diseases known, it's an acute respiratory illness caused by a virus in the paramyxovirus family

Treatment An inexpensive vaccine has been available for more than 40 years

Outlook Now rare in the industrial world but still common in developing nations

Depiction of the plague in 1564

PLAGUE

182 DEATHS (2003)

Cause The *Yersinia pestis* bacterium infects fleas and rodents, which bring disease into human homes

Treatment Antibiotics, such as streptomycin and tetracycline

Outlook Endemic to many countries, particularly in Africa and Asia. Incidence has increased recently

CHOLERA

1,894 DEATHS (2003)

Cause The *Vibrio cholerae* bacterium causes acute intestinal infection and is spread through water and food

Treatment Most cases can be cured with oral rehydration salts. Three oral vaccines are available

Outlook Nearly every developing country faces an outbreak or the threat of one

INFLUENZA

250,000 DEATHS A YEAR

Cause A virus that attacks the upper respiratory tract. It's easily transmitted through the air when an infected person coughs or sneezes

Treatment Vaccines available, but the virus's genetic makeup is constantly changing

Outlook Millions infected every year. The elderly and chronically ill are most at risk

YELLOW FEVER

650-3,250 DEATHS (2004)*

Cause Carried by the *Aedes* and *Haemogogus* mosquitoes, which mainly pass the virus from monkeys to humans

Treatment No specific treatment. Vaccine confers immunity within a week

Outlook Once nearly eliminated, epidemics occur intermittently in Africa and South America

*Estimate

POLIOMYELITIS

126 DEATHS (2004)

Cause The highly infectious poliovirus invades the nervous system and destroys the nerve cells that activate muscles

Treatment There's no cure, but vaccines have been around since the 1950s

Outlook A qualified success story. Polio is now found only in parts of Africa and South Asia

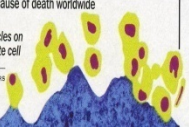
AIDS

3.1 MILLION DEATHS (2004)

Cause The human immunodeficiency virus (HIV) slowly attacks and destroys the immune system, leaving the victim vulnerable to infections that can lead to death

Treatment No cure or effective vaccine. Antiretroviral drugs can help, and their cost has fallen sharply

Outlook HIV infection rates are on the rise, and AIDS is now the No. 4 cause of death worldwide



HIV virus particles on a T4 lymphocyte cell

EMERGING THREATS

New diseases continue to threaten the human population. Since 2003, a strain of **avian-flu virus** called H5N1 has infected more than 110 people in Southeast Asia and killed at least 60. In 2002, a coronavirus likely jumped from a palm civet to a human in southern China—the first known case of **SARS.** Before it was contained in 2003, SARS infected 8,098 people worldwide and killed 774. In the western hemisphere, another avian virus, **West Nile,** took root in 1999. To date, it has infected more than 16,000 people in the U.S. alone and killed more than 600.


Source of the next pandemic

Examples of Emerging and Re-Emerging Diseases

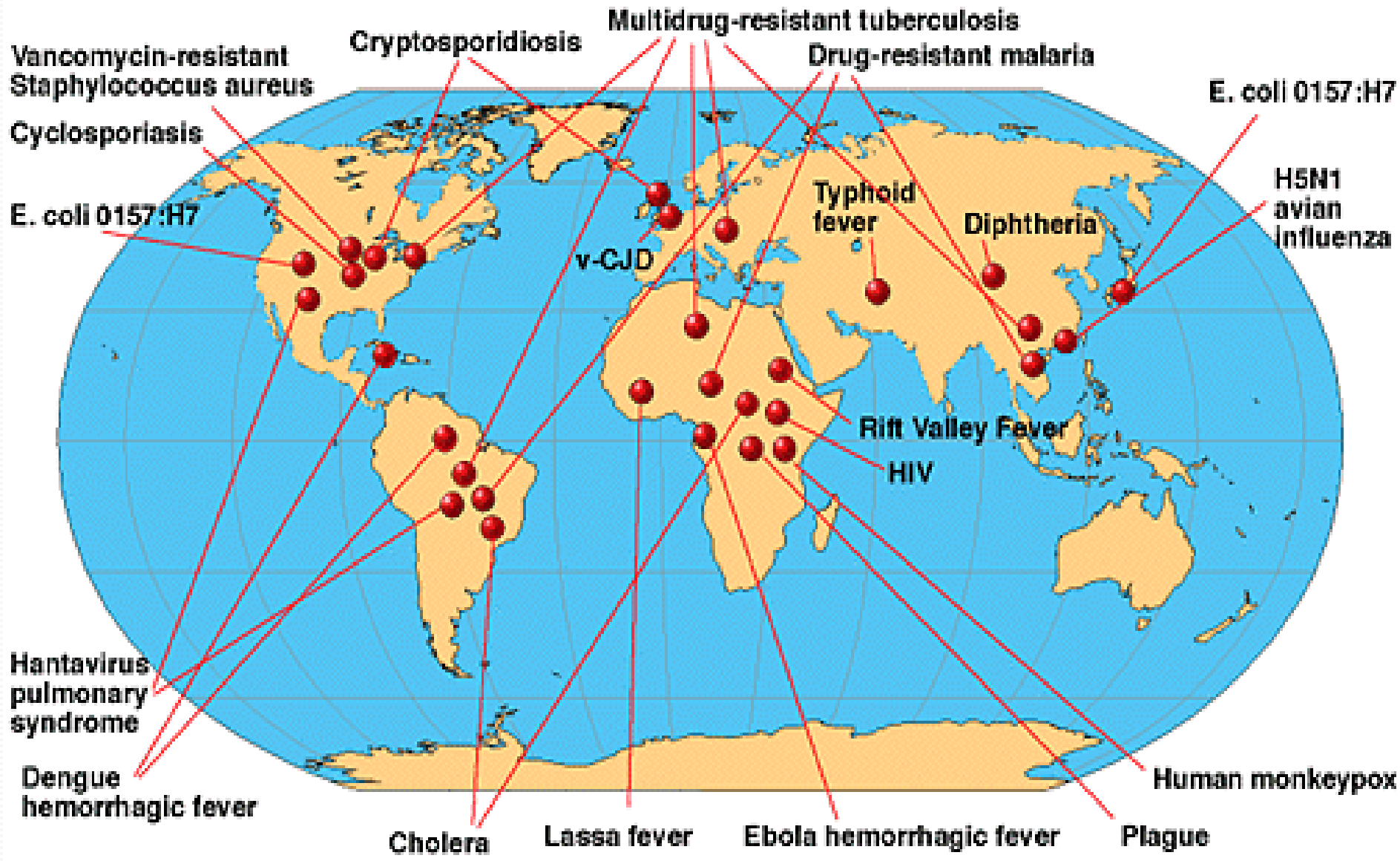


Table 1: *Newly discovered organisms of public health importance*

Year	Microbe
1973	Rotavirus
1975	Parvovirus B-19
1976	*Cryptosporidium parvum*
1977	Ebola virus
1977	*Legionella pneumophila*
1977	Hantaan virus
1977	*Campylobacter jejuni*
1980	Human T-lymphotropic virus I (HTLV-I)
1981	Toxin producing strains of *Staphylococcus aureus*
1982	*Escherichia coli* O157:H7
1982	HTLV-II
1982	*Borrelia burgdorferi*
1983	Human immunodeficiency virus
1983	*Helicobacter pylori*
1985	*Enterocytozoon bieneusi*
1986	*Cyclospora cayatanensis*
1988	Hepatitis E virus
1989	*Ehrilichia chafeensis*
1989	Hepatitis C
1991	Guanarito virus
1991	*Encephalitozoon hellem*
1991	New species of *Babesia*
1992	*Vibrio cholerae* O139
1992	*Bartonella henselae*
1993	Sin nombre virus
1993	Encephalitozoon cunculi
1994	Sabia virus
1995	HHV-8
1999	Nipah virus
2002	SARS virus

Table 1

Examples of recently emerging pathogens

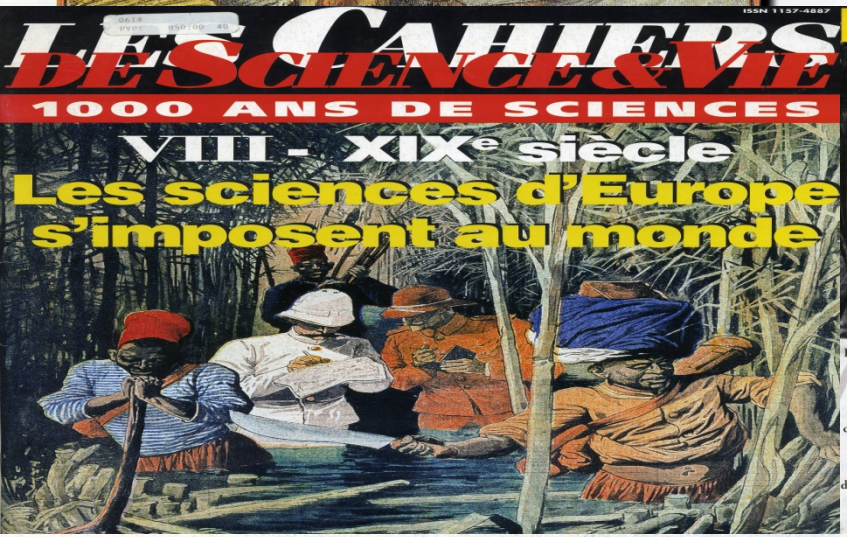
Microbe	Disease	Year
Rotavirus	Infantile gastroenteritis	1973
Legionella pneumophila	Legionnaires disease	1977
Ebola virus	Ebola hemorrhagic fever	1977
Borrelia burgdorferi	Lyme disease	1982
HIV	AIDS	1983
Hepatitis C virus	Hepatitis	1989
Vibrio cholerae O139	Cholera	1992
Sin Nombre virus	Hantavirus pulmonary syndrome	1993
Human herpesvirus 8	Kaposi sarcoma in AIDS patients	1995
Influenza virus A H5N1	Influenza	1997[A]
SARS coronavirus	Severe acute respiratory syndrome	2002

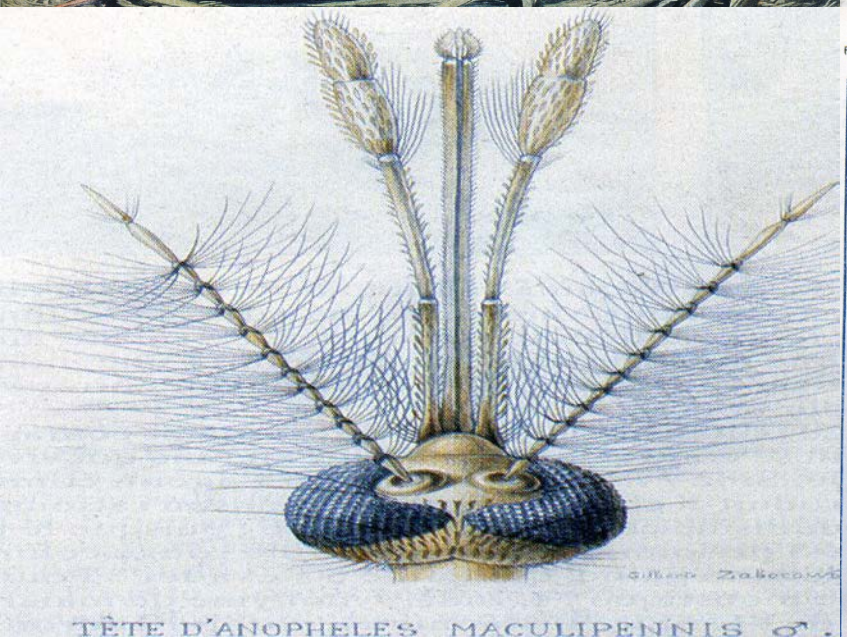
[A]First human cases; virus previously known to infect birds.

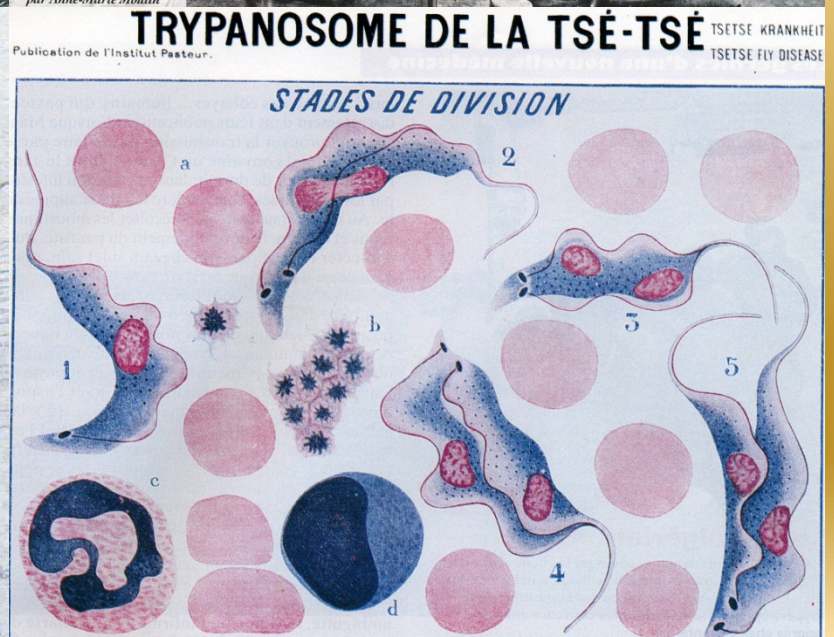
Sciences nouvelles

The Spread of Western Medicine

MICHAEL WORBOYS







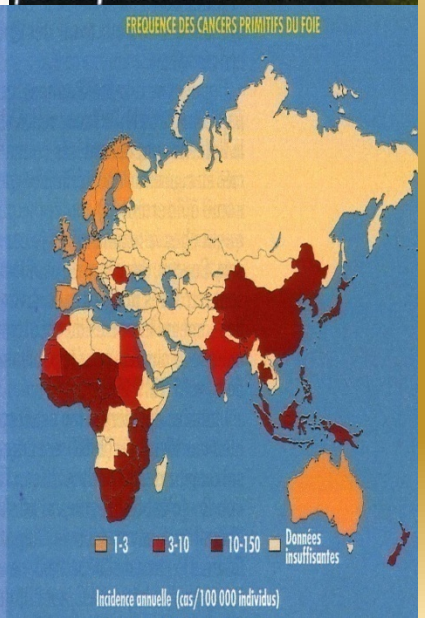
Les Six virus cancérogènes chez l'homme

L'Américain Francis Rous est, en 1910, le premier à établir une relation entre virus et cancers.

15 % des cancers humains sont d'origine virale. Le nombre de virus identifiés comme cancérogènes est pourtant très faible. De surcroît, l'infection ne semble pas suffire, à elle seule, à provoquer la maladie.

Virus cancérogènes chez l'homme

Virus	Symbole	Famille	Type de cancers
Virus de la leucémie T de l'adulte	HTLV-I	Rétrovirus	Leucémies T
Virus du papillome	HPV16 et HPV18 HPV5 et HPV17	Papovavirus	Cancer du col de l'utérus Cancers ano-génitaux Cancers cutanés
Virus d'Epstein-Barr	EBV	Herpèsvirus	Lymphome de Burkitt, cancer du nasopharynx et maladie de Kaposi
Virus Saimiri		Herpèsvirus	Maladie de Kaposi
Virus de l'hépatite B	HBV	Hepadnavirus	Hépatocarcinome
Virus de l'hépatite C	HCV	Flavivirus	Hépatocarcinome



SOFIA A. SOULI

The Love Life of the Ancient Greeks

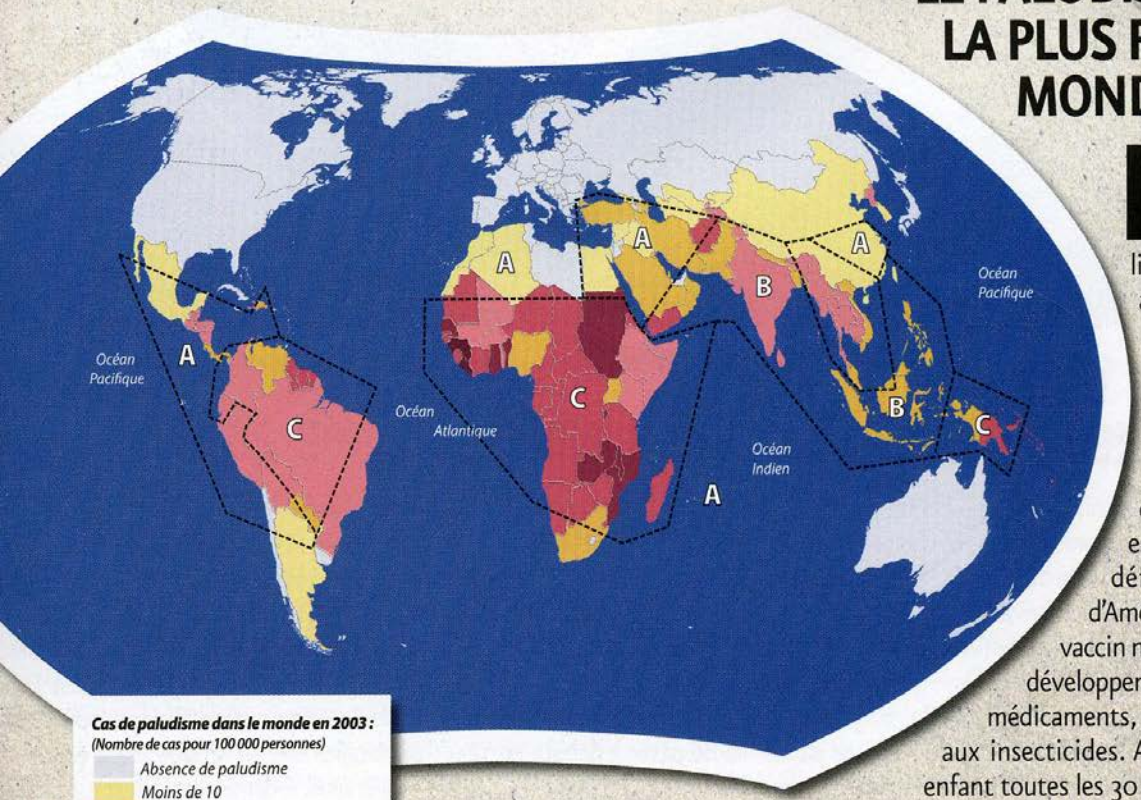
THE ILLUSTRATED

Kama Sutra

ANANGA-RANGA • PERFUMED GARDEN

PALUDISMO

LE PALUDISME, LA MALADIE LA PLUS RÉPANDUE AU MONDE



Cas de paludisme dans le monde en 2003 :
(Nombre de cas pour 100 000 personnes)

- Absence de paludisme
- Moins de 10
- 10 à 100
- 100 à 1 000
- 1 000 à 10 000
- 10 000 à 25 000
- Plus de 25 000

Risques que le paludisme résiste aux traitements (selon l'OMS) :
ZONE A : risque généralement faible et saisonnier.
ZONE B : risque faible.
ZONE C : risque élevé.

Sources : Organisation Mondiale de la Santé, Institut Pasteur.

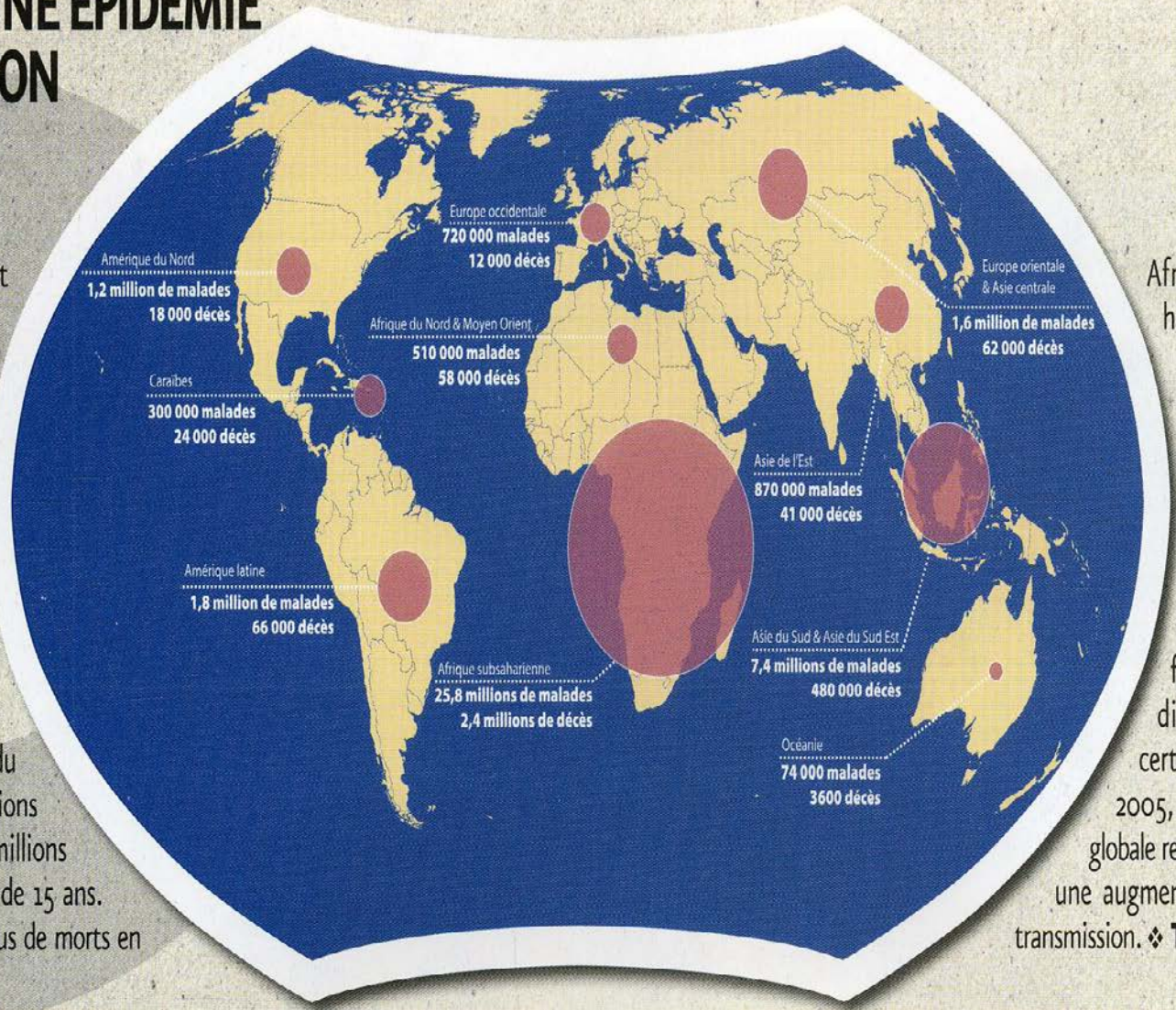
En 2004, le paludisme était la maladie la plus répandue dans le monde. Avec 500 000 millions de nouveaux malades chaque année, la maladie tue entre 1 et 3 millions de personnes par an selon les estimations de l'OMS. Avec 40 % de la population mondiale exposés à la maladie, le paludisme – qui se contracte par la piqûre d'un moustique femelle – touche essentiellement les zones tropicales défavorisées d'Afrique, d'Asie et d'Amérique latine. Il est à noter qu'aucun vaccin n'existe à ce jour, et que les parasites développent de plus en plus de résistance aux médicaments, tout comme les moustiques face aux insecticides. Aujourd'hui, le paludisme tue un enfant toutes les 30 secondes en Afrique. ❖ **T.D.**

Sida, une Crise mondiale

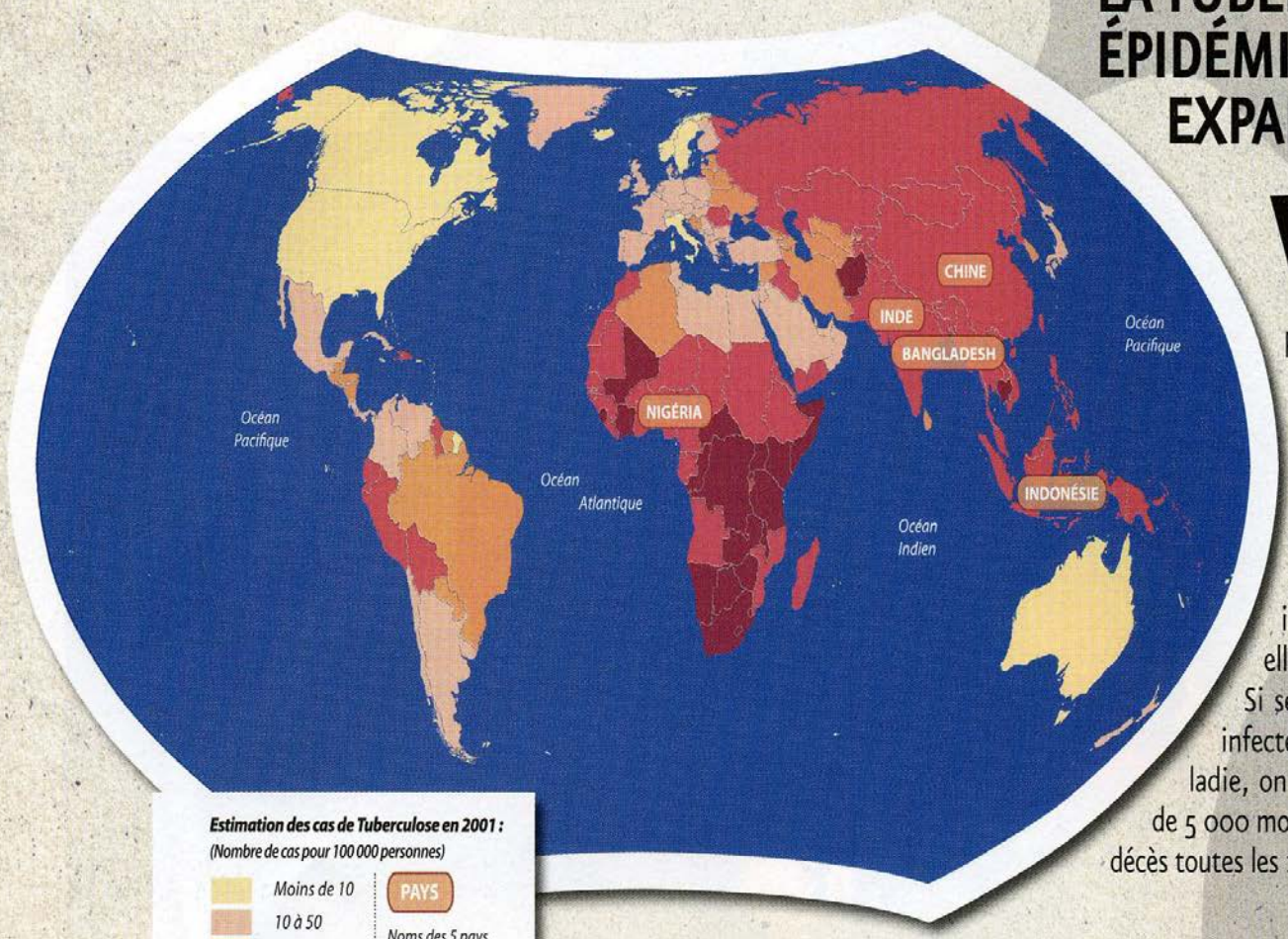
Le sida
Jusqu'à quand ?

LE SIDA, UNE ÉPIDÉMIE À DIFFUSION RAPIDE

Le SIDA est une maladie récente, décrite en 1981, mais qui était déjà présente dès 1959 chez certaines populations isolées d'Afrique. Aujourd'hui, 40,3 millions de personnes vivent avec le virus du sida, dont 17,5 millions de femmes et 2,3 millions d'enfants de moins de 15 ans. La maladie fait le plus de morts en Afrique subsaharienne avec 2,5 millions de décès en 2005 pour 25,8 millions de malades. Si les taux d'infection ont diminué dans certains pays en 2005, la tendance globale reflète toujours une augmentation de la transmission. ❖ **T.D.**



TUBERCULOSE

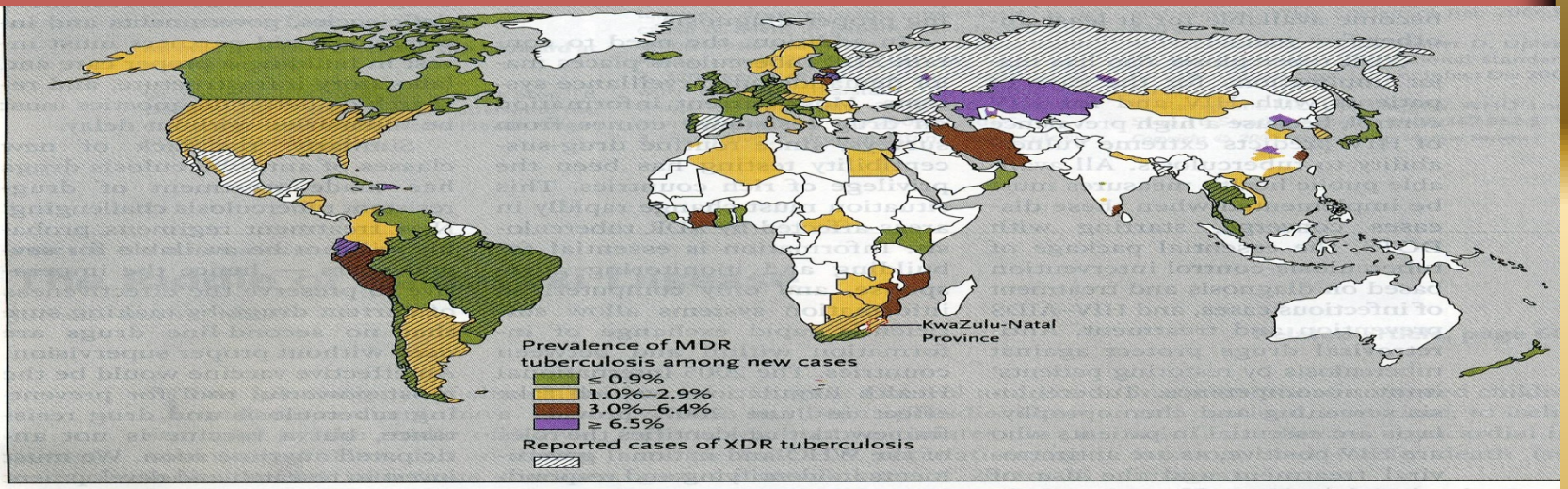


LA TUBERCULOSE, UNE ÉPIDÉMIE EN PLEINE EXPANSION

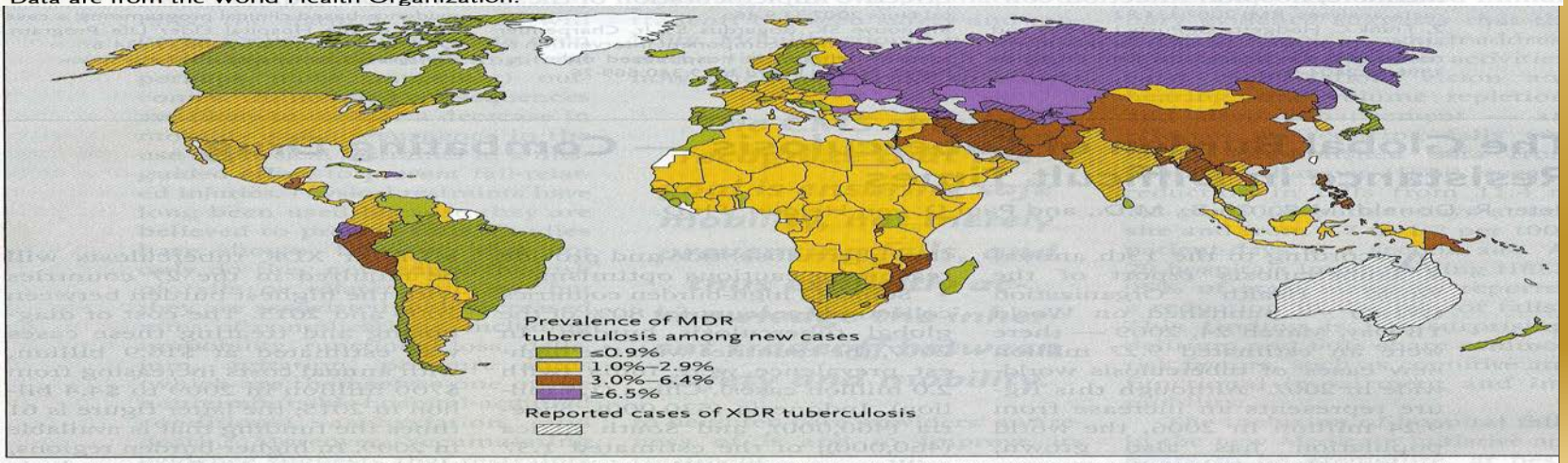
Vieille de 3 millions d'a
nées, la tuberculose t
aujourd'hui 2 millions
personnes chaque année. Elle
considérée par l'OMS comme r
ponsable d'une épidémie mondi
de plus en plus dangereuse. U
estimation prévoit qu'entre 20
et 2020, c'est près d'un milliard
personnes qui seront nouvelleme
infectées et que 35 millions d'en
elles en mourront, si rien n'est fa
Si seulement 5 à 10 % des personn
infectées contractent réellement la r
ladie, on compte, en 2006, une moyer
de 5 000 morts par jour dans le monde, soit
décès toutes les 15 secondes. ❖ **T.D.**

XDR Tuberculosis — Implications for Global Public Health

Mario C. Raviglione, M.D., and Ian M. Smith, M.B., Ch.B.



Prevalence of MDR Tuberculosis among New Cases of Tuberculosis, 1994–2002, and Countries with at Least One Reported Case of XDR Tuberculosis as of January 2007.
Data are from the World Health Organization.



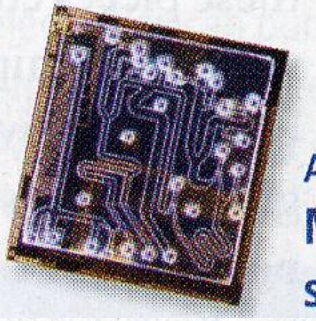
Prevalence of MDR Tuberculosis among New Cases of Tuberculosis, 2007, and Countries with at Least One Reported Case of XDR Tuberculosis as of December 2008.
Data are from the World Health Organization.

O FUTURO

Big Lab on a Tiny Chip

Squeezing a chemistry lab down to fingernail size could provide instant medical tests at home and on the battlefield

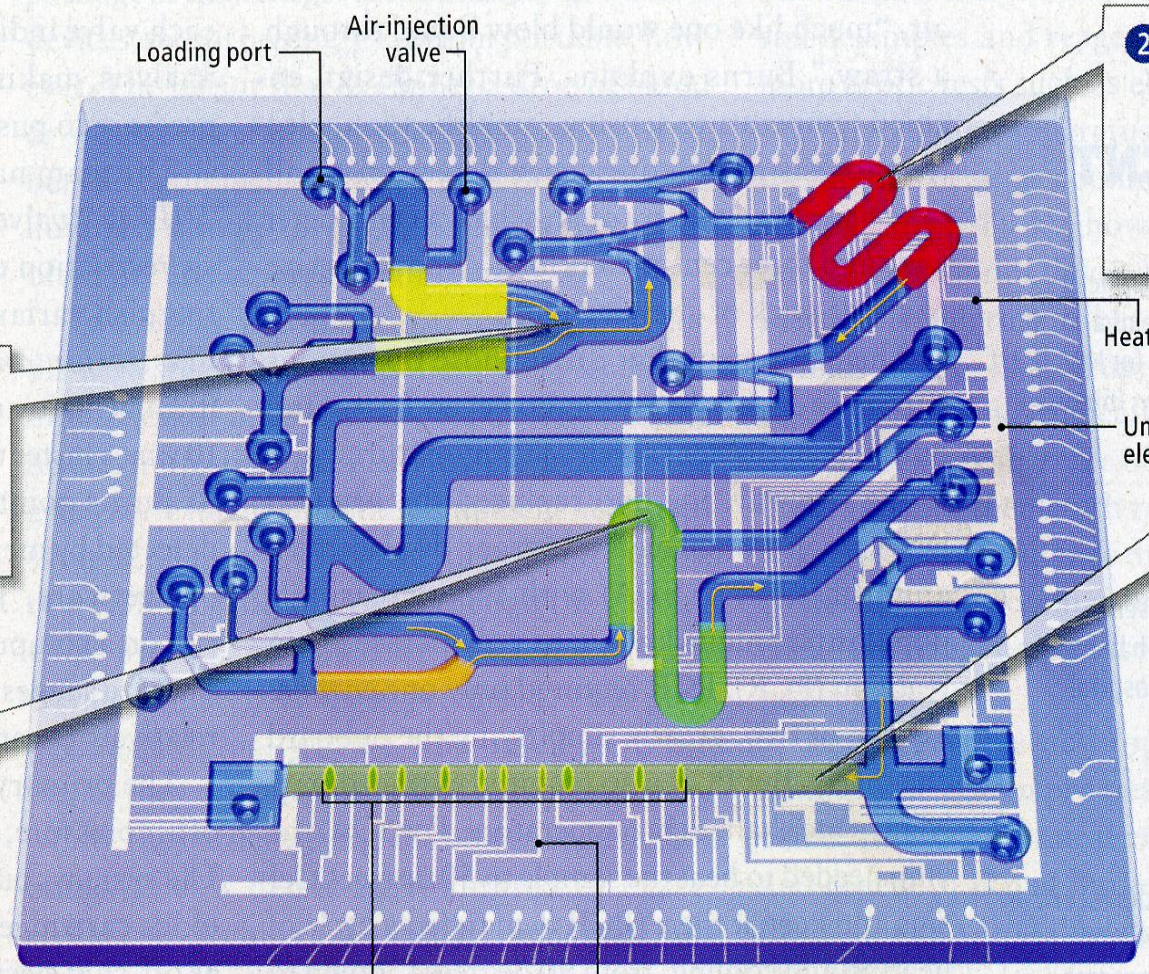
By Charles Q. Choi



ACTUAL SIZE: The University of Michigan's influenza chip measures 1.5 by 1.6 centimeters.

Influenza Detector

A prototype from the University of Michigan moves droplets through a microfluidic maze. Tests on a blood sample could show influenza or other pathogens within 15 minutes.



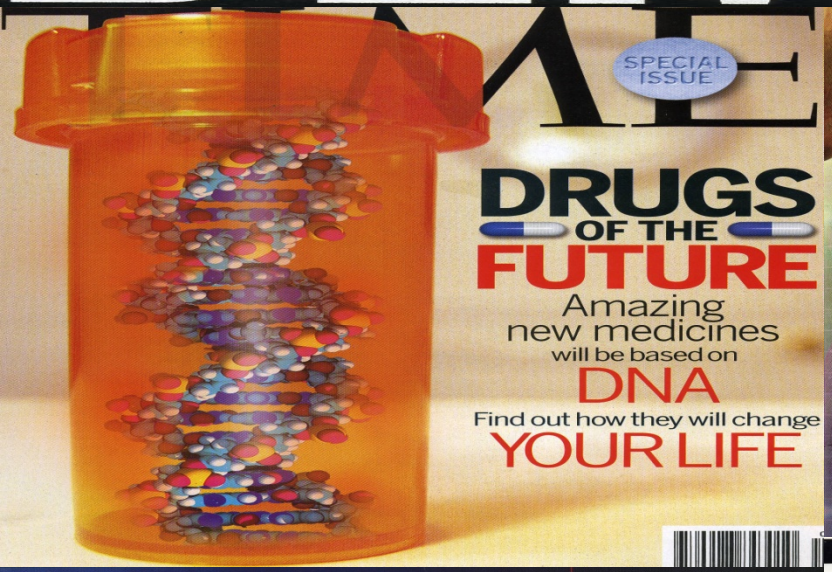
1 LOAD
Blood sample (*yellow*) and amplification reagent (*green*) are loaded, then pushed along by air pressure.

2 AMPLIFY
Any DNA in the sample is amplified in a PCR chamber (*red*), which heats and cools 35 times.

3 REACT
Amplified DNA mixes with a reagent (*gold*) that reacts to influenza inside a reaction chamber (*green*).

4 ANALYZE
An electrophoresis channel read with ultraviolet light indicates a telltale signature if pathogens are present.

LA GALÉNIQUE DE DEMAIN

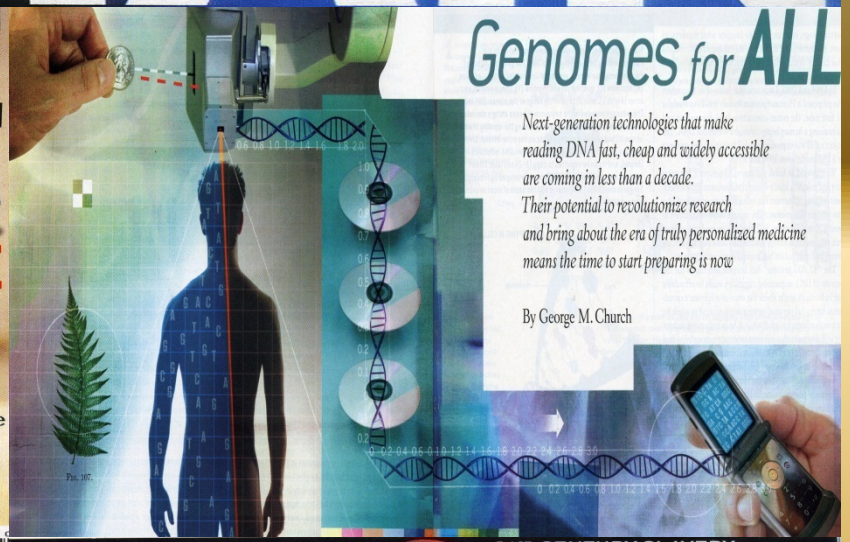


SPECIAL ISSUE

DRUGS OF THE FUTURE

Amazing new medicines will be based on DNA

Find out how they will change YOUR LIFE



Genomes for ALL

Next-generation technologies that make reading DNA fast, cheap and widely accessible are coming in less than a decade. Their potential to revolutionize research and bring about the era of truly personalized medicine means the time to start preparing is now

By George M. Church

SEEING GRAVITY WAVES

21ST-CENTURY SLAVERY

SCIENTIFIC AMERICAN

How Cassini Will Explore Saturn

JUNE 2004
WWW.SCIAM.COM

SCIENTIFIC AMERICAN

APRIL 2002
WWW.SCIAM.COM

NANOTECH and DNA

Construction with the Double Helix

Turning Stem Cells into Therapies

Nuclear Attacks in Orbit

Q&A with Bill Gates

Proteomics

Biotech's Next Big Challenge

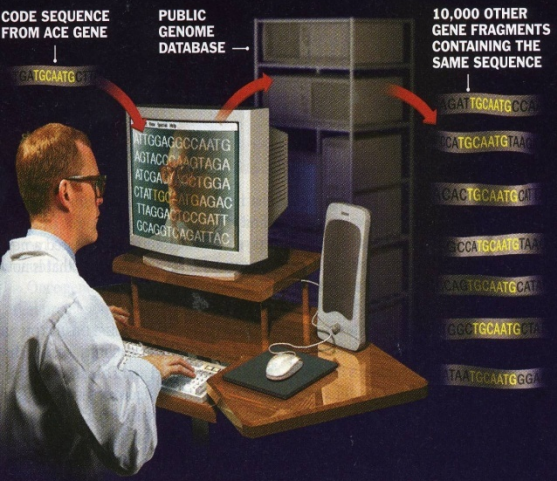
PLUS:
Virtual Captions for the Real World
Fighting Bad Breath

Drug Design in the Fast Lane

Pharmaceutical companies used to spend $500 million and 15 years to create a new drug. With genome-based technologies, however, it may be possible to develop more effective medications in less time and for half the price. Here's how Millennium Pharmaceuticals plans to do it:

1 MINING THE DATABASE

Millennium is trying to make a better blood-pressure drug by improving today's popular ACE inhibitors. These drugs reduce blood pressure by blocking an enzyme that converts angiotensin to an active form that constricts blood vessels. The first step for Millennium's researchers is searching the huge **public genome database** for snippets of DNA that resemble the known ACE enzyme. From this search they get **10,000 computer matches**, each of them gene fragments representing potential ACE inhibitors.

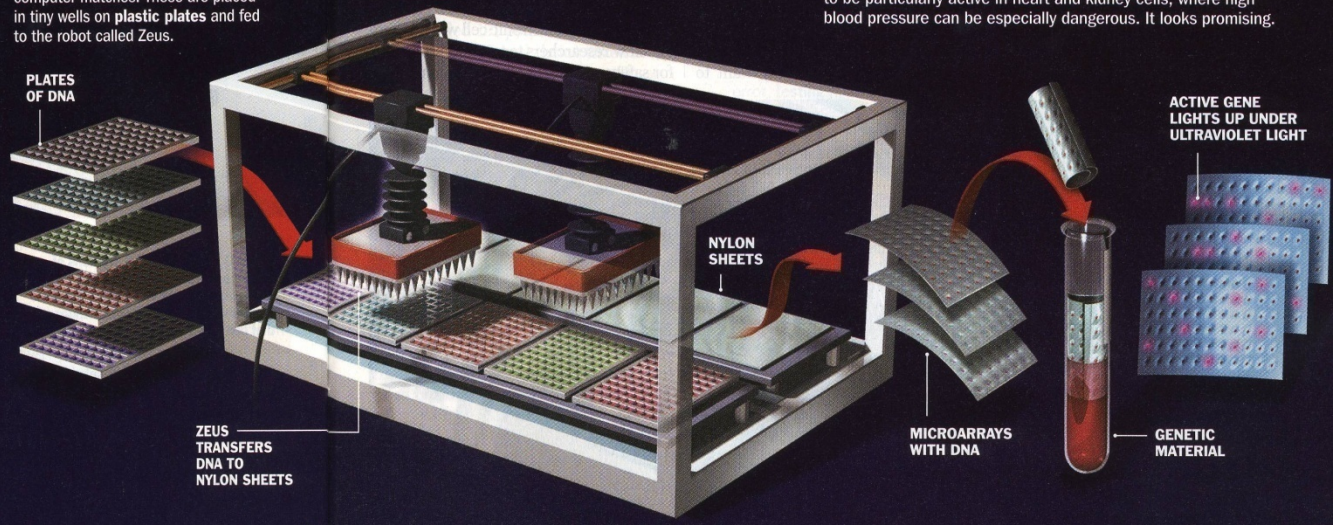


2 NARROWING CHOICES

The researchers then turn to their library of several million frozen DNA fragments and pull out 10,000 snippets corresponding to those computer matches. These are placed in tiny wells on **plastic plates** and fed to the robot called Zeus.

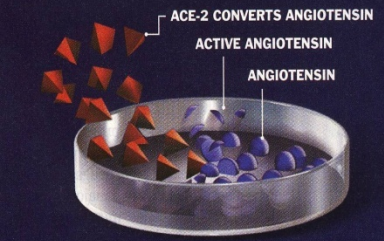
Waving its mechanical arms, **Zeus** dips tiny needles into the wells, picks up microscopic droplets of DNA and spots them onto a sheet of **nylon paper**, creating a so-called **microarray**. These sheets are rolled up and slipped into **test tubes**.

The test tubes are then washed with **genetic material** from a wide range of tissue cells that have been labeled with a radioactive dye. When a **gene is active** in a particular cell type, the **spot lights up under UV**. By comparing patterns of brightness, the researchers isolate one gene, which they call ACE-2, that appears to be particularly active in heart and kidney cells, where high blood pressure can be especially dangerous. It looks promising.



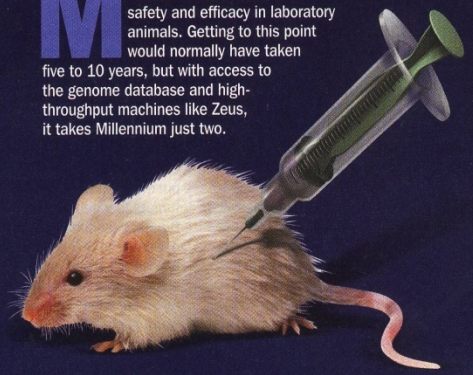
3 ISOLATING THE DRUGS

After confirming that **ACE-2** does indeed convert **angiotensin**, the researchers start looking for a chemical that will inhibit ACE-2. They have a head start in this because they know what ACE inhibitors look like. In their library of molecules they find one that works against ACE-2. This is their drug candidate.



4 TESTING IN ANIMALS

Millennium scientists then test that ACE-2 inhibitor molecule for safety and efficacy in laboratory animals. Getting to this point would normally have taken five to 10 years, but with access to the genome database and high-throughput machines like Zeus, it takes Millennium just two.



5 TESTING IN HUMANS

If the ACE-2 inhibitor is safe and effective in animals, studies in people will begin next. Millennium also plans to save time and money at this stage in the process by screening human subjects for genetic compatibility with the drugs. This makes it easier for the researchers to measure success.

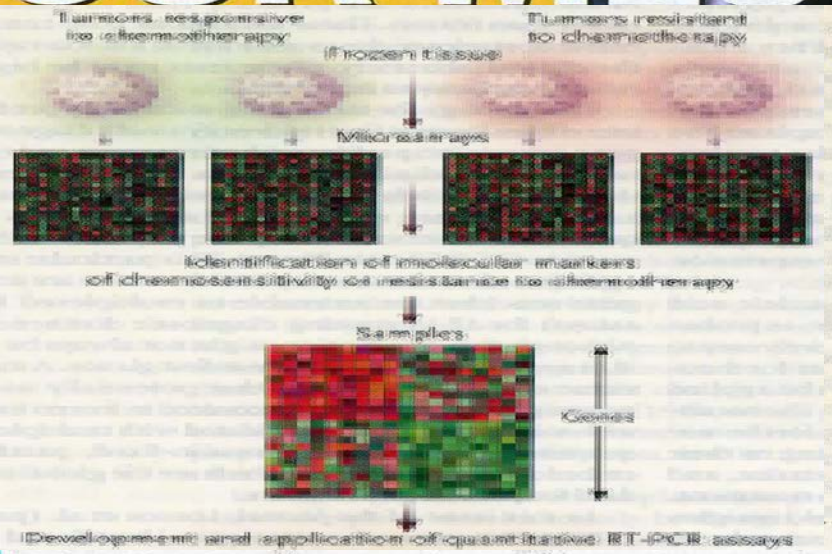
6 FDA APPROVAL

Once the human trials are complete and an ACE-2 inhibitor is shown to be both safe and effective, it will be ready for review by the FDA and commercial production and distribution following regulatory approval. If all goes according to Millennium's plans, a new drug could be available within five years.

TIME Graphic by Ed Gabel, Joe Lertola and Lon Tweeten

Source: Millennium Pharmaceuticals

DES MÉDICAMENTS SUR MESURE



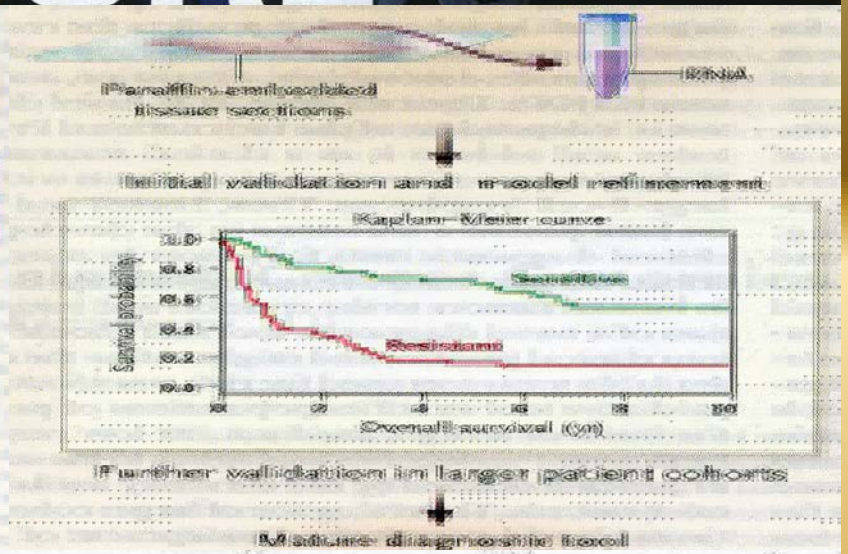


Table 1. Human cancers caused by viruses and their potential targets for RNA interference

Virus	Cancer	Viral target
Epstein–Barr virus	Burkitt's lymphoma	EBNA-1
	Hodgkin's disease	EBNA-2
	Post-transplant lymphoproliferative disorder	LMP1
	AIDS-related central nervous system lymphoma	
Human papillomavirus	Anogenital cancers	E6 E7
Human T cell leukaemia virus-1	Adult T-cell leukaemia	Tax
Kaposi's sarcoma-associated herpes-virus	Kaposi's sarcoma	LANA
	Multicentric Castleman's disease	vcyclin
	Primary effusion lymphoma	VFLIP
		vIL-6/ORF50
Hepatitis B or C viruses	Hepatocellular carcinoma	Hepatitis B surface or core antigen
		HBx potential oncogene
		Hepatitis C virus viral proteases

AIDS	Acquired Immune Deficiency Syndrome
EBNA-1/ EBNA-2	Epstein–Barr virus Nuclear Antigen 1/2
LMP1	Latent Membrane Protein 1
LANA	Latency Associated Nuclear Antigen
ORF50	Open Reading Frame 50
Tax HTLV-1	Transactivator
vFLIP	viral FLICE inhibitory protein
vIL-6	viral interleukin 6

PHARMACIENS SANS FRONTIERES

LES JIVAROS

Apothicaires en Amazonie

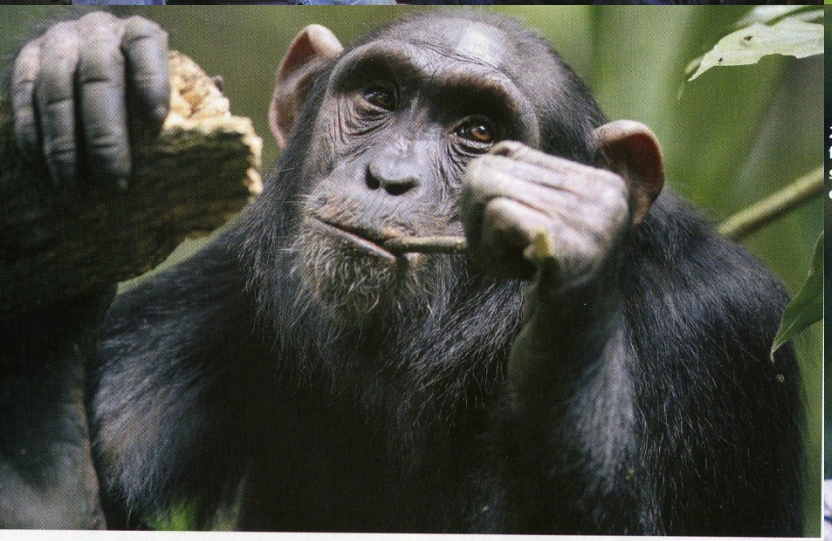
Malgré une insertion de plus en plus grande dans l'économie marchande, les Jivaros n'ont jusqu'à récemment disposé d'aucun service de santé, même modeste. Par Emmanuel Thévenon

La pharmacopée des chimpanzés

Sabrina KRIEF

L'observation des grands singes indique l'existence de comportements d'automédication. Les plantes que ces animaux sélectionnent pour « se soigner » deviendront-elles nos médicaments de demain ?

1. Les chimpanzés consomment des plantes ayant des propriétés antimicrobiennes, comme ces fruits de *Phyolacca dodecandra*. Il pourrait les associer à d'autres substances pour éviter de pâtir de leur toxicité.



3. Kilimi, une femelle chimpanzé, souffrait de parasitisme intestinal. Elle a mangé de l'écorce d'un arbre *Albizia grandibracteata*, alors que ses congénères n'en consommaient pas : deux jours après, les selles ne contenaient plus de parasites.

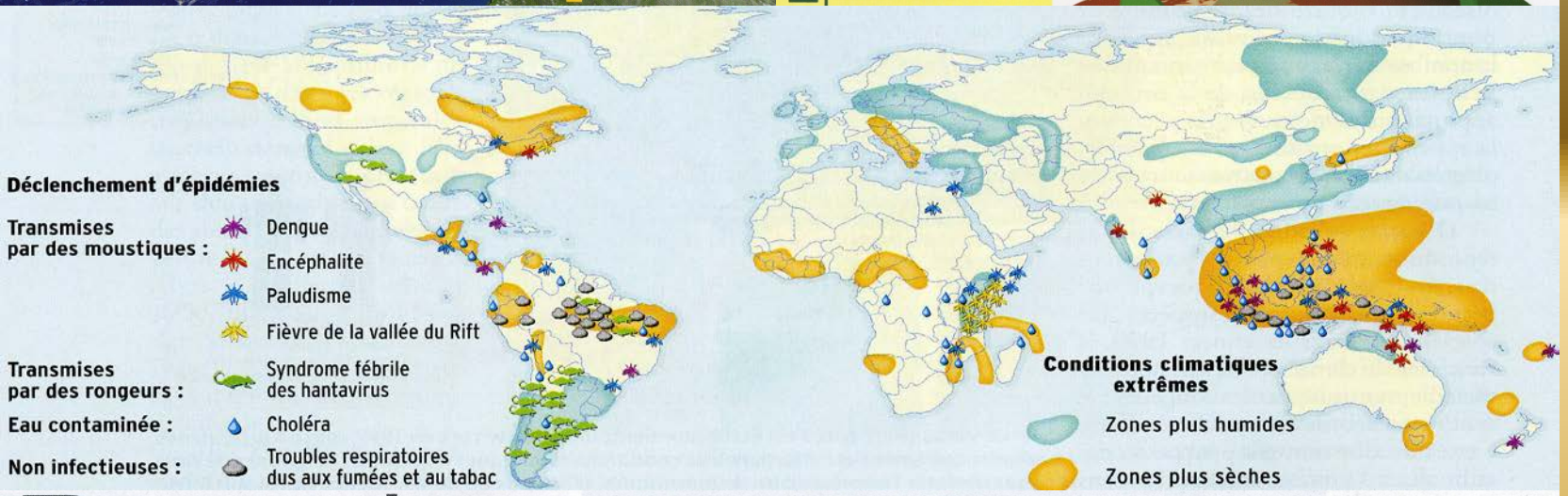
2. Ce chimpanzé consomme des feuilles de *Trichilia rubescens*, qui se sont révélées comporter des composés antipaludiques.

Le risque climatique

pourlascience.com
DOSSIER
POUR LA SCIENCE
Édition française de Scientific American

LES FAITS
- LES CANICULES
- LES MALADIES
- LES CYCLONES

CLIMAT
Comment éviter la surchauffe ?



Parasites en tout genre

Paludisme, dengue, fièvre jaune, peste : les trois dernières décennies ont vu une recrudescence mondiale de plusieurs maladies infectieuses. Certaines ont gagné des aires géographiques nouvelles, comme la fièvre du Nil, responsable depuis 1999 de centaines de morts aux États-Unis. La faute au réchauffement de la planète ? La question a donné lieu à des annonces parfois catastrophistes, souvent contradictoires. Pourquoi ces divergences de vue ?

AU BURUNDI, campagne de lutte contre les moustiques du genre anophèle, vecteurs du paludisme. ©Ian Berry/Magum Photos

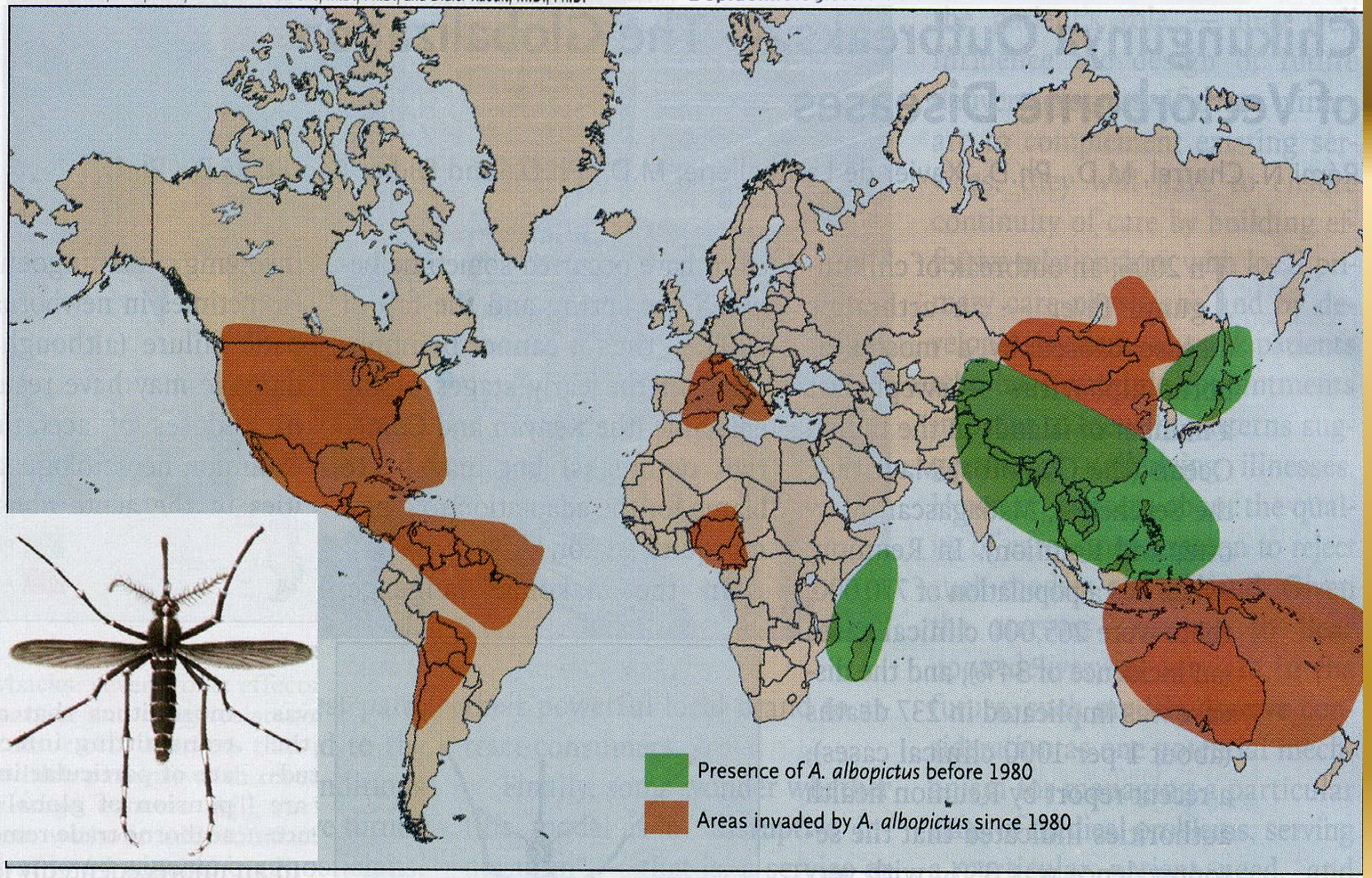
Chikungunya Outbreaks — The Globalization of Vectorborne Diseases

Rémi N. Charrel, M.D., Ph.D., Xavier de Lamballerie, M.D., Ph.D., and Didier Raoult, M.D., Ph.D.

Alerte au virus
comment agir ?

Dounia BITAR et Didier CHE

L'apparition d'un nouveau virus dans une population impose des mesures sanitaires adaptées et rapides. L'épidémiologiste aide à définir les bonnes réactions.



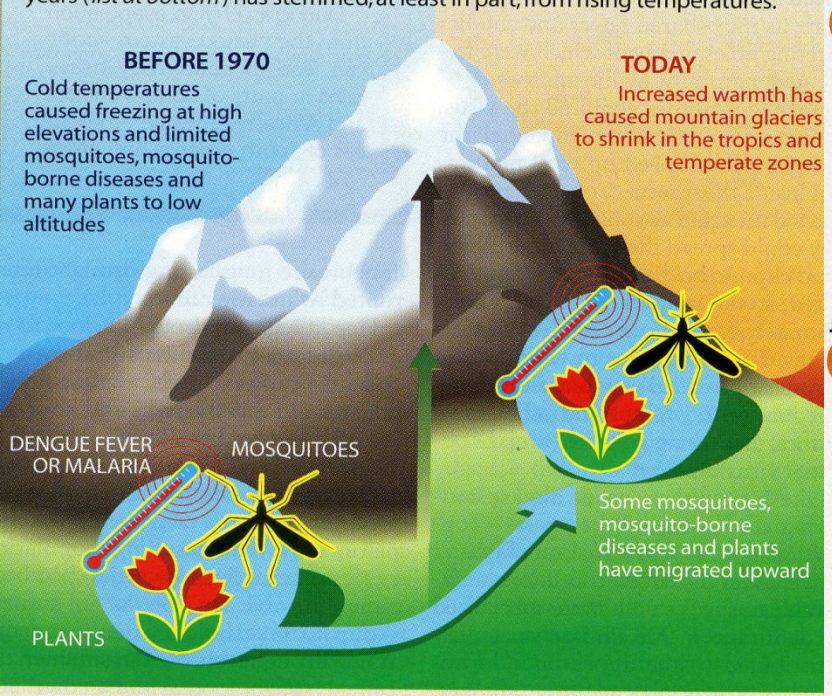
World Distribution of the *Aedes albopictus* Mosquito.

MALARIA...WEST NILE VIRUS...HANTAVIRUS...DENGUE...CHOLERA...

Global Warming: The Hidden Health Risk

Changes Are Already Under Way

Computer models have predicted that global warming would produce several changes in the highlands: summit glaciers (like North Polar sea ice) would begin to melt, and plants, mosquitoes and mosquito-borne diseases would migrate upward into regions formerly too cold for them (*diagram*). All these predictions are coming true. This convergence strongly suggests that the upward expansion of mosquitoes and mosquito-borne diseases documented in the past 15 years (*list at bottom*) has stemmed, at least in part, from rising temperatures.



WHERE DISEASES OR THEIR CARRIERS HAVE REACHED HIGHER ELEVATIONS

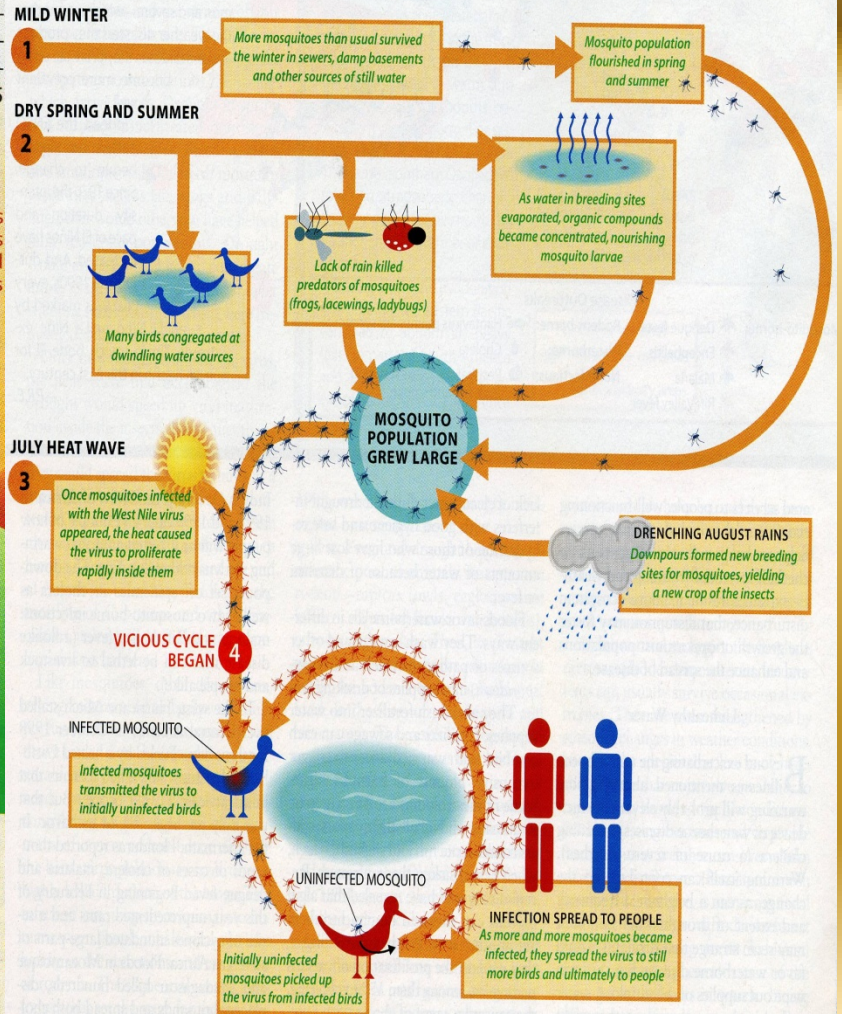
Malaria
Highlands of Ethiopia, Rwanda, Uganda and Zimbabwe
Usamabara Mountains, Tanzania
Highlands of Papua New Guinea and West Papua (Irian Jaya)

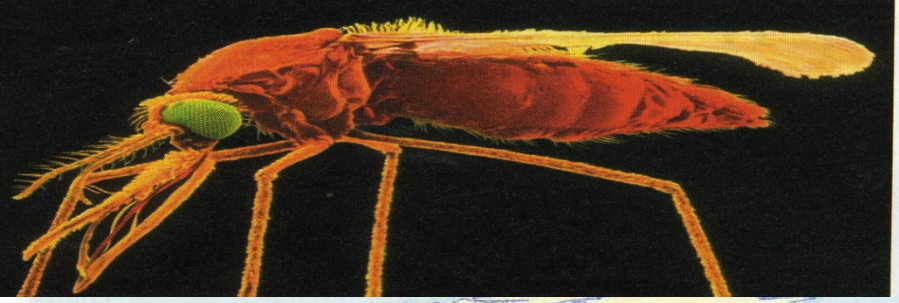
Dengue fever
San Jose, Costa Rica
Taxco, Mexico

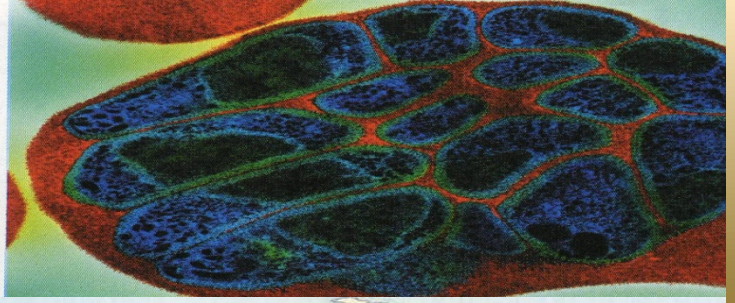
***Aedes aegypti* mosquitoes**
(can spread dengue fever and yellow fever)
Eastern Andes Mountains, Colombia
Northern highlands of India

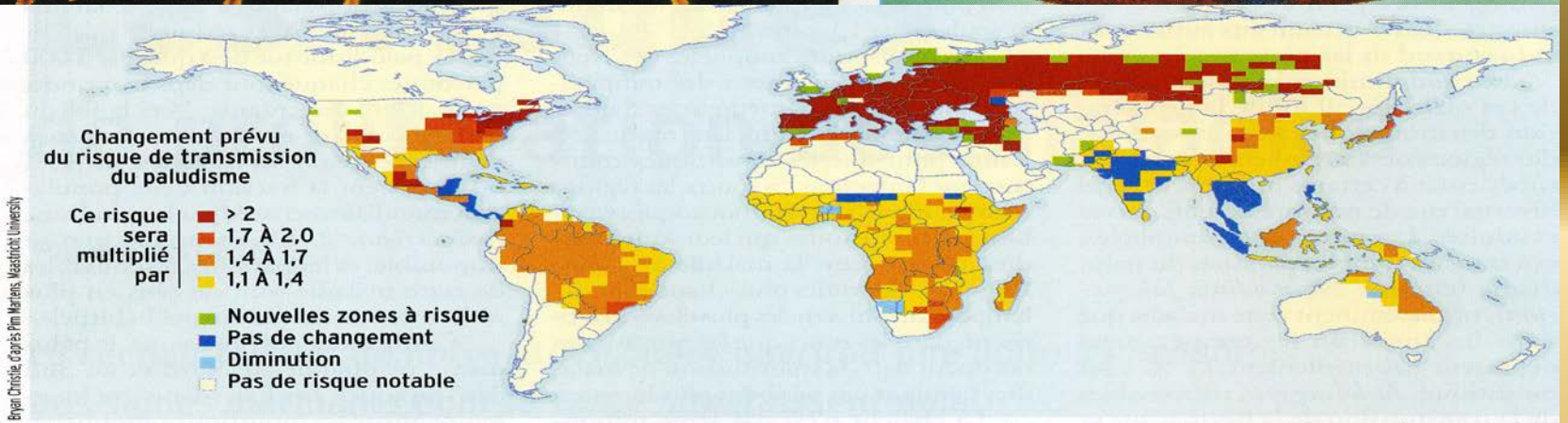
Weather and the West Nile Virus

This diagram offers a possible explanation for how a warming trend and sequential weather extremes helped the West Nile virus to establish itself in the New York City area in 1999. Whether the virus entered the U.S. via mosquitoes, birds or people is unknown. But once it arrived, interactions between mosquitoes and birds amplified its proliferation.





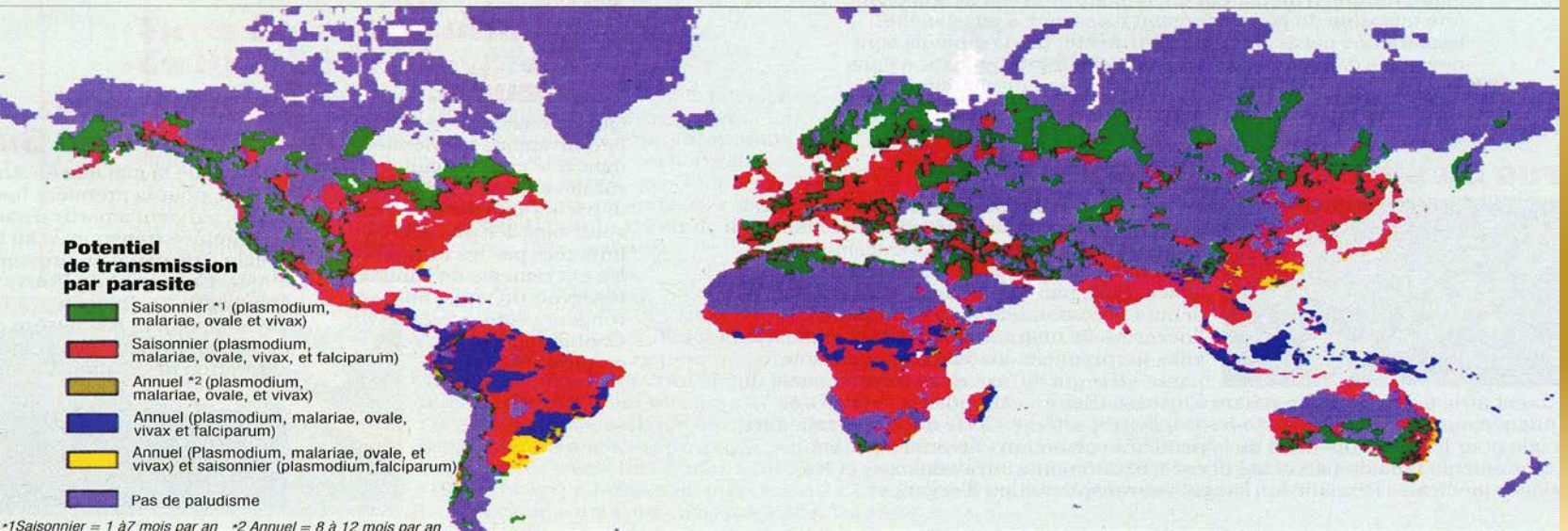




Bryan Christie, d'après Pim Martens, Maastricht University

2. LE RISQUE DE TRANSMISSION DU PALUDISME aux alentours de 2020 aura augmenté dans de nombreuses parties du monde (en comparaison avec le risque moyen dans les années 1961 à 1990), selon des projections fondées sur un accroissement de la température de 1 °C. L'analyse ne tient compte que de la variation de température et pas des autres facteurs qui agiraient sur l'extension du paludisme.

Potentiel de transmission du paludisme en 2025-2045



*1Saisonnier = 1 à 7 mois par an *2 Annuel = 8 à 12 mois par an

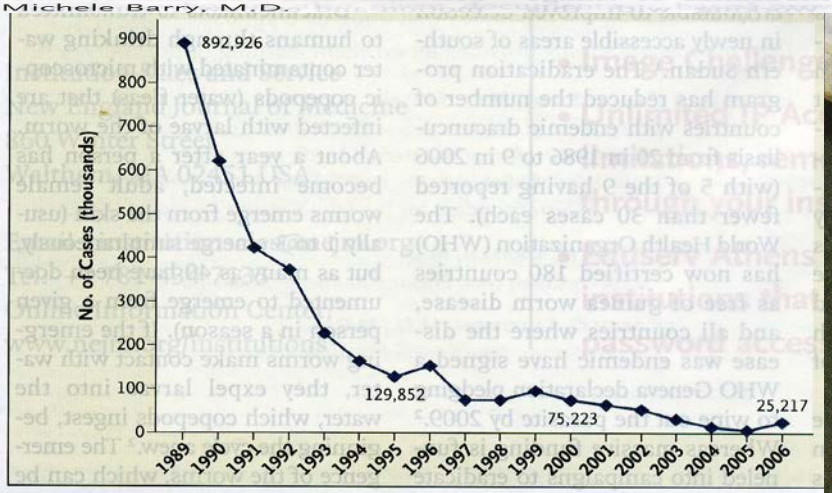
The NEW ENGLAND JOURNAL of MEDICINE

Perspective

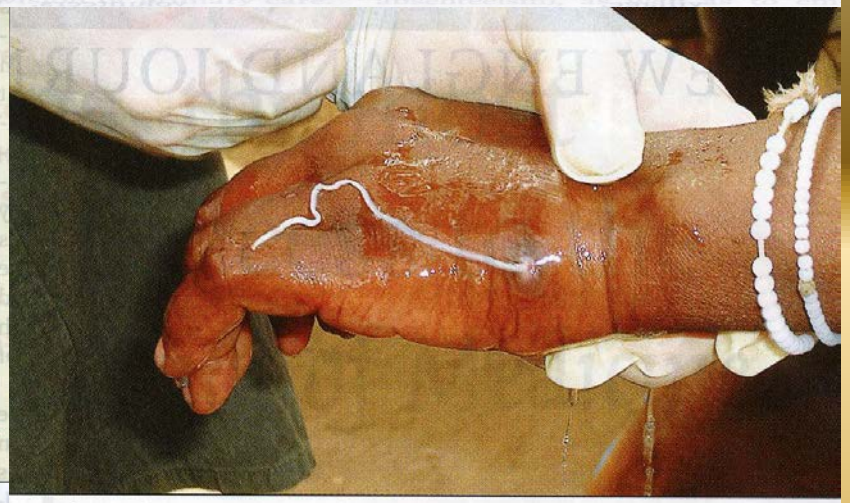
JUNE 21, 2007

The Tail End of Guinea Worm — Global Eradication without a Drug or a Vaccine

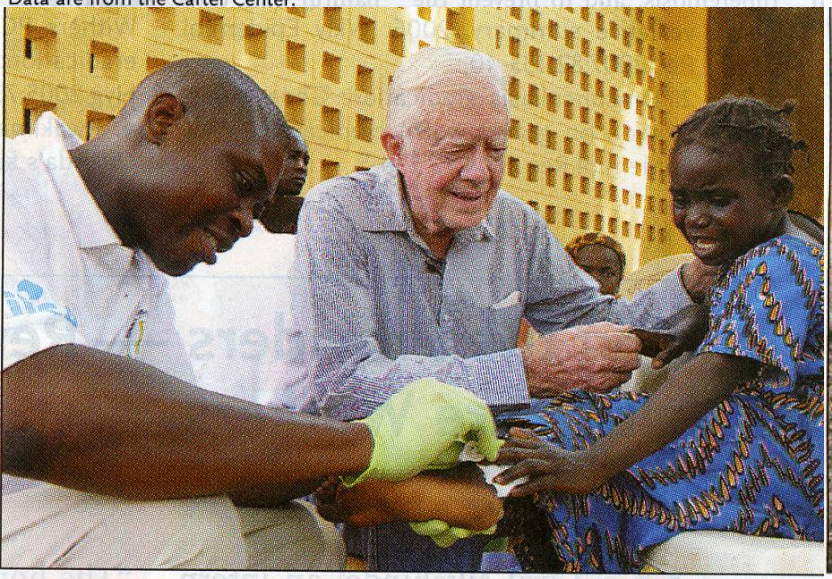
Michele Barry, M.D.



Number of Reported Cases of Dracunculiasis Worldwide, 1989–2006.
Data are from the Carter Center.



Emerging Guinea Worm.



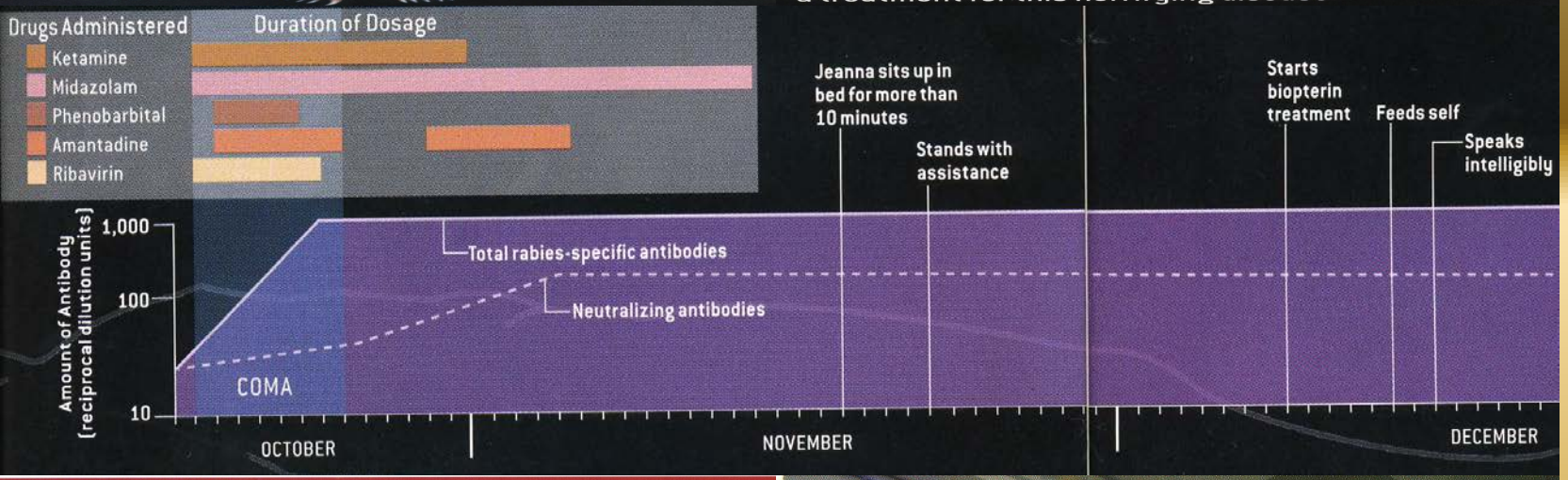
Jimmy Carter in Ghana.

Manual Extraction of Guinea Worm.

A CURE for RABIES?

By Rodney E. Willoughby, Jr.

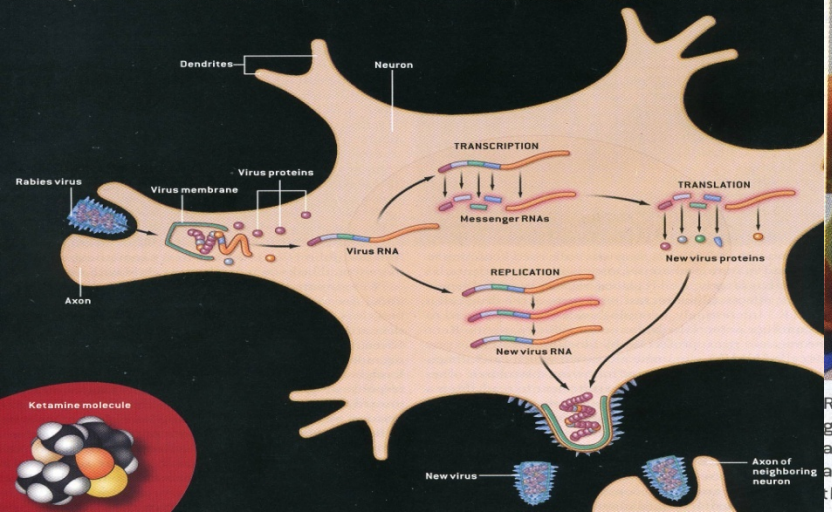
The survival of a Wisconsin teenager who contracted rabies may point the way to a treatment for this horrifying disease

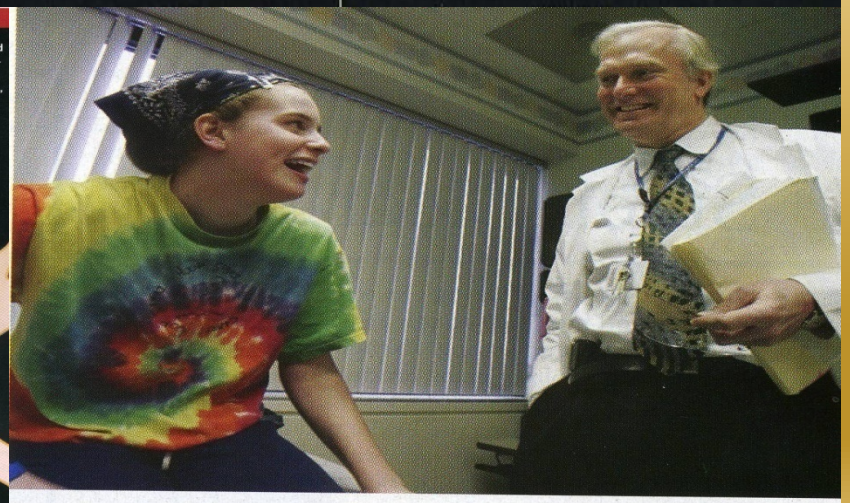


CURBING A DEADLY VIRUS

After the rabies virus penetrates the axon of a neuron, the microbe sheds its membrane and releases its proteins and RNA, which travel to the cell body. The viral RNA generates messenger RNAs (transcription), which in turn use the cell's machinery to produce the virus's five proteins (translation).

Then the viral RNA creates copies of itself, which are assembled with the proteins into new microbes that emerge from the neuron's dendrites to attack the next nerve cell. Studies indicate that ketamine (*inset*), a compound long used as an anesthetic, inhibits the transcription stage of the virus's life cycle.





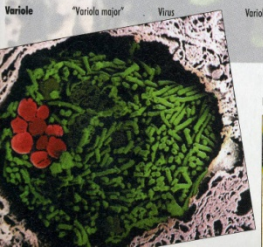
REMARKABLE RECOVERY: Jeanna Giese (*shown with the author*) is graduating from high school this year and hopes to become a veterinarian. The only lingering reminders of her battle with rabies are a small area of numbness on the bitten finger, an alteration in the tone of her left arm and a wider gait when she runs.

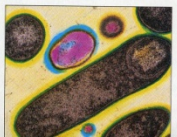
Le dossier du bioterrorisme

BIOTERRORISME

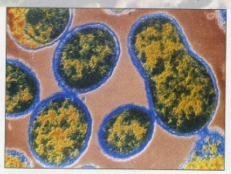
QUATORZE AGENTS DE BIOTERRORISME OU DE GUERRE BIOLOGIQUE

NOM D'USAGE COURANT	NOM SCIENTIFIQUE DE L'AGENT	NATURE DE L'AGENT	NOM DE LA MALADIE	MODE D'INFECTION	CONTAGIOSITÉ	MORTALITÉ	SYMPTÔMES
Anthrax, charbon	"Bacillus anthracis"	Bactérie (libère une toxine) Souches plus ou moins virulentes	Charbon pulmonaire (maladie des trieurs de laine ; le charbon cutané est le plus souvent bénin)	Par inhalation des spores	Nulle	Très élevée	Temps d'incubation généralement court (deux à quatre jours). Premiers symptômes comparables à ceux d'une forte grippe, avec vomissements. Puis oppression respiratoire, grosseurs sombres sur la poitrine et le cou
Botulisme	"Clostridium botulinum"	Toxine de la bactérie	Botulisme	Par ingestion (ou inhalation de la toxine cristallisée)	Non	Forte quelques nanogrammes de toxine suffisent	Vision brouillée, difficulté à avaler, faiblesse puis paralysie musculaire
Brucellose	"Brucella suis"	Bactérie	Brucellose	Par ingestion ou infection par plaie cutanée	Non	Très faible (agent incapacitant)	N'apparaissent qu'après une longue période d'incubation. Fièvre, toux sèche, douleurs abdominales. Peuvent devenir chroniques
Choléra	"Vibrio cholerae"	Bactérie (libère une toxine)	Choléra (infection de l'intestin grêle)	Par ingestion d'eau ou de nourriture contaminée	Oui	Moyenne	Après incubation de 12 à 28 heures, diarrhée fulgurante, vomissements, déshydratation générale
Ebola	Virus d'Ebola	Virus (filovirus)	Fièvre hémorragique d'Ebola	Par contact direct avec animal ou humain contaminé ou par inhalation	Très grande	Entre 70 % et 90 %. Dépend de la souche	Une semaine d'incubation, symptômes grippaux puis hémorragies
Encéphalite du Vénézuéla	Virus EEV	Virus à ARN	Encéphalomyélite équine du Vénézuela	Dans la nature, par piqûre de moustique		Agent incapacitant. Risque d'effets permanents sur le système nerveux central et périphérique. Mortalité faible	Malaise grave, forte fièvre, nausées, céphalées, diarrhées
Fièvre Q	"Coxiella burnetii"	Rickettsie	Fièvre Q	Par inhalation. Une seule bactérie peut créer la maladie.	Forte	Agent incapacitant. Mortalité très faible en cas de traitement	D'abord comparables à une grippe, puis deux semaines d'hallucinations, douleurs de la face et de la tête, forte fièvre
Marbourg	Virus de Marbourg (Marburg)	Filavirus	Fièvre hémorragique de Marbourg	Par contact direct avec animal ou humain contaminé	Très élevée	Très élevée	D'abord des ecchymoses, puis hémorragie générale
Morve	"Burkholderia mallei"	Bactérie	Morve	Par contact direct avec animaux malades (chiens, chats...)	Modérée	De modérée à élevée	Fièvres, douleurs musculaires, Risque de pneumonie
Peste	"Yersinia pestis"	Bactérie	Peste pulmonaire (la peste bubonique n'est plus considérée comme une arme)	Habituellement transmise du rat à l'homme par piqûre de puce. L'URSS a développé un aérosol	Très élevée (par inhalation)	Très élevée	Premiers symptômes comparables à une grippe puis toux expectorante (sang), pneumonie
Salmonelle	"Salmonella enterica typhimurium"	Entérobactérie	Salmonellose (la typhoïde est provoquée par une autre salmonelle)	Par ingestion	Non	Agent incapacitant. Mortalité rare	Diarrhée et nausée soudaines, prostration, fièvre
Staphylocoque doré	Entérotoxine staphylococcique B	Toxine de la bactérie	Septicémie	Par ingestion ou par inhalation	Non	Agent incapacitant. Mortalité faible	D'abord comparables à une grippe, puis très forte fièvre, douleurs musculaires, céphalées, toux
Tularémie	Francisella tularensis	Bactérie	Tularémie	Par inhalation, ingestion, égratignure, ou via moustiques et animaux. Une centaine de germes par individu suffisent	Rare	Agent incapacitant. Mortalité 30 % en l'absence de soins	Frissons, nausées, migraine, fièvre pendant deux à quatre semaines
Variole	"Variola major"	Virus	Variole	Moins de cinq particules suffisent pour infecter des animaux. Par contact ou inhalation	De modérée à élevée (par inhalation ; il peut suffire d'une quinte de toux)	De modérée à élevée (plus élevée chez ceux qui sont trop jeunes pour avoir été vaccinés ; vaccination arrêtée en 1979)	Incubation de deux semaines, puis éruption de lésions rouges qui se transforment en pustules



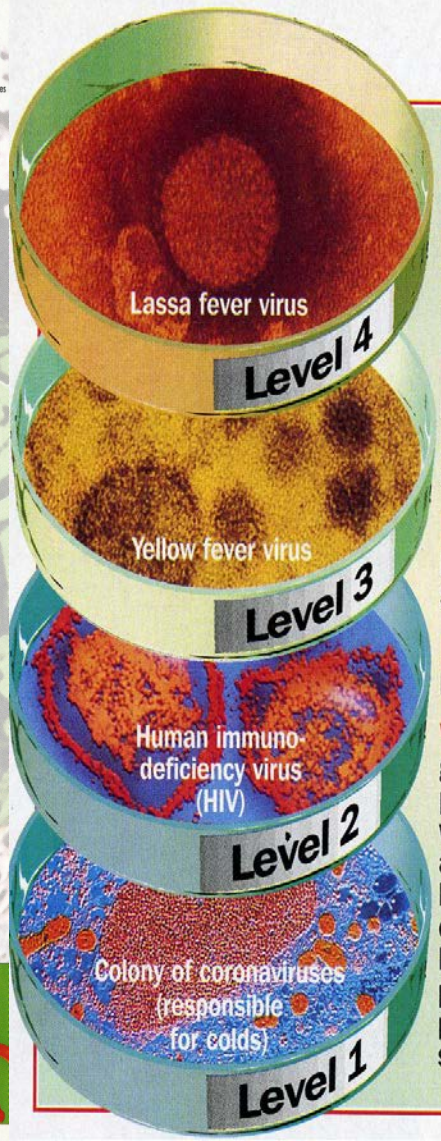


Botulisme



Brucellose

Choléra



The virus hierarchy

LEVEL 4: eg: Lassa fever, Marburg, Ebola Zaire viruses
No known cure. Highly infectious. Fast acting. High mortality rates.

LEVEL 3: eg: Yellow fever, dengue haemorrhagic fever virus
Easily contracted. Potentially fatal, and serious when not fatal.

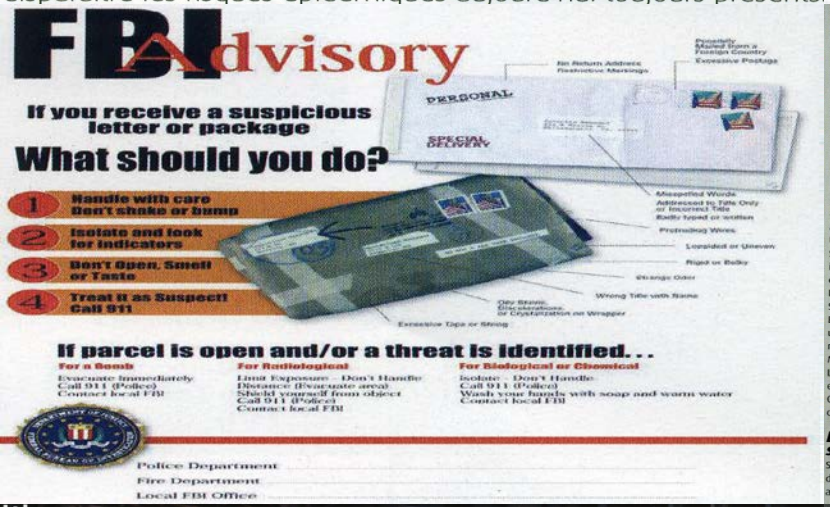
LEVEL 2: eg: HIV (Aids)
Difficult to contract. Easily destroyed. Serious, possibly fatal.

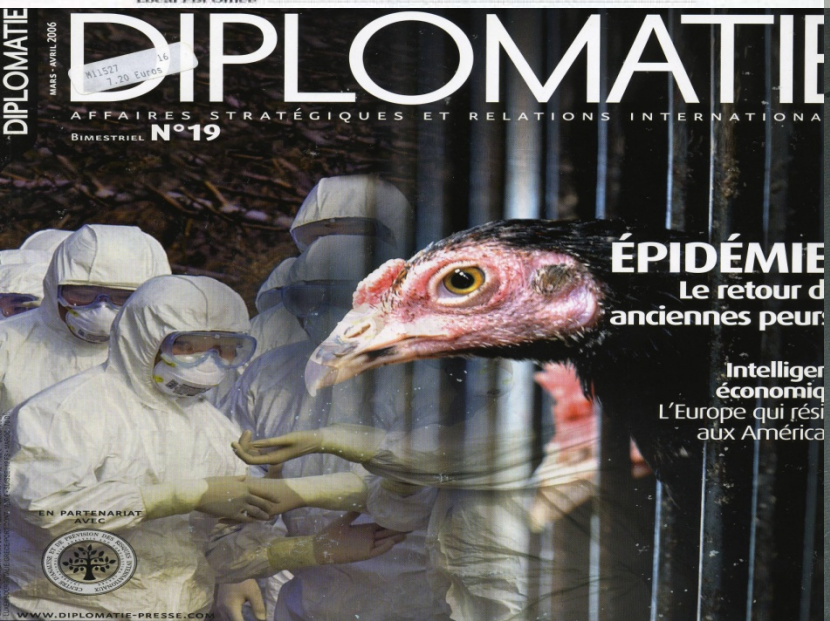
LEVEL 1: eg: cold viruses
Relatively innocuous – not fatal.

VIRUSES are infectious packages of genetic material (DNA or RNA) in a protein coat. There is debate about whether they should be considered alive: their only activity is to take over living cells of other organisms, without which they cannot survive. Despite these limitations, viruses plague us: flu, colds, glandular fever, polio, some eye infections, possibly some cancers – all are viruses.

Les risques épidémiques intentionnels

L'avènement de la microbiologie pasteurienne, suivi des grandes découvertes sur les vaccins et les antibiotiques, n'a pas fait disparaître les risques épidémiques aujourd'hui toujours présents.





Gestion du risque épidémique et technologies de l'information

La Surveillance Spatiale des Épidémies (S2E)

Le Consortium Surveillance Spatiale des Épidémies fut créé en 1999 et associe le Centre National d'Études Spatiales (CNES, et ses filiales Médias-France, CLS et MEDES) ; l'Institut Pasteur, l'Institut National de Recherche Agronomique et l'École vétérinaire de Lyon.

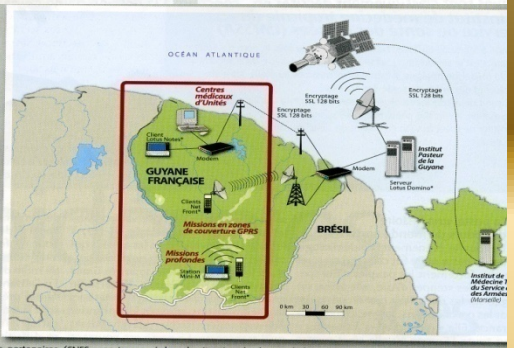
Selon les projets, les financements sont assurés par le CNES, le ministère de la Recherche, l'Agence Spatiale Européenne et la Délégation Générale pour l'Armement.

Les projets de surveillance spatiale couvrent bon nombre de régions « à risque », comme la vallée du Rift en Afrique, les zones de reproduction des oiseaux migrateurs (Camargue), les forêts tropicales humides, comme la Guyane.

Au Sénégal et en Mauritanie (S2E EMERCASE), le projet concerne le système de collecte et de transmission par satellite de données épidémiologiques sur la fièvre de la vallée du Rift, en collaboration avec des équipes de recherches françaises (INRA, CIRAD, CNRS, CEA, Université de Marseille, Université de Lyon, Université de Grenoble, Service de Santé des Armées, CNES, MEDES, Médias-France) ; des industriels (Calystène, Géosys, SOGREAH, MSSI, EADS) et des équipes de recherches sénégalaises (DIREL, Institut Pasteur de Dakar, IRD, ISRA, Université Cheikh Anta Diop, Météorologie Nationale du Sénégal).

En Camargue, le projet S2E Oiseaux Migrateurs s'attache à effectuer une surveillance spatiale des épidémies introduites par les oiseaux migrateurs (grippe aviaire, virus West Nile), en association avec des partenaires (CNES, Médias-FRANCE, CLS, Institut Pasteur à Paris, Fondation Sansouire, AFSSA).

La Guyane accueille les projets S2E Dengue (surveillance de la dengue, une collaboration entre l'Institut Pasteur de Guyane, l'IRD, le MEDES, Médias-France, INRA-ENV Lyon et Calystène) et S2E-FAG (schéma ci-contre) qui concerne pour sa part la surveillance spatiale des épidémies au sein des forces armées françaises.



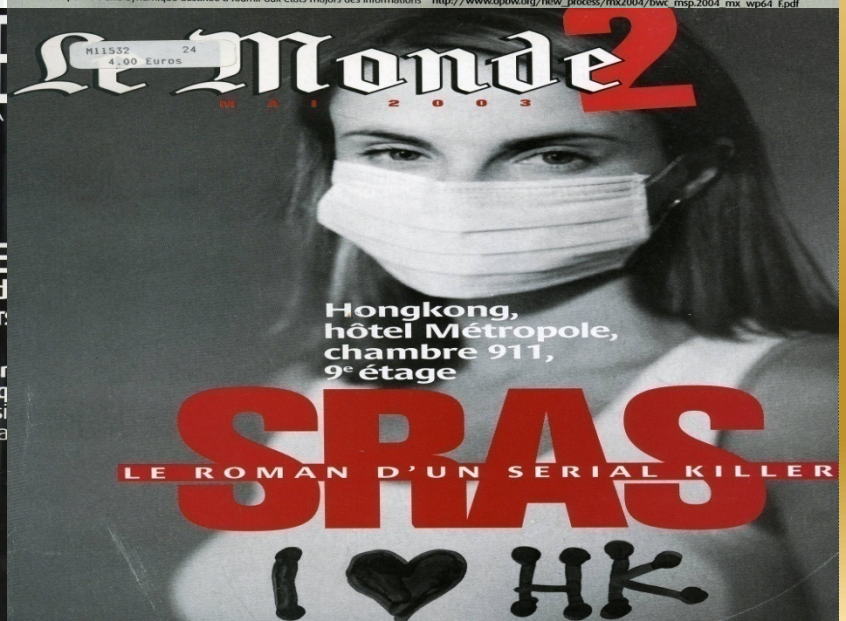
Les forces armées, sentinelles de la surveillance spatiale (S2E-FAG)

S2E-FAG est destiné à connaître en temps réel la disponibilité sanitaire des forces et de détecter au plus tôt tout phénomène sanitaire anormal. Ces travaux du service de santé des armées font partie d'une dynamique destinée à fournir aux états-majors des informations en temps réel sur la situation du champ de bataille. Ainsi, S2E-FAG a non seulement pou objectif d'opérer une surveillance des épidémies mais de la conduire en temps réel, avar de la généraliser sous la forme d'un système de surveillance en temps réel interopérabl – en effet ce type de politique doit être mis en commun au sein des pays de l'OTAN.

Pour en savoir plus sur les projets S2E :

Institut Pasteur :
http://www.pasteur.fr/pasteur/international/Dai/s2e.html

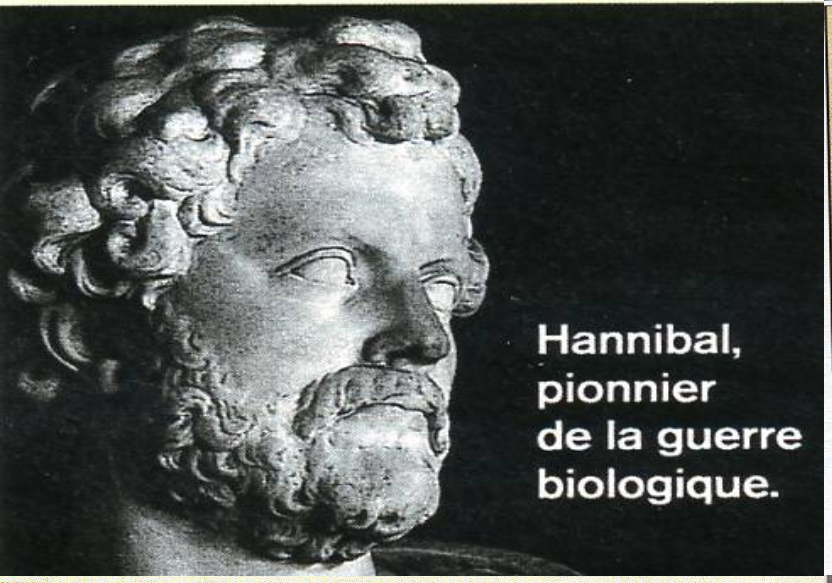
Réunion des États parties à la Convention sur l'interdiction de la mise au point, de l fabrication et du stockage des armes bactériologiques (biologiques) ou à toxines et su leur destruction :
http://www.opbw.org/new_process/mx2004/bwc_msp.2004_mx_wp64_f.pdf



Le bioterrorisme commence il y a trois mille ans

Gaz mystérieux utilisé par les Russes pour libérer le théâtre de Moscou en octobre dernier, alerte à l'anthrax aux Etats-Unis en 2001, inquiétude sur une épidémie "préméditée" de variole : l'heure est à la psychose. Retour sur un procédé qui remonte au VIII[e] siècle avant notre ère.

par Pierre Kohler



Hannibal, pionnier de la guerre biologique.

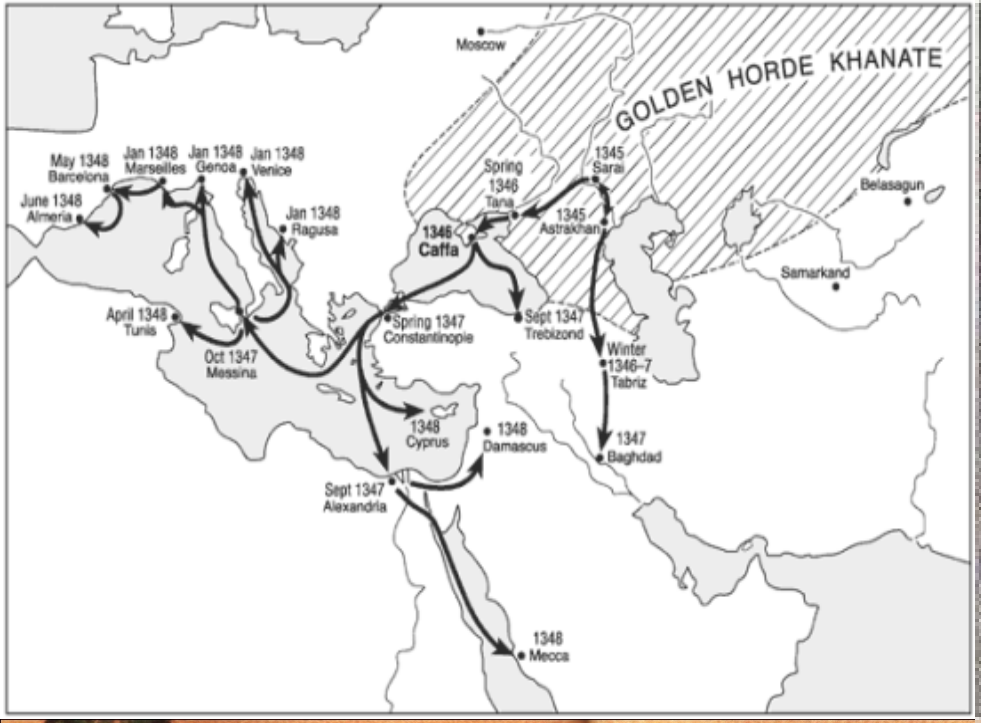
© Bridgeman/Giraudon

La technique consistant à expédier des objets « biodérangeants » est très ancienne. Ici au siège de la turque Nicée en Asie Mineure par les Croisés en 1097, ceux-ci catapultèrent des têtes humaines. En 1846, lors du siège de Caffa, sur la mer Noire, où la peste sévissait, les Tatars musulmans rendirent aux chrétiens la monnaie de leur pièce : ils catapultèrent des cadavres sur les bateaux gènois.

1763 : la variole propagée par les Anglais décime les Indiens.

Le vaccin comme seule défense

En 1940, pendant la guerre sino-japonaise, les Nippons larguent des bombes infestées du virus de la peste et du choléra sur plusieurs villes chinoises. Les civils doivent être vaccinés au plus vite.


GOLDEN HORDE KHANATE
Moscow
May 1348 Barcelona
Jan 1348 Marseilles
Jan 1348 Genoa
Jan 1348 Venice
June 1348 Almeria
Jan 1348 Ragusa
Spring 1346 Tana
1345 Sarai
1345 Astrakhan
1346 Caffa
Belasagun
Samarkand
April 1348 Tunis
Oct 1347 Messina
Spring 1347 Constantinople
Sept 1347 Trebizond
Winter 1346–7 Tabriz
1348 Cyprus
1348 Damascus
1347 Baghdad
Sept 1347 Alexandria
1348 Mecca

Bioterrorism and Bioterrorism Preparedness: Historical Perspective and Overview

Nancy Khardori, MD, PhD

Division of Infectious Diseases, Department of Internal Medicine, Southern Illinois University School of Medicine, 701 North First Street, Room A 484, Springfield, IL 62794-9636, USA

Impact of Plague on Human History

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Table 1
Examples of political attempts at bioterrorism

Year	Group	Attempt	Outcome
1970	Weather Underground	A US revolutionary group intended to obtain agents from Ft. Detrick by blackmail and to incapacitate US cities temporarily to demonstrate the "impotence of the federal government"	Report originated with a US Customs informant. The case later appeared to be apocryphal
1972	R.I.S.E.	A group of college students influenced by ecoterrorist ideology and 1960s drug culture planned to use agents of typhoid fever, diphtheria, dysentery, and meningitis, initially to target the entire world population, but later narrowed the plan to five cities near Chicago	The attack was aborted when cultures were discarded
1978	Unknown	Bulgarian defector Georgi Markov was assassinated in London when a spring-loaded device disguised in an umbrella was used to implant a ricin-filled pellet in his thigh	Similar device used against a second defector in the same area was unsuccessful
1979	Accidental	Accidental release of anthrax spores from a bioweapons facility in Sverdlovsk, Russia, caused an epidemic of inhalational anthrax	At least 77 cases and 60 deaths
1980	Red Army Faction	Members of a Marxist revolutionary ideology group allegedly cultivated botulinum toxin in a safe house in Paris and planned attacks against at least nine German officials and civilian leaders	This probably was an erroneous report, later repudiated by the German government
1984	Rajneeshee Cult	An Indian religious cult headed by Rajneesh plotted to contaminate a restaurant salad bar in Dalles, Oregon, with *Salmonella typhimurium*. The motivation was to incapacitate voters, win local elections, and seize political control of the county	The incident resulted in a large community outbreak of salmonellosis involving 751 patients and at least 45 hospitalizations. The plot was revealed when the cult collapsed and members turned informants
1991	Minnesota Patriots Council	A right-wing "Patriot" movement obtained ricin extracted from castor beans by mail order. They planned to deliver ricin through the skin with dimethyl sulfoxide and aloe vera or as dry aerosol against Internal Revenue Service officials, US Deputy Marshals, and local law enforcement officials	The group was infiltrated by Federal Bureau of Investigation informants
1995	Aum Shinrikyo	A New Age doomsday cult seeking to establish a theocratic state in Japan attempted at least 10 times to use anthrax spore, botulinum toxin, Q fever agent, and Ebola virus in aerosol form	Multiple chemical weapon attacks with sarin, Vx, and hydrogen cyanide in Matsumator and Tokyo and assassination campaigns were conducted. All attempts with use of biological weapons failed. The nerve gas sarin killed 12 and injured 5500 in a Tokyo subway
1997	Disgruntled employee in Texas	Intentional contamination of muffins and donuts with laboratory cultures of *Shigella dysenteriae*	Caused gastroenteritis in 45 laboratory workers, 4 of whom were hospitalized
2001	Unknown	Intentional dissemination of anthrax spores through the US Postal System led to the deaths of 5 people, infection of 22 others, and contamination of several government buildings	Investigation into the attacks so far has not reached a conclusion

Adapted from Khardori N, Kanchanapoom T. Overview of biological terrorism: potential agents and preparedness. Clin Microbiol News 2005;27:1–8. with permission.

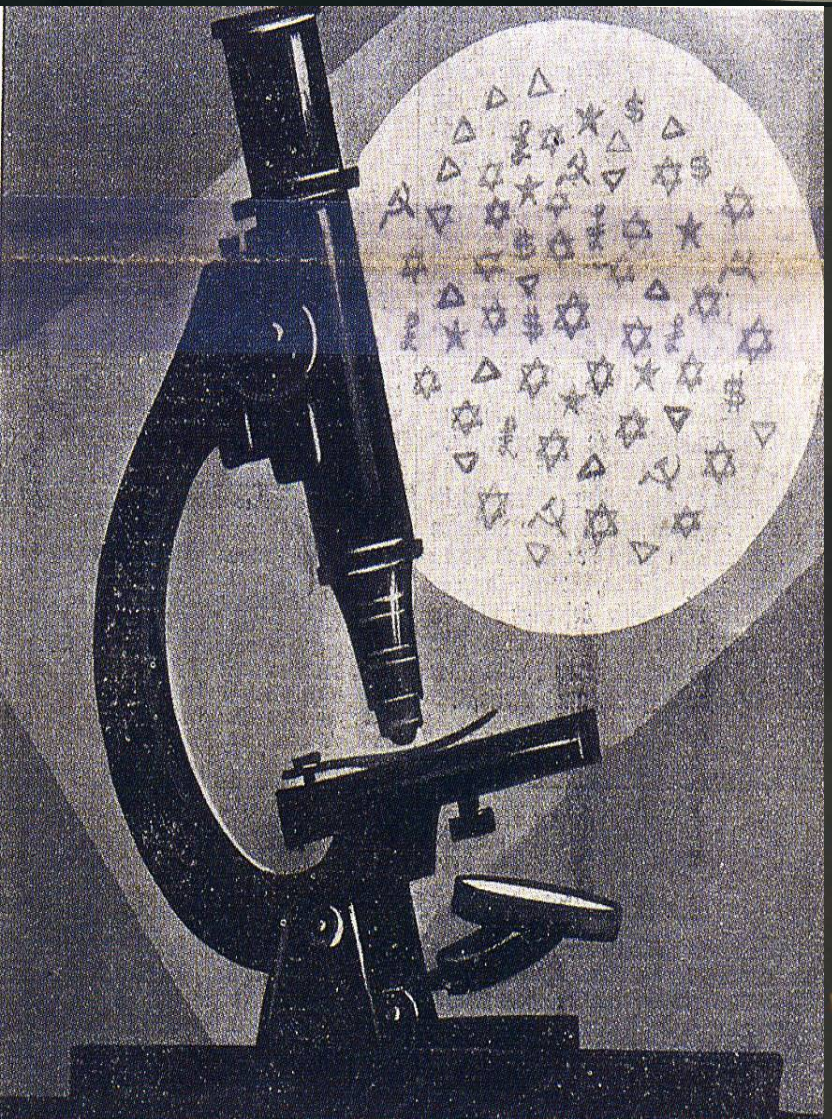
Table 5
Plague pandemics

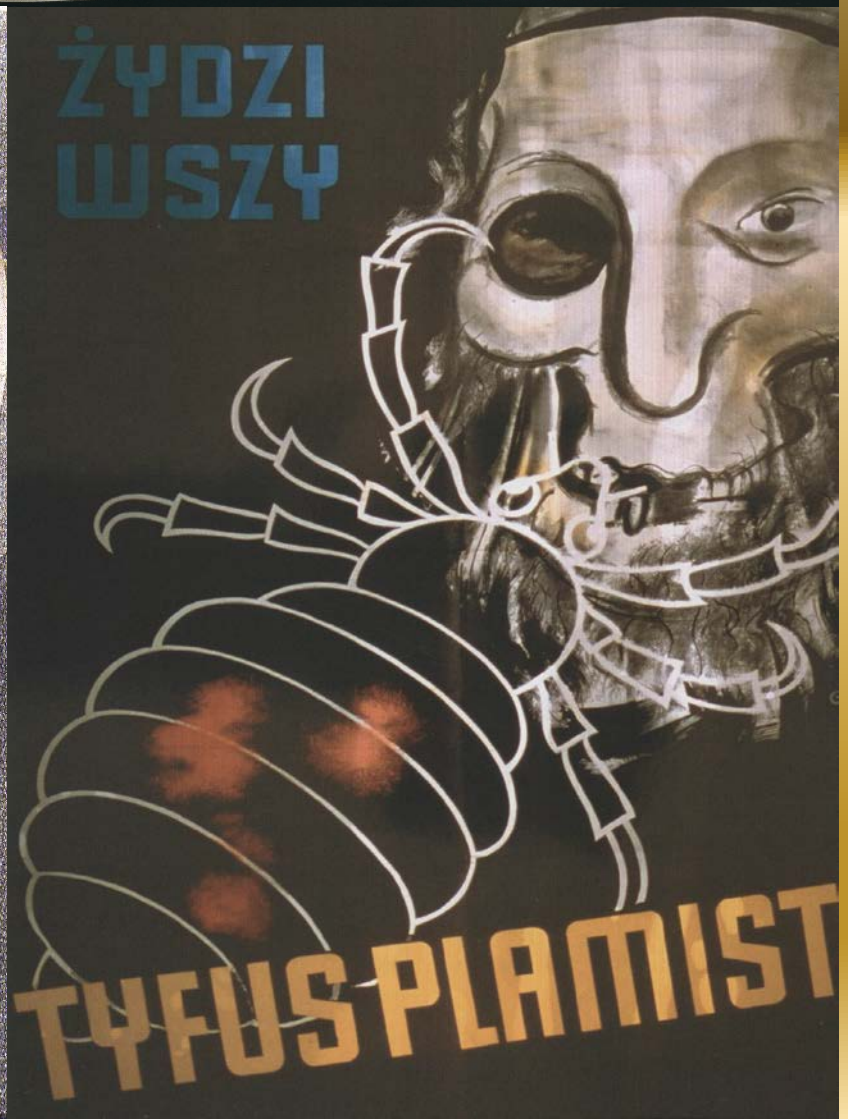
Plague pandemic	Year	Location	Vector	Historical significance
Plague of Athens	430–426 BC	Athens	Unknown. No antecedent rat deaths described	Decimated military/civilian population of Athens. Pericles died of plague. Spartans victorious over Athens. End of Greece's Golden Age. Western civilization changed 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].

DEADLY MEDICINE

CREATING THE MASTER RACE





New Antidotes to

ANTHRAX

ATTACKING ANTHRAX

Recent discoveries are suggesting much-needed strategies for improving prevention and treatment. High on the list: ways to neutralize the anthrax bacterium's fiendish toxin

by John A. T. Young and R. John Collier

ANTHRAX IN ACTION

Physicians classify anthrax according to the tissues that are initially infected. The disease turns deadly when the causative bacterium, *Bacillus anthracis*, reaches the bloodstream and proliferates there, producing large amounts of a dangerous toxin. Much research is now focused on neutralizing the toxin.

THREE TYPES

INHALATION ANTHRAX
Spores are breathed in

GASTROINTESTINAL ANTHRAX
Spores are ingested by eating contaminated meat

CUTANEOUS ANTHRAX
Spores penetrate the skin through a break

HOW INHALATION ANTHRAX ARISES

Inhalation anthrax is the most dangerous form, probably because bacteria that land in the lungs are more likely to reach the bloodstream and thus disseminate their toxin through the body.

1 Immune system cells called macrophages ingest *B. anthracis* spores and carry them to lymph nodes in the chest. En route, or in the macrophages, the spores transform into actively dividing cells

2 Proliferating *B. anthracis* cells erupt from macrophages and infiltrate the blood readily

3 In the blood, the active bacteria evade destruction by macrophages and other cells of the immune system by producing a capsule (*detail*) that blocks the immune cells from ingesting them and by producing a toxin that enters immune cells and impairs their functioning

4 Protected from immune destruction, the bacteria multiply freely and spread through the body

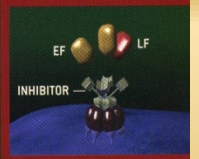
MACROPHAGE
SPORE
REPLICATING BACTERIAL CELLS
BACTERIUM
CAPSULE
BACTERIA IN BLOOD
CELL
MACROPHAGE FILLED WITH TOXIN
TOXIN MOLECULES

HOW THE TOXIN INVADES CELLS ... AND HOW TO STOP IT

THE ANTHRAX TOXIN must enter cells to hurt the body. It consists of three collaborating proteins: protective antigen (PA), edema factor (EF) and lethal factor (LF). The last two disrupt cellular activities, but only after protective antigen delivers them to the cytosol—the matrix surrounding the cell's intracellular compartments. Molecular understanding of how the factors reach the cytosol has led to ideas for blocking that journey and thus for neutralizing the toxin and saving lives. The antitoxins depicted in the boxes have shown promise in laboratory studies.

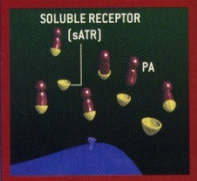
LF
EF
HEPTAMER
PA
1 PA binds to its receptor on a cell
ANTHRAX TOXIN RECEPTOR (ATR)
2 PA gets cleaved
3 Seven copies combine, forming a heptamer
4 Up to three copies of EF or LF or a combination of the two bind to the heptamer
5 The heptamer complexed with EF and LF is delivered to a membrane-bound compartment called an endosome
HEPTAMER COMPLEX
ENDOSOME
6 Mild acidity in the endosome causes the heptamer to inject EF and LF into the cytosol
CYTOSOL
7 EF causes tissues to swell and prevents immune system cells from ingesting and degrading bacteria
8 LF is believed to be important in causing disease and death, but exactly how it does so is in question

TREATMENT IDEA



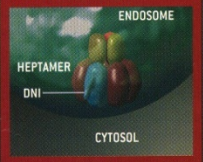
Keep EF and LF from attaching to their binding sites on PA heptamers. Plug those sites with linked copies of a molecule that also has affinity for the sites.

TREATMENT IDEA

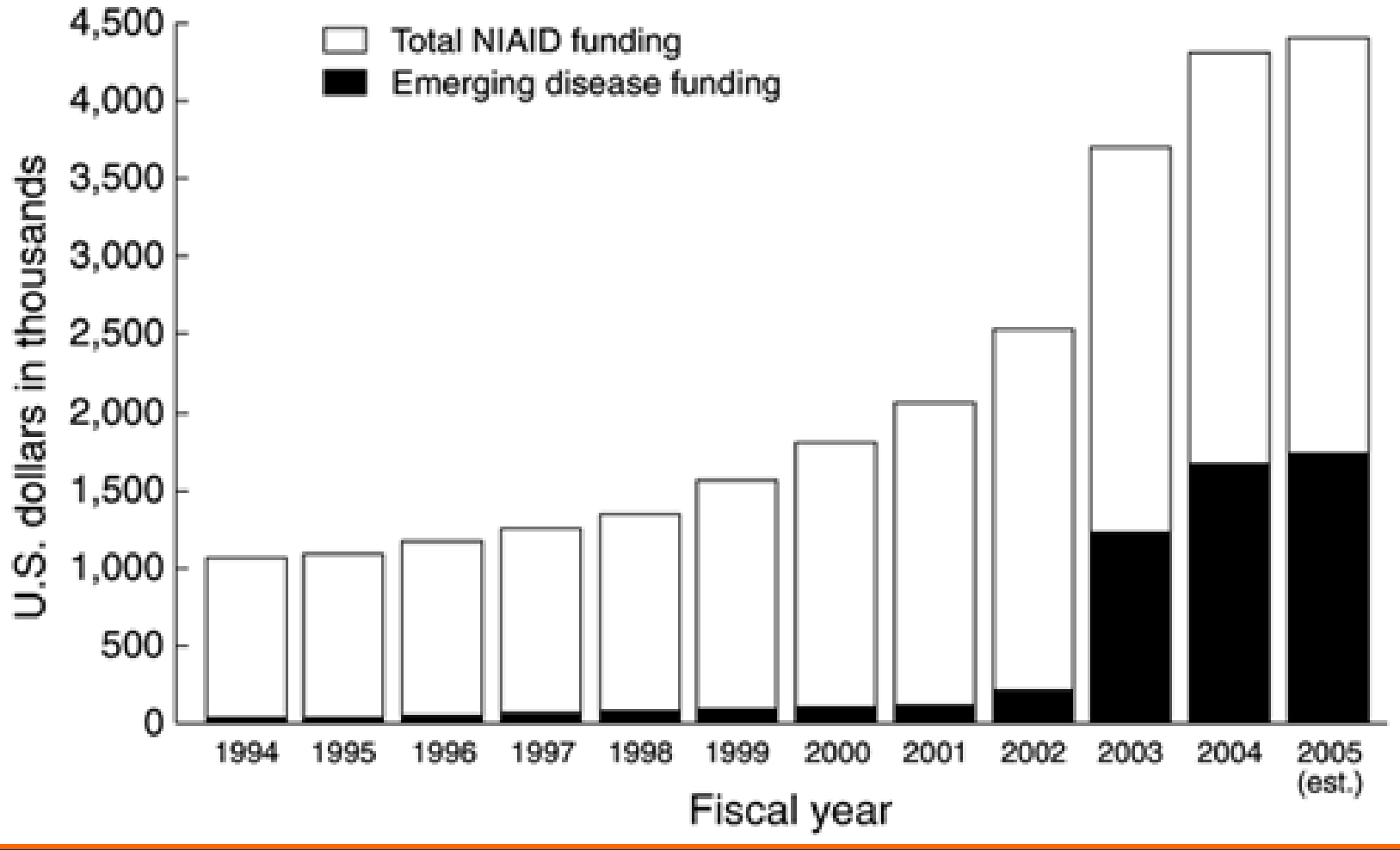


Prevent PA from linking to its receptor on cells. Induce it to bind instead to decoys, such as soluble copies of the toxin receptor's PA binding site.

TREATMENT IDEA



Block transport of EF and LF from the endosome into the cytosol by causing newly forming heptamers to incorporate a version of PA known as a dominant negative inhibitor (DNI). DNI-containing heptamers cannot move EF and LF across the endosome's membrane.

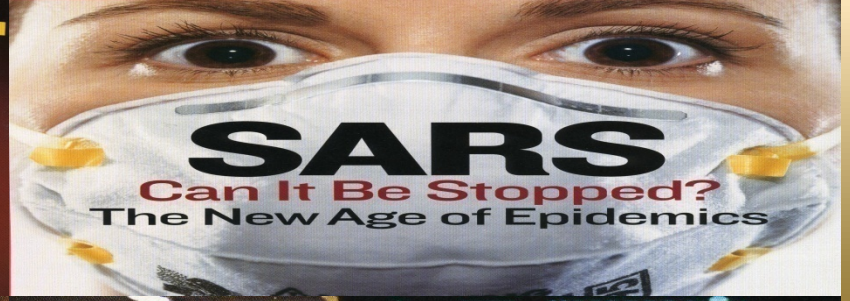


Flu Fever

The Vaccine Crisis
Who Should Get Shots?
The Scary Future Of Winter Bugs

SARS

Can It Be Stopped?
The New Age of Epidemics



CAMPING OUT: Miriam Majors, 82, and 400 others wait in the rain at a Roanoke, Va., clinic

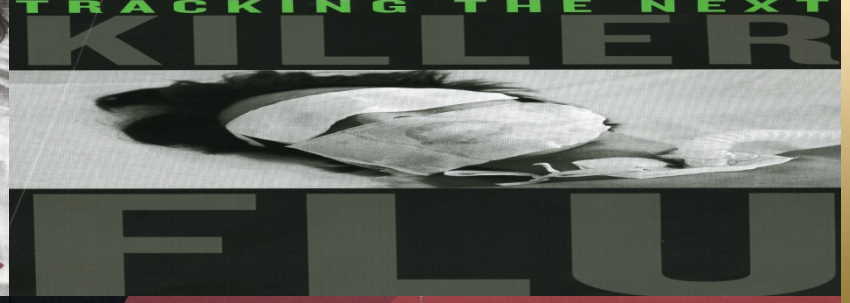
The Mystery of SARS

As this strange new virus continues its spree, killing hundreds and infecting thousands more, scientists are working overtime, trying to keep people from harm

EMERGENCY: A patient and a paramedic at a Toronto hospital are suited up against the virus

The Next Killer Flu

Can we stop it?



TRACKING THE NEXT KILLER FLU

1918
50-100 MILLION DEATHS
Bird origin suspected

TODAY
180-360 MILLION COULD DIE

1900 | 1910 | 1920 | 1930 | 1940 | 1950 | 1960 | 1970 | 1980 | 1990 | 2000 | ?

50 million

100 million

180 million

360 million

7.4 mi

OVERDUE FOR A FLU PANDEMIC?

Three times in the 20th century a new flu virus spread through the world's population, causing an unusual number of deaths because people had little immunity to it. Nearly 40 years have passed since the last pandemic. The world may be ripe for a new one as a dangerous bird flu circulates in Asia.

SPANISH FLU 1918-19
The most deadly outbreak in history, the Spanish flu is believed to have originated in birds sometime before 1918. It swept the globe in 1918 and early 1919. Except for a few Pacific islanders, everyone on Earth was exposed to the disease, and half got sick.

Bird and human viruses mix.

1,000,000 DEATHS

ASIAN FLU 1957
The pandemic emerged in southern China when a bird and a human flu swapped genes, probably after infecting a pig. The result was a new and deadly virus.

Bird and human viruses mix.

750,000 DEATHS

HONG KONG FLU 1968
A bird and a human flu again swapped genes, creating a new virus first seen in Hong Kong. Similarities to the 1957 virus meant people had some immunity, which helped reduce deaths.

Since 1997, outbreaks of H5N1 bird flu have alarmed experts.

THE NEXT KILLER FLU
The H5N1 bird-flu virus killing poultry and people in Asia could cause the next global pandemic if it gains the ability to spread quickly from person to person. Estimated deaths in such a pandemic range from 7.4 million to an apocalyptic 180 million to 360 million, extrapolating 1918 deaths to today's population.

A VIRUS MOVES TWICE AS FAST NOW

The last pandemic, in 1968, took a year to spread around the world. More than three decades later, increased jet travel could halve that time—limiting the opportunity for slowing the spread with a vaccine.

KEY
In each city, flu cases rise to a peak several weeks after the first reported infection, then gradually taper off.

Flu cases per city

Hong Kong, Sydney, Bangkok, Mumbai (Bombay), São Paulo, Lagos, Caracas, Havana, Washington, Rome, Shanghai, Tehran

HYPOTHETICAL PANDEMIC: 180 DAYS (MODELED FOR 2000)

52 CITIES
The flu could spread to these cities twice as fast as it did in 1968 (data graphed below).

Hong Kong, Bangkok, Mumbai (Bombay), Washington, Tehran, Rome, Shanghai, Lagos, Caracas, Havana, São Paulo, Sydney

THE LAST PANDEMIC, IN 1968: 342 DAYS

RESPONSE: DAY 1
As soon as a pandemic begins, countries with stockpiles of antiviral drugs can begin distributing them.

DAY 100
If a vaccine were developed and tested in advance, distribution could begin within three months of the start of the pandemic.

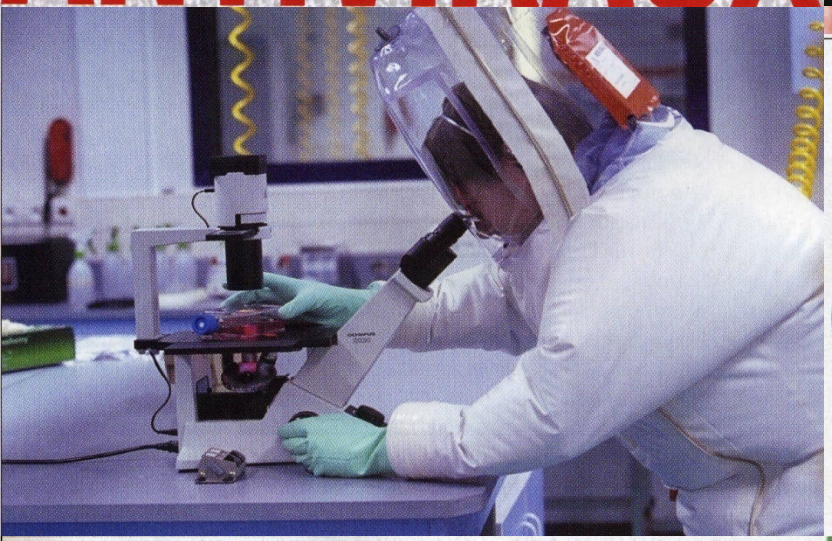
DAY 250
It normally takes about this long to develop a vaccine, test it, amass the millions of fertilized eggs needed to make it, and get it to market.

PANDEMIC MORTALITY RATES (TOP): MICHAEL T. OSTERHOLM, UNIVERSITY OF MINNESOTA; WORLD HEALTH ORGANIZATION. SPREAD MODELS (BOTTOM): REBECCA F. GRAIS, J. HUGH ELLIS, GREGORY E. GLASS, JOHNS HOPKINS UNIVERSITY. NGM ART

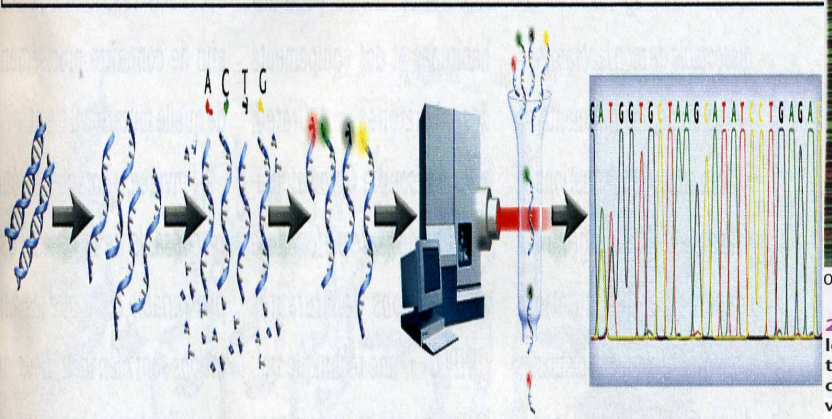
LE DÉFI DES ANTIVIRAUX

Ebola
Marburg
Lassa
Grippe...

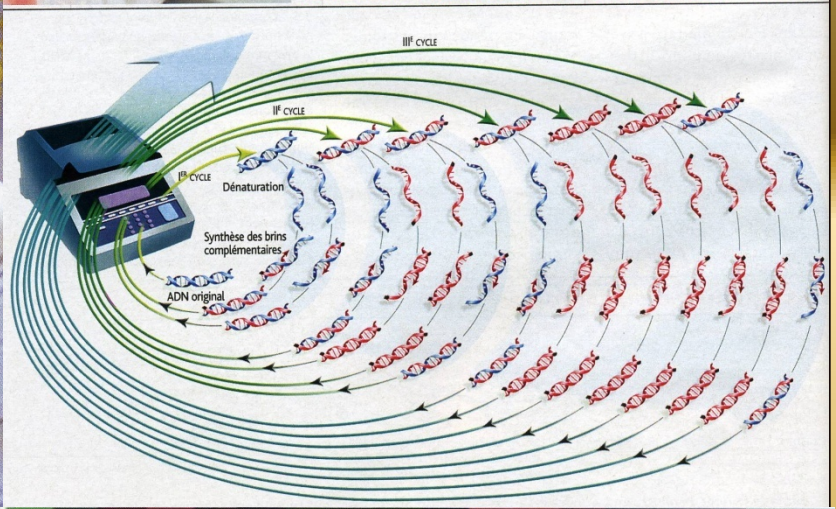
Vaincre les virus

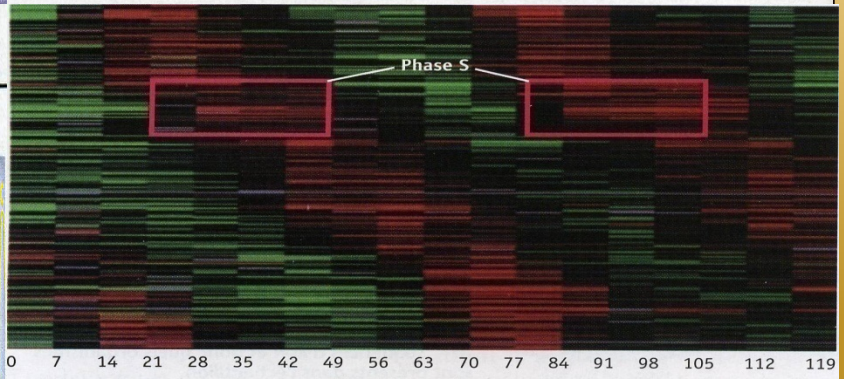


Une technique de séquençage d'un gène



Réaction de polymérisation en chaîne : la PCR





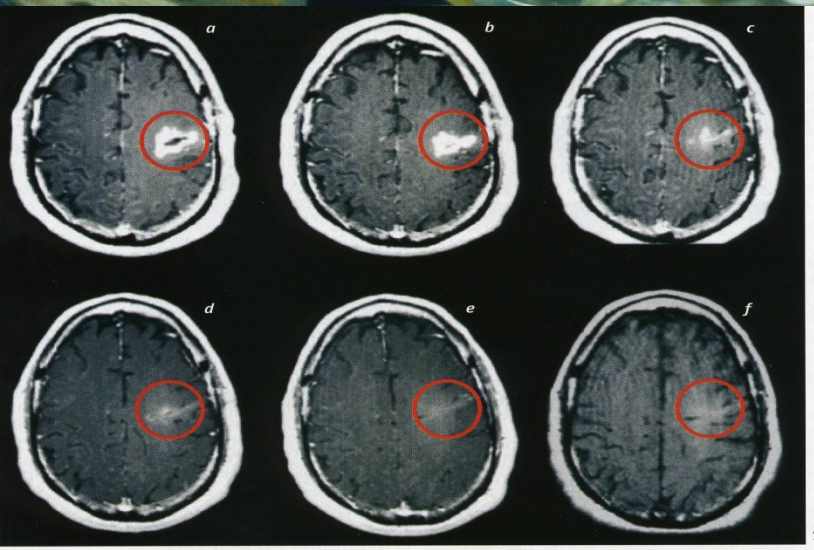
2. Le cycle cellulaire révélé par les puces à ADN. On identifie les gènes qui contrôlent ce cycle à l'aide des puces à ADN (après synchronisation des cellules) en analysant les transcriptomes des cellules au cours du temps. Après traitement bio-informatique des données (regroupement des gènes ayant un comportement semblable), on observe des vagues d'expression de gènes *(l'expression est représentée ici par une échelle allant du vert – le gène s'exprime peu – au rouge – le gène s'exprime beaucoup)* que l'on peut relier à l'état de la cellule. Dans le cas de la levure de boulanger, environ 800 gènes (sur les 6 000 gènes que compte cet organisme) s'expriment de façon cyclique. Les gènes de la même vague d'expression partagent des signaux similaires et des fonctions biologiques communes. Ainsi, chez la levure, les gènes exprimés pendant la phase S *(les rectangles rouges)* sont majoritairement requis pour la synthèse de l'ADN.

Des cancers
traités par des virus

J. ROMMELAERE, C. DINSART, A. RÉGNIER-VIGOUROUX, N. SALOMÉ, J. SCHLEHOFER

Les traitements conventionnels contre les cancers ont une efficacité limitée dans de nombreux cas. La thérapie oncolytique, fondée sur l'utilisation de virus tueurs de tumeurs, offre de nouvelles perspectives dans la lutte contre ce fléau mondial.

1. Cette bulle stérile protégeait David, atteint d'un déficit immunitaire combiné sévère (DICS), maladie héréditaire. Un essai de thérapie génique, réalisé en 1999 à l'Hôpital Necker de Paris, a permis de soigner huit enfants. Par la suite, des améliorations des vecteurs rétroviraux ont été proposées.

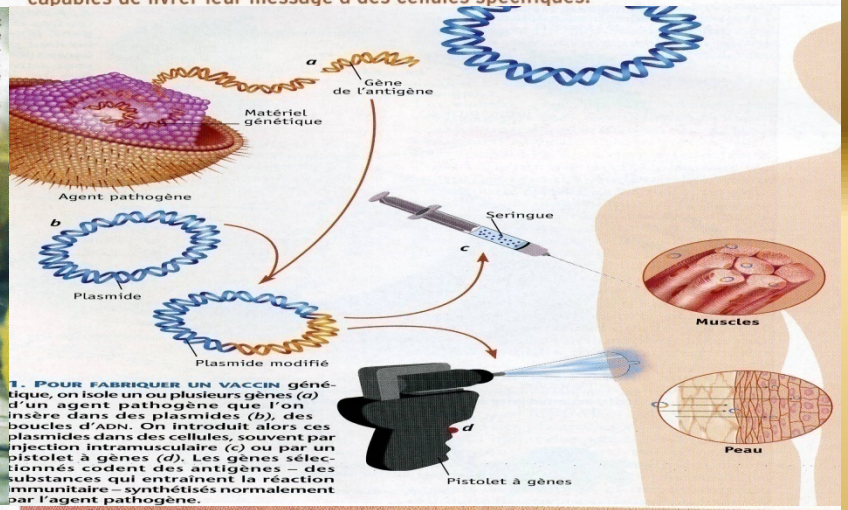


3. Régression d'une tumeur cérébrale. Des essais cliniques ont montré l'efficacité de la thérapie oncolytique sur des cellules gliales cancéreuses du cerveau. L'injection de virus de la maladie de Newcastle a provoqué la régression de la tumeur *(de a à f)*, comme le montrent les images par résonance magnétique prises lors du test, en 2006.

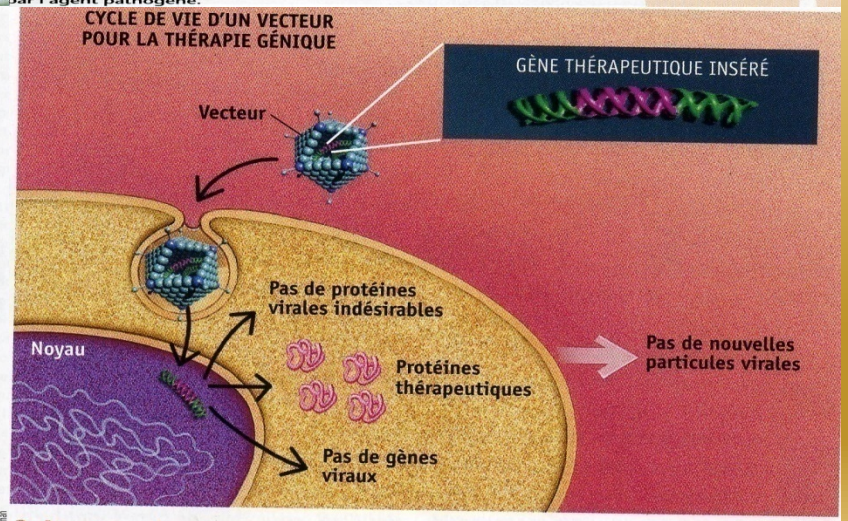
Les virus vecteurs
de molécules thérapeutiques

Jean-Christophe PAGÈS et Éric PIVER

En désamorçant leur pouvoir pathogène, on convertit des virus en vecteurs d'instructions génétiques. Ceux-ci deviennent des outils thérapeutiques, capables de livrer leur message à des cellules spécifiques.



1. Pour fabriquer un vaccin génétique, on isole un ou plusieurs gènes *(a)* d'un agent pathogène que l'on insère dans des plasmides *(b)*, des boucles d'ADN. On introduit alors ces plasmides dans des cellules, souvent par injection intramusculaire *(c)* ou par un pistolet à gènes *(d)*. Les gènes sélectionnés codent des antigènes – des substances qui entraînent la réaction immunitaire – synthétisés normalement par l'agent pathogène.



A. Freeman

3. Le cycle d'un vecteur viral est tronqué par rapport à celui d'un virus : ne sont conservés que l'entrée et le transfert nucléaire du génome, qui permettront l'expression du gène thérapeutique. Comme les gènes structuraux ne sont plus présents dans le génome du vecteur, celui-ci est incapable de se multiplier.

CONCLUSÕES

SCIENTIFIC AMERICAN HISTÓRIA

O HOMEM EM BUSCA DAS *Origens*

Como a humanidade entendeu o fenômeno da vida, da mitologia ao Projeto Genoma

Mitos e metáforas procuram explicar o surgimento da vida e a criação do mundo. Ciência e religião se complementam como conhecimento.

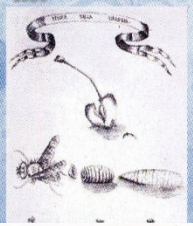
Antiguidade

500 a.C.

Anaxágoras cunha o termo panspermia, que em grego significa sementes em toda a parte.

A filosofia continua a questionar a origem da vida e a gênese das espécies, com teorias sobre animalculismo, ovismo, pré-formação e cosmogênese.

1668



Experiências sobre a geração de insetos é publicada por Redi

1730/31

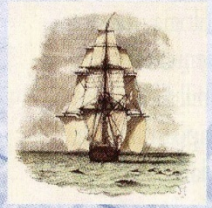
Lineu elabora o sistema de classificação que leva seu nome.

1770

Spallanzani refaz experiências sobre a geração espontânea.

1798

Publicação de *Essay on population*, por Malthus.



1831 a 1836

Darwin faz a famosa viagem no *Beagle*.

1809

Lamarck publica *Filosofia zoológica*.

1838

Schleiden propõe a teoria celular para as plantas.

1839

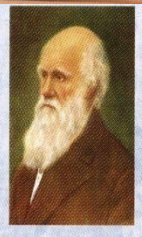
Schwann propõe a teoria celular para o reino animal.

1846 a 1852

Wallace e Bates aventuram-se na Amazônia.

1858

Wallace envia a Darwin o trabalho *On the tendency of varieties to depart indefinitely from the original type*.

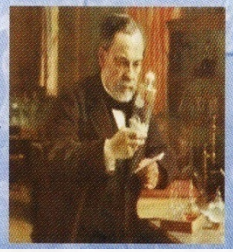


1859

Darwin publica *A origem das espécies*.

1862

Pasteur põe fim à teoria da geração espontânea.



1865

Mendel descobre as leis da genética.

1870

Wallace publica *Contribution to the theory of natural selection*.

1950

Miller e Ulrey demonstram a possibilidade da panspermia.

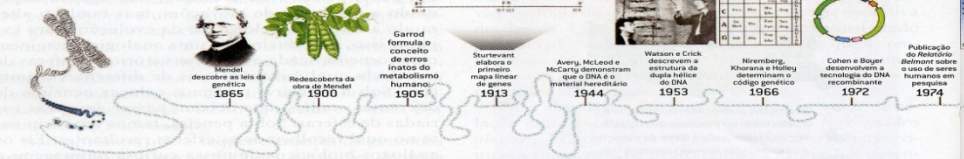
1953

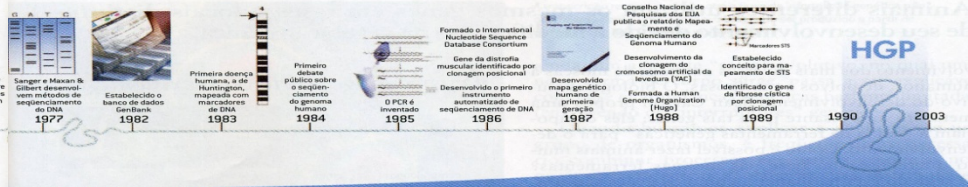
Watson e Crick descrevem a estrutura da dupla hélice do DNA.

2001

Publicado o rascunho do seqüenciamento do genoma humano.

Principais acontecimentos na história da genética, de 1865 até hoje





1990

Projeto Genoma Humano (HGP) lançado nos EUA

Programas sobre Implicações Éticas, Legais e Sociais (ELSI) estabelecidos nos Institutos Nacionais de Saúde (NIH) e no Departamento de Energia (DOE) dos EUA

Mapeado primeiro gene do câncer de mama (BRCA1)

1991

Fundados primeiros centros de genoma americanos

1992

Desenvolvido mapa genético humano de segunda geração

Estabelecidas pelo NIH e DOE diretrizes para rápida divulgação de dados

1993

Publicado nos EUA novo plano de cinco anos para o HGP

Sanger Centre é fundado (depois renomado como Wellcome Trust Sanger Institute)

1994

Atingido objetivo de mapeamento genético humano do HGP

1995

Atingido objetivo de mapeamento físico humano do HGP

Seqüenciado primeiro genoma de bactéria (H. influenzae)

Comissão para oportunidade iguais de trabalho americana divulga políticas sobre discriminação genética no emprego

1996

Estabelecido primeiro mapa genético humano

Projetos-piloto para seqüenciamento do genoma humano começam nos EUA

Seqüenciado primeiro genoma primitivo

Seqüenciado genoma de levedura (S. cerevisiae)

Atingido objetivo de mapeamento genético do camundongo pelo HGP

Estabelecidos princípios para a rápida publicação e abertura de dados em Bermuda

1997

O DOE forma o Joint Genome Institute

Seqüenciado genoma da *E. coli*

Fundado o Genescope, centro nacional francês de seqüenciamento genômico

1998

Incorporados 30 mil genes ao mapa genômico humano

Publicado novo plano de cinco anos do HGP nos EUA

Estabelecido o centro Rijen de ciências genômicas no Japão

Seqüenciado o genoma do nematelminto *C. elegans*

GTGCT
GTCCT

Fundados os centros nacionais chineses de genoma humano, em Pequin e Xangai

1999

Começa o seqüenciamento humano em escala completa

Finalizado o seqüenciamento do primeiro cromossomo humano (cromossomo 22)

2000

Completado o rascunho do seqüenciamento do genoma humano

O presidente Clinton (EUA) e o primeiro-ministro Blair (Inglaterra) apóiam o acesso livre e gratuito da informação genômica

Seqüenciado o genoma da drosófila (*D. melongaster*)

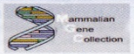
Seqüenciado o genoma da *A. thaliana*

Diretiva do Executivo bane a discriminação genética em cargos federais nos EUA

2001

Publicado o rascunho do seqüenciamento do genoma humano

Seqüenciadas 10 mil cDNAs na sua totalidade



2002

O rascunho do seqüenciamento de genoma do camundongo é finalizado e publicado

Finalizado o seqüenciamento do genoma da ratazana

Finalizada e publicado o rascunho do genoma do arroz

2003

Completada a versão final do seqüenciamento do genoma humano

HGP termina com todos os objetivos atingidos

Continua...

SPECIAL ISSUE on the Most Powerful Idea in Science

SCIENTIFIC AMERICAN

January 2009 www.SciAm.com

EVOLUTION AT WORK
How Doctors, Police and Others Use It on the Job

The Evolution of EVOLUTION

How Darwin's Theory Survives, Thrives and Reshapes the World

The Future of Human Evolution

Molecular Proof of Natural Selection

How Life Invents Complex Traits

Creationists' Latest Tricks

Evolution before and after Darwin

The concept of evolution stretches back to ancient times. Here are some key events in a history that has been marked by continual change.

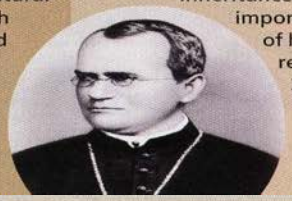
610–546 B.C.: Greek philosopher Anaximander suggests that all life-forms evolved from fish in the seas and went through a process of modification once they were established on land.

1735: Carl Linnaeus publishes the first volume of *Systema Naturae,* which laid the foundations for taxonomy. Later he suggested that plants descend from a common ancestor.

1838: Charles Darwin formulates the theory of natural selection, which is not published for more than 20 years.

1859: *On the Origin of Species* sells out as soon as it is published.

1865: Czech monk Gregor Mendel publishes his research on inheritance, but the importance of his work is not recognized for 35 more years.



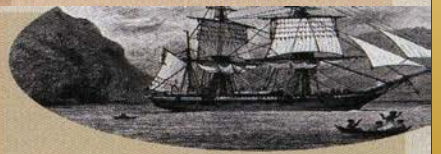
1871: In *The Descent of Man,* Darwin ties the human lineage to primate ancestors, provoking outrage in some quarters and the caricaturing of his image.

1882: Darwin dies.

1925: The Scopes Monkey trial in Tennessee tries a teacher based on a law that made it illegal to teach any theory that denies divine creation.

1809: Darwin (*shown opposite his younger sister*) is born in Shrewsbury, England, into the comfort of a wealthy family.

1830: Charles Lyell publishes *Principles of Geology,* a formative influence on Darwin's thinking about the gradualism of natural processes as can be witnessed in the Grand Canyon (*right*).



1831: Darwin leaves on a five-year around-the-world journey on the HMS *Beagle.*

1936–1947: The modern synthesis combines Darwin's evolutionary theory with Mendelian genetics.

1953: James D. Watson and Francis Crick discover the structure of DNA, making it possible to study the molecular biology of evolution.

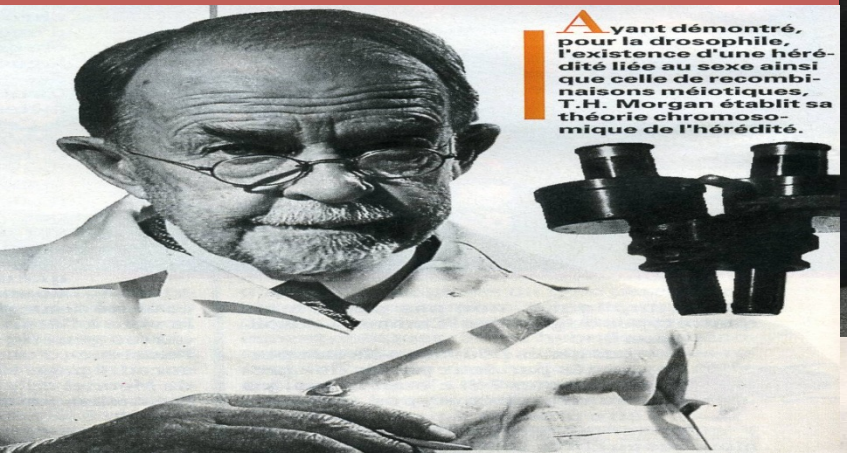
Mid-2000s: Genetic analyses have shown evidence of relatively recent human evolution—dating back several thousand years.

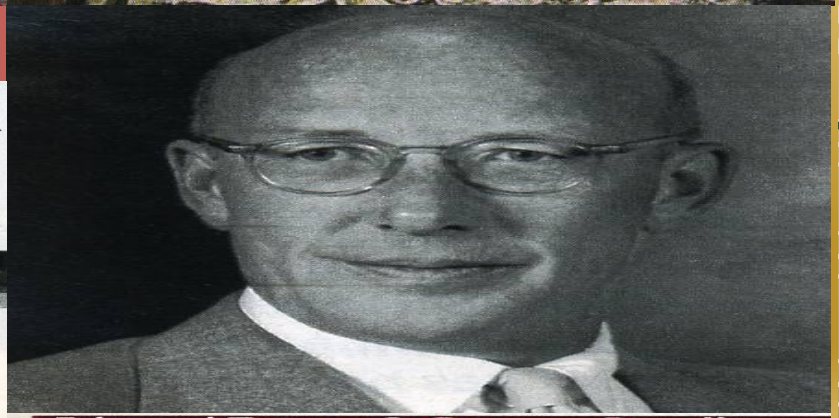
2009: Darwin Day marks the naturalist's birthday on February 12 and will be observed with dozens of events in at least 10 countries. Stay abreast of what's happening at www.darwinday.org

- *(Charles Darwin – 1859)*

- *(Gregor Mendel -1865)*

- 1910 (*Thomas Morgan*)

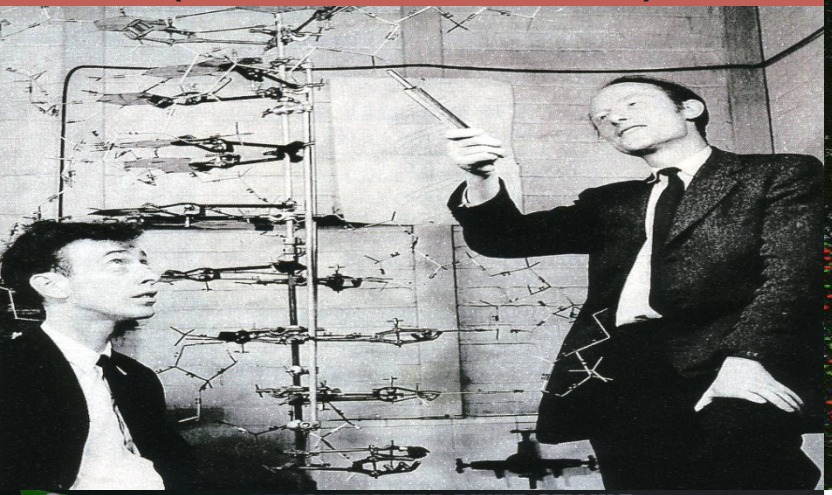


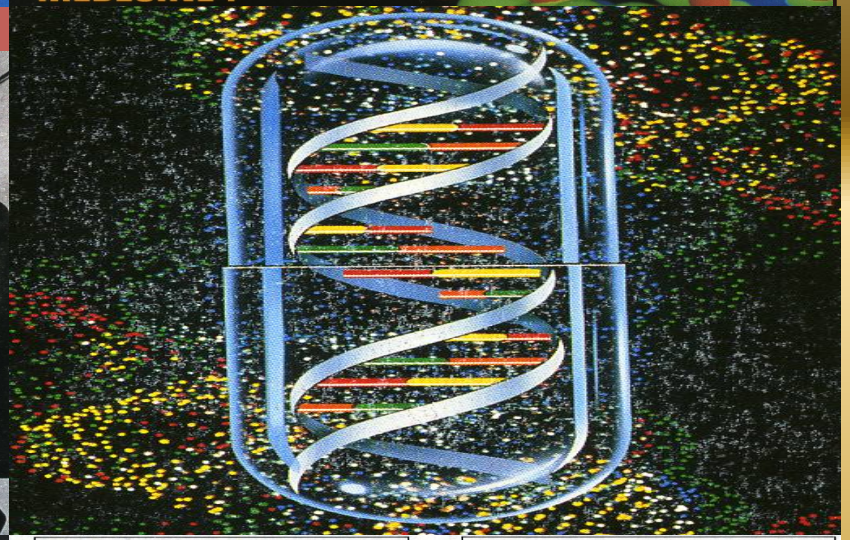


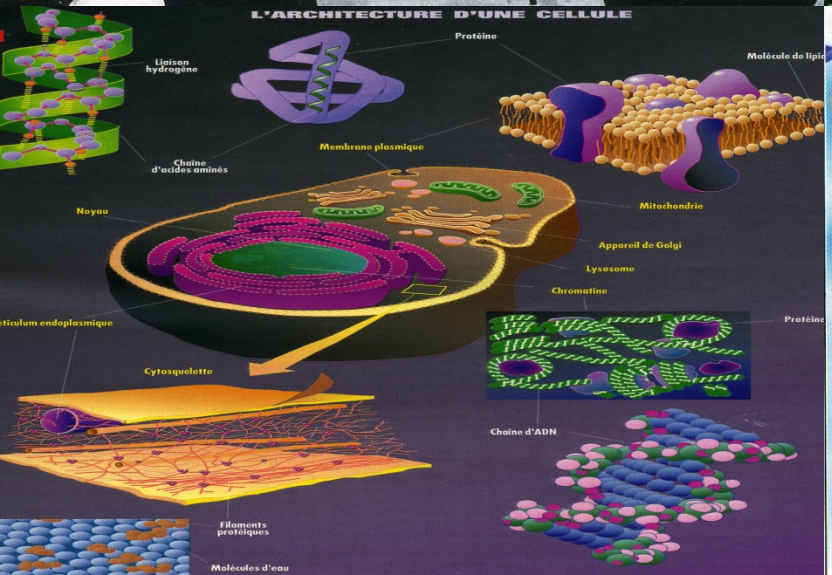
Edward Tatum & George Beadle

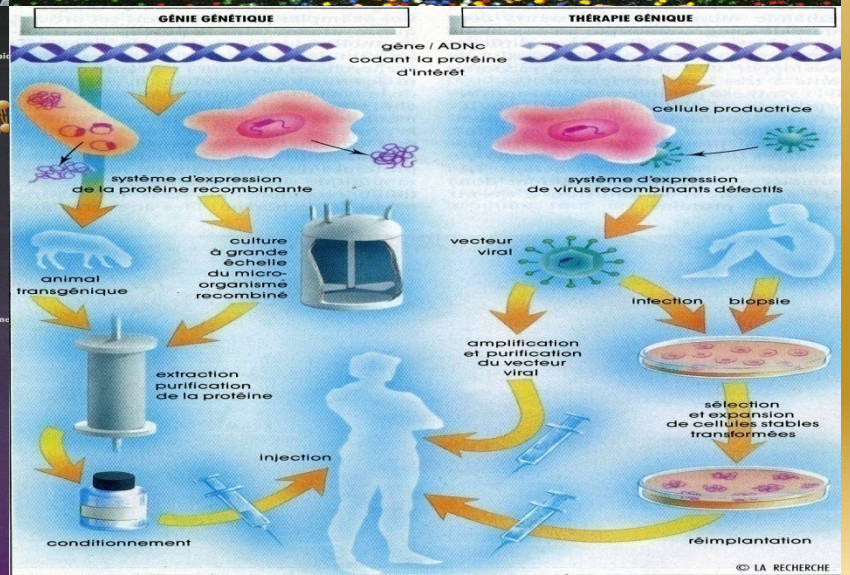
« Un gène - une enzyme » : cette expression mémorable est formulée en 1941 par Edward Tatum et George Beadle pour résumer le fait que chaque gène semble alors gouverner la synthèse d'une enzyme.

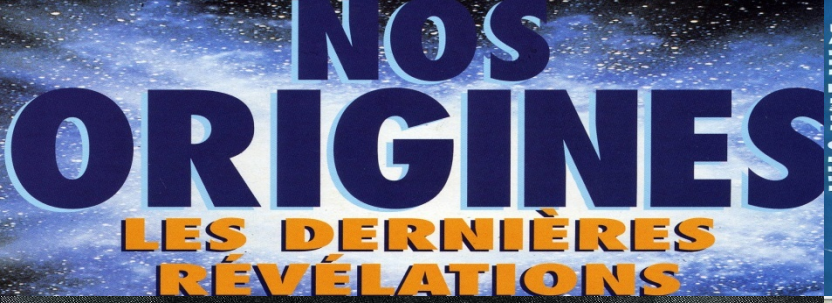
1953 (*James Watson e Francis Crick*)

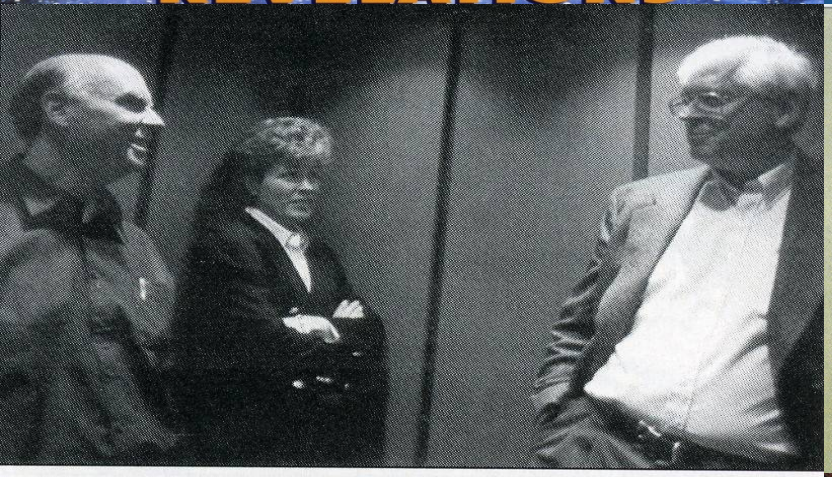


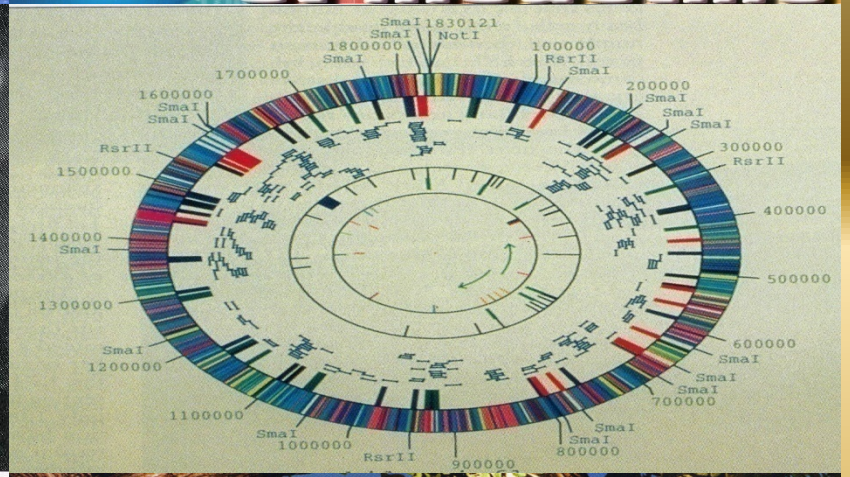






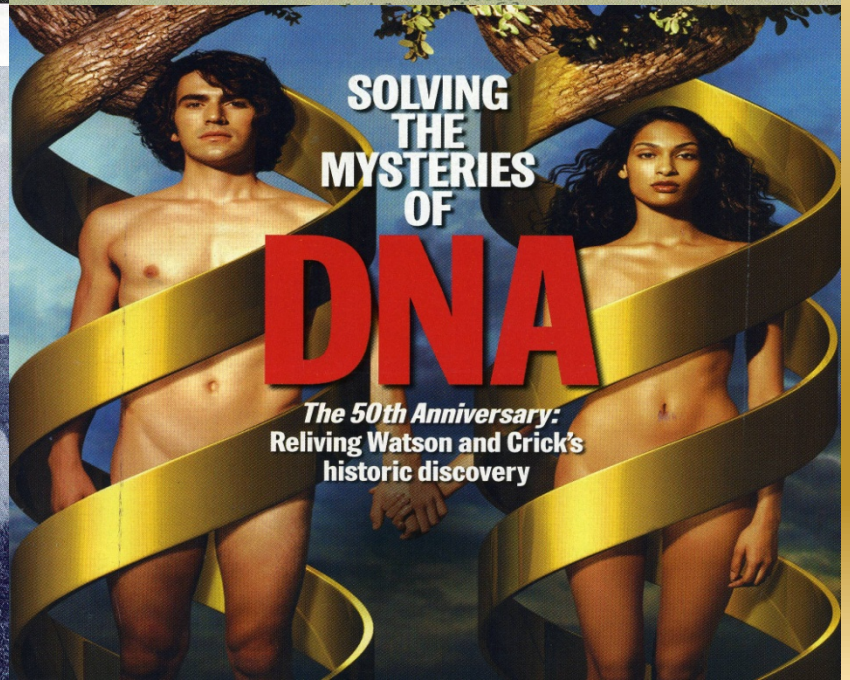






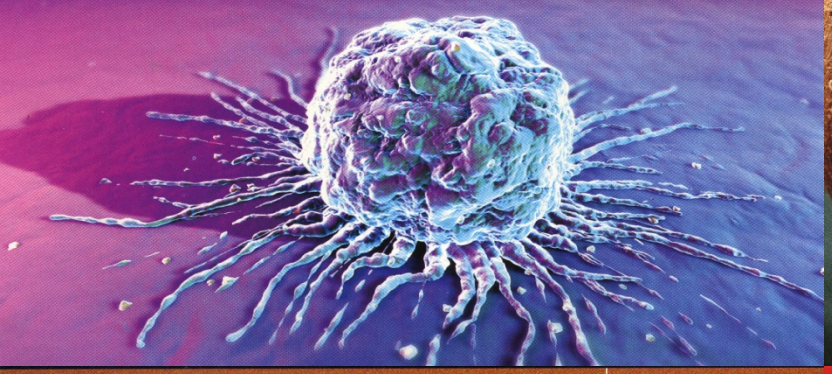
Left to right: Craig Venter, Claire M. Fraser, and Hamilton O. Smith

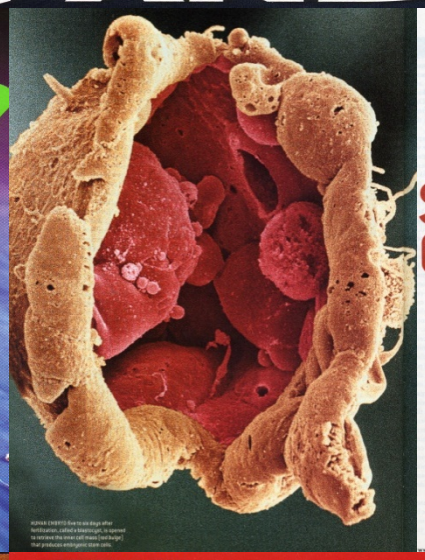
Mirror, mirror. Only the photographer knows who's fairest in this digitally manipulated portrait of Dolly with her creator, Ian Wilmut.



BABY, IT'S YOU! AND YOU, AND YOU

DO STEM CELLS CAUSE CANCER?





Stem cells raise the prospect of regenerating failing body parts and curing diseases that have so far defied drug-based treatment. Patients are buoyed by reports of the cells' near-miraculous properties, but many of the most publicized scientific studies have subsequently been refuted, and other data have been distorted in debates over the propriety of deriving some of these cells from human embryos.

Provocative and conflicting claims have left the public (and most scientists) confused as to whether stem cell treatments are even medically feasible. If legal and funding restrictions in the U.S. and other countries were lifted immediately, could doctors start treating patients with stem cells the next day? Probably not. Many technical obstacles must be overcome and unanswered questions resolved before stem cells can safely fulfill their promise.

For instance, just identifying a true stem cell can be tricky. For scientists to be able to share results and gauge the success of techniques for controlling stem cell behavior, we must first know that the cells we are studying actually possess the ability to serve as the source, or "stem," of a variety of cell types while themselves remaining in a generic state of potential. But for all the intensive scrutiny of stem cells, they cannot be distinguished by appearance. They are defined by their behavior.

Most versatile are embryonic stem (ES) cells, first isolated in mice more than 20 years ago. ES cells come from the portion of a very early-stage embryo that would normally go on to form three distinctive germ layers within a later embryo [*see illustration on page 63*] and ultimately all the different tissues of the body. ES cells retain this potential ability to produce any cell type in the body, making them pluripotent.

Most of the existing human ES cell lines in the world were derived from unused embryos created for couples seeking in vitro fertilization (IVF). Researchers working with these cells have found that they usually recover after freezing and thawing and can differentiate into assorted cell types in a culture dish. But it is becoming clear that not all human ES cell lines are the same.

The Stem Cell Challenge

What hurdles stand between the promise of human stem cell therapies and real treatments in the clinic?

By Robert Lanza and Nadia Rosenthal

SCIENTIFIC AMERICAN
JANUARY 2002
WWW.SCIAM.COM

EXCLUSIVE REPORT

THE FIRST Human Clone

The Clone Makers Tell Their Story

FEBRUARY 19, 2001

IMMIGRATION
EUROPE UNDER SIEGE

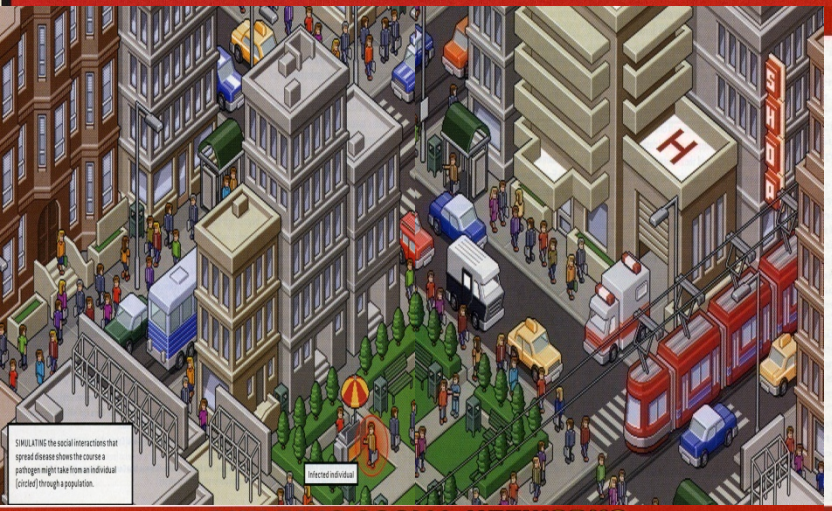
HUMAN CLONING IS CLOSER THAN YOU THINK

For couples who can't have a child—or who have lost one—the unthinkable may soon be possible. Here are the perils

IF SMALLPOX STRIKES PORTLAND ...

BY CHRIS L. BARRETT, STEPHEN G. EUBANK AND JAMES P. SMITH

"EPISIMS" UNLEASHES VIRTUAL PLAGUES IN REAL CITIES TO SEE HOW SOCIAL NETWORKS SPREAD DISEASE. THAT KNOWLEDGE MIGHT HELP STOP EPIDEMICS

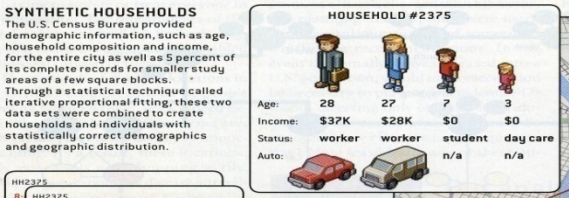


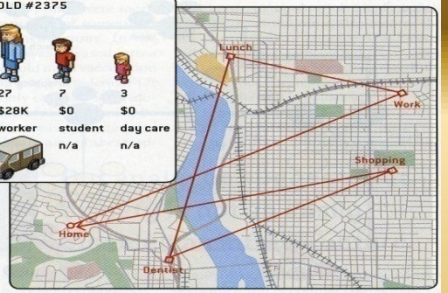
CREATING THE EPISIMS

The original EpiSims model was based on Portland, Ore., but gathering sufficiently detailed information about 1.6 million real people and their activities would have been difficult and intrusive. A synthetic population, statistically indistinguishable from the real one, could nonetheless be constructed and given realistic daily lives using publicly available data.

SYNTHETIC HOUSEHOLDS

The U.S. Census Bureau provided demographic information, such as age, household composition and income, for the entire city as well as 5 percent of its complete records for smaller study areas of a few square blocks. Through a statistical technique called iterative proportional fitting, these two data sets were combined to create households and individuals with statistically correct demographics and geographic distribution.





ACTIVITIES

Most metropolitan planning offices conduct detailed traveler activity surveys for small population samples of a few thousand. These logs track the movements of each household member over the course of one or more days, noting the time of each activity. By matching the demographics of survey respondents to the entire synthetic population, realistic daily activities can be generated for every synthetic household member.

LOCATIONS

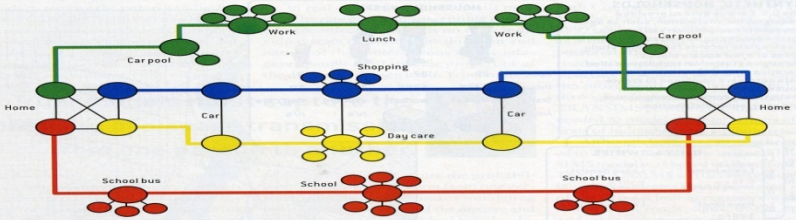
Setting the population in motion requires assigning locations to every household's activities. Land-use data for buildings, parking lots, parks and other places were associated with 180,000 locations in the model, providing estimates of the number of people performing various types of activities there. Activities were anchored to individuals' work or school locations, and then places were chosen for additional activities, such as grocery shopping or recreation, taking into account their distance and other measures of their appeal.

BUILDING SOCIAL NETWORKS

TYPICAL HOUSEHOLD'S CONTACTS

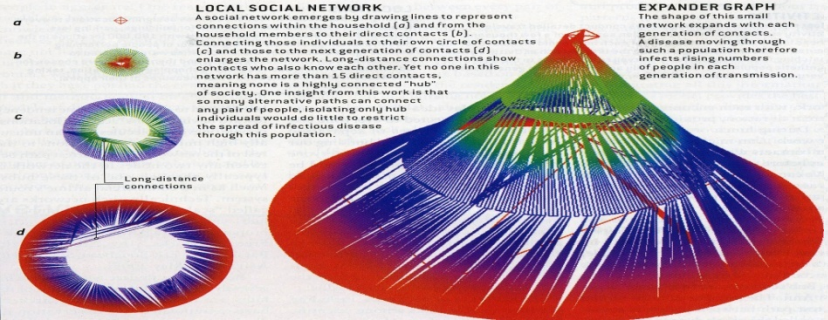
Constructing a social network for a household of two adults and two children starts by identifying their contacts with other people throughout a typical day.

This diagram shows where the household members go and what they do all day but reveals little about how their individual contacts might be interconnected or connected to others.



LOCAL SOCIAL NETWORK

A social network emerges by drawing lines to represent connections within the household (*a*) and from the household members to their direct contacts (*b*). Connecting those individuals to their own circle of contacts (*c*) and those to the next generation of contacts (*d*) enlarges the network. Long-distance connections show contacts who also know each other. Yet no one in this network has more than 15 direct contacts, meaning none is a highly connected "hub" of society. One insight from this work is that so many alternative paths can connect any pair of people, isolating only hub individuals would do little to restrict the spread of infectious disease through this population.



EXPANDER GRAPH

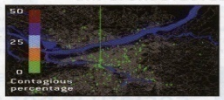
The shape of this small network expands with each generation of contacts. A disease moving through such a population therefore infects rising numbers of people in each generation of transmission.

SIMULATED SMALLPOX ATTACKS

EpiSims animations depict simulated outbreaks and the effects of official interventions. In the still frames below, vertical lines indicate the number of infected people present at a location, and color shows the percentage of them who are contagious. In both scenarios shown, smallpox is released at a university in central Portland, but the attack is not detected until victims start experiencing symptoms 10 days later. The left-hand images show no public health response as a baseline. In the right-hand images, infected and exposed individuals are targeted for vaccination and quarantine. Results from a series of such simulations (*bottom*) show that people withdrawing to their homes early in an outbreak makes the biggest difference in death toll. The speed of official response, regardless of the strategy chosen, proved to be the second most important factor.

DAY 1: UNDETECTED SMALLPOX RELEASE

NO RESPONSE



INFECTED: 1,281
DEAD: 0

TARGETED VACCINATION AND QUARANTINE STARTING DAY 14

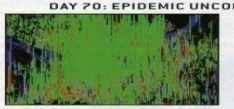
INFECTED: 1,281
QUARANTINED: 0
VACCINATED: 0
DEAD: 0

DAY 35: SMALLPOX EPIDEMIC

INFECTED: 23,919
DEAD: 551

INFECTED: 2,564
QUARANTINED: 29,910
VACCINATED: 30,560
DEAD: 312

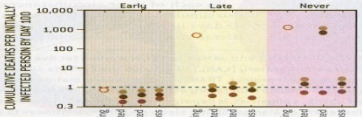
DAY 70: EPIDEMIC UNCONTAINED OR CONTAINED



INFECTED: 380,582
DEAD: 12,499

INFECTED: 2,564
QUARANTINED: 36,725
VACCINATED: 37,207
DEAD: 435

WITHDRAWAL TO HOME



INTERVENTION KEY
- No vaccine
- 10-day delay
- 7-day delay
- 4-day delay

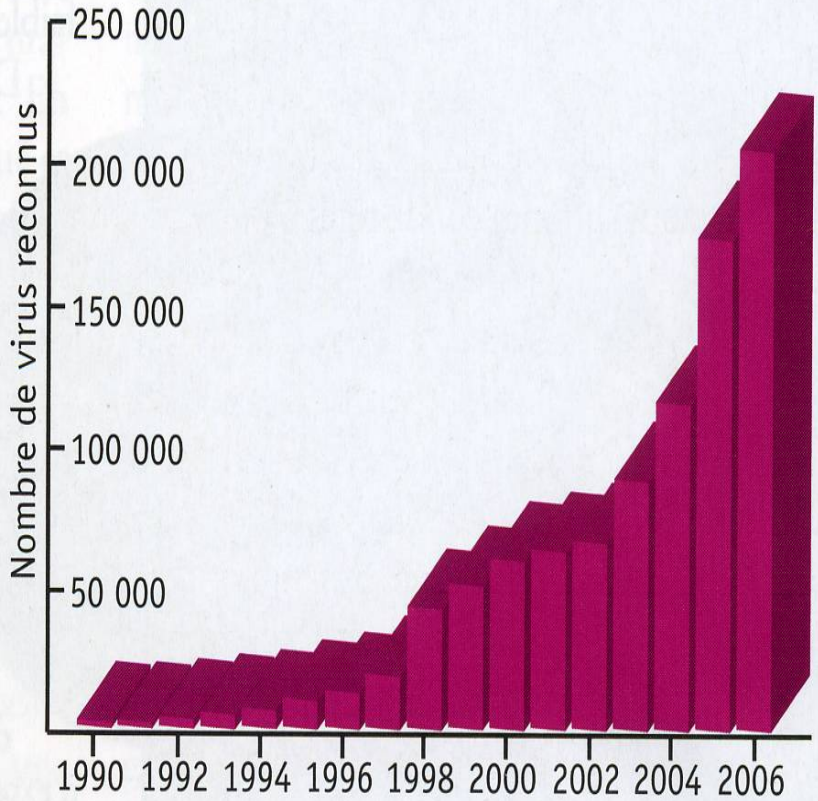
RESPONSE EFFECTIVENESS

Simulations allowed people to withdraw to their homes because they felt ill or were following officials' instructions. Withdrawal could be "early," before anyone became contagious, or "never," meaning people continued moving about unless they died. "Late" withdrawal, 24 hours after becoming contagious, was less effective than early withdrawal, which prevented an epidemic without other intervention. Official responses included doing nothing, or targeted vaccination and quarantine with unlimited personnel, or targeted vaccination limited by only half the necessary personnel being available, or mass vaccination of the entire population. The interventions began four, seven or 10 days after the first victims became symptomatic.

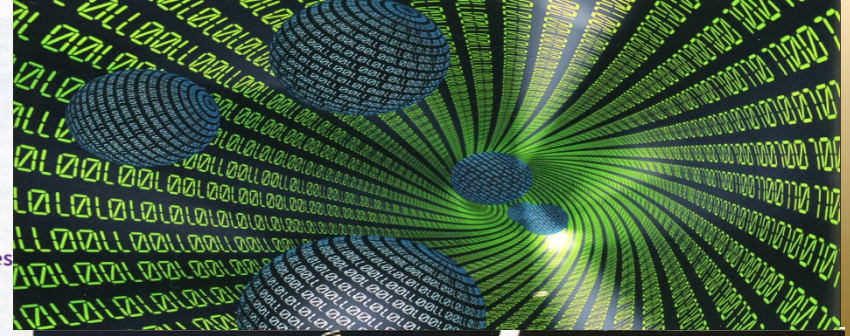
La virologie informatique

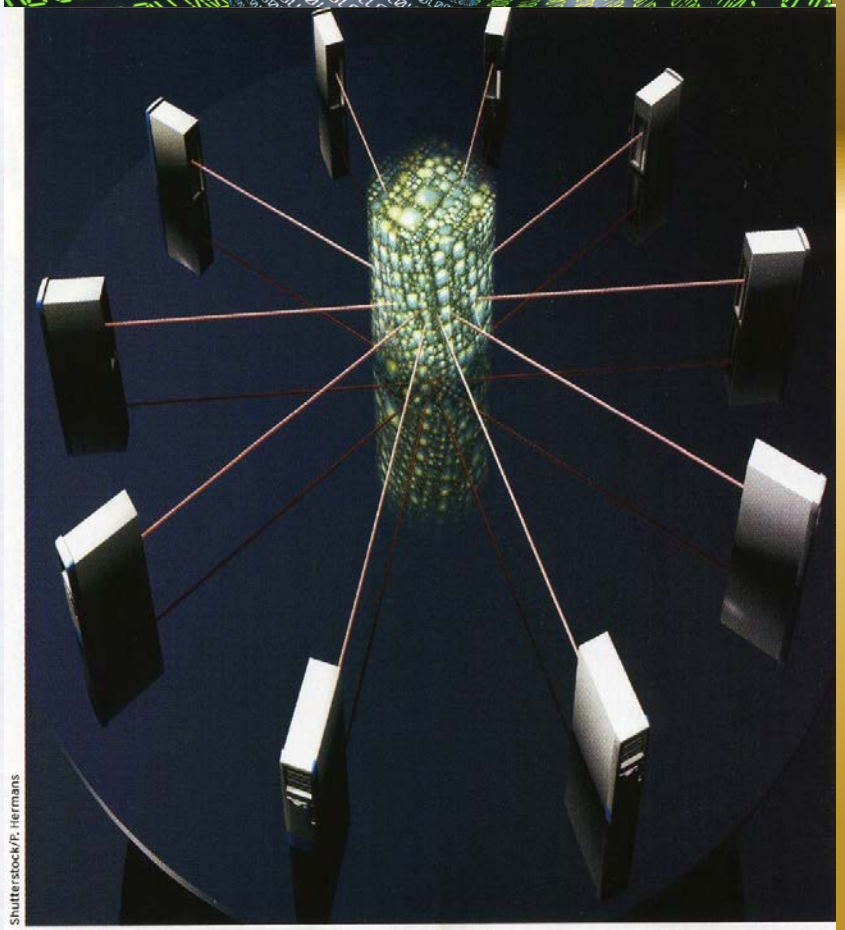
Éric FILIOL et Jean-Yves MARION

L'émergence des virus informatiques échappe à tout contrôle. Seules des mesures « sanitaires » de prévention et de surveillance nous permettront de juguler les épidémies virales sur les réseaux.



2. ÉVOLUTION DU NOMBRE DE VIRUS répertoriés dans les bases de données des logiciels antivirus. Une signature numérique identifie chaque virus et permet ainsi de les repérer lorsque le logiciel filtre les programmes contenus dans l'ordinateur. La barre des 200 000 virus a été dépassée en 2006.



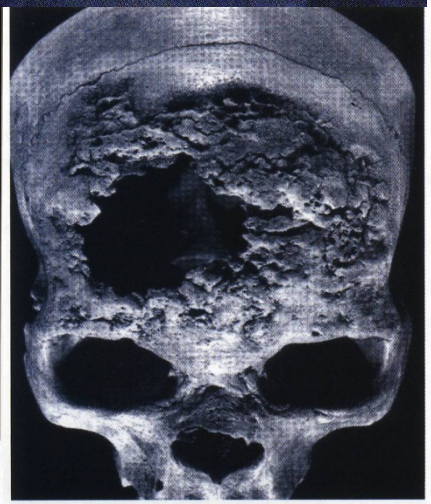


Shutterstock/P. Iiermans

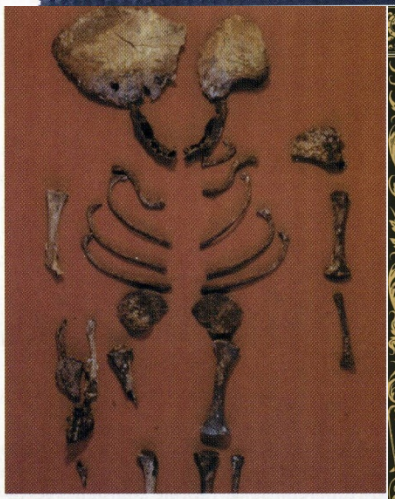
3. LA RÉPLICATION DES VIRUS INFORMATIQUES passe par l'infection d'autres ordinateurs connectés au réseau. Dans le foyer infectieux central, le virus est copié en autant d'exemplaires qu'il existe de cibles. Ce processus diffère de la réplication biologique où les virus se multiplient au sein d'une cellule hôte en des centaines, voire des milliers, d'exemplaires, puis s'en échappent à la recherche d'autres cellules saines.

PALEOPATOLOGIA

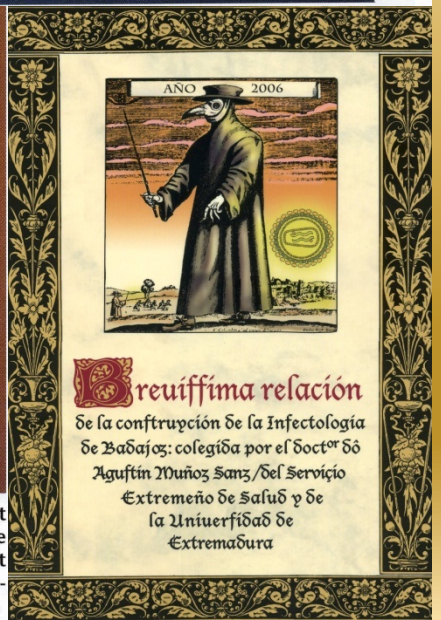
8. Tibia droit d'une jeune femme (Gloucester, XIII^e^-XIV^e^ siècles) présentant une lésion liée à une tréponématose. Antérieur à 1493, ce cas, avec d'autres observations réalisées en Grande-Bretagne, conforte la thèse d'une origine européenne de la syphilis.



9. Crâne féminin présentant des lésions typiques de tréponématose (Mexique, époque pré-colombienne). Les lésions du tréponème, prennent, sur le crâne, un aspect de nodules, nommés gommes.



10. Fœtus d'environ sept mois présent dans la cavité pelvienne de sa mère (Costebelle, IV^e^ siècle). Les lésions résultent d'une syphilis congénitale et infirment l'origine américaine de la maladie.

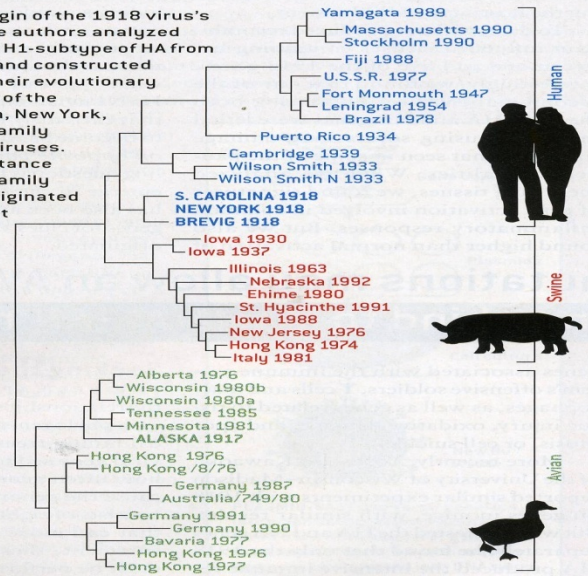


Capturing a Killer Flu virus

INFLUENZA VICTIMS lie at U.S. Army Camp Hospital No. 45, Aix-les-Bains, France, in 1918. Flu killed 43,000 American servicemen mobilized for World War I, representing nearly 40 percent of U.S. military casualties.

Flu Family Tree

Seeking clues to the origin of the 1918 virus's hemagglutinin (HA), the authors analyzed gene sequences for the H1-subtype of HA from a variety of flu strains and constructed a phylogeny showing their evolutionary relationships. Samples of the 1918 strain (S. Carolina, New York, Brevig) fell within the family of human-adapted flu viruses. The 1918 H1 gene's distance from the known avian family could indicate that it originated in an avian flu strain but spent time evolving in an unidentified host before emerging in 1918. Supporting this conclusion, a contemporary avian strain found in a preserved Brant goose (Alaska 1917) was evolutionarily distant from the 1918 strain and more similar to modern bird flus.



GENETIC TRAPS for VIRUSES

REVERSE ENGINEERING THE FLU

When analyzing the genes of the 1918 virus revealed no definitive reasons for the pandemic strain's virulence, our group turned to reverse genetics—a method of understanding the function of genes by studying the proteins they encode. In collaboration with scientists from the Mount Sinai School of Medicine, the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, the University of Washington and the Scripps Research Institute, we "built" influenza viruses containing one or more of the 1918 virus's genes, so we could see how these recombinant viruses behaved in animals and human cell cultures.

To construct these viruses, we employed a new technique called plasmid-based reverse genetics, which requires first making DNA copies of flu genes that normally exist in RNA form. Each DNA gene copy is then inserted into a tiny ring of DNA called a plasmid. Different combinations of these plasmids can be injected into living cells, where cellular machinery will execute the genetic instructions they bear and manufacture flu viruses with only the desired combination of genes.

Reverse genetics not only allows us to study the 1918 virus, it will allow scientists in the U.S. and Europe to explore how great a threat the H5N1 avian flu virus poses to humans. Since January 2004, that strain—which is now present in birds in 10 Asian countries—has infected more than 40 people, killing more than 30 of them. One of the casualties was a mother who is believed to have contracted the virus from her daughter, rather than directly from a bird.

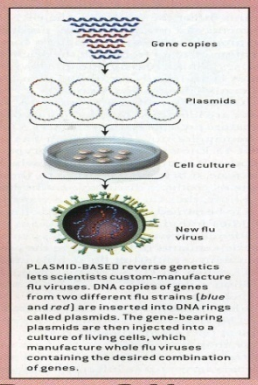
Such human-to-human transmission could suggest that in their case the avian virus had adapted to be more easily spread between humans, either by mutating or by acquiring new genes through reassortment with a circulating human flu strain. That dreaded development would increase the possibility of a human pandemic. Hoping to predict and thereby prevent such a disaster, scientists at the CDC and Erasmus University in the Netherlands are planning to test combinations of H5N1 with current human flu strains to assess the likelihood of their occurring naturally and their virulence in people.

What these experiments will reveal, as in our group's work with the 1918 virus genes, is crucial to understanding how influenza pandemics form and why they cause disease. Some observers have questioned the safety of experimenting with lethal flu strains, but all of this research is conducted in secure laboratories designed specifically to deal with highly pathogenic influenza viruses.

What is more, re-creating the 1918 virus proteins enabled us to establish that currently available antiviral drugs, such as amantadine or the newer neuraminidase inhibitors, such as oseltamivir (Tamiflu), would be effective against the 1918 strain in the case of an accidental infection. The H5N1 viruses are also sensitive to the neuraminidase inhibitors.

Scientists in the U.S. and U.K. also recently employed plasmid-based reverse genetics to create a seed strain for a human vaccine against H5N1. They made a version of the H5N1 virus lacking the wild strain's most deadly features, so that manufacturers could safely use it to produce a vaccine [see "The Scientific American 50," December 2004]. Clinical trials of that H5N1 vaccine were scheduled to begin at the end of 2004.

—J.K.T., A.H.R. and T.G.F.



PLASMID-BASED reverse genetics lets scientists custom-manufacture flu viruses. DNA copies of genes from two different flu strains (*blue* and *red*) are inserted into DNA rings called plasmids. The gene-bearing plasmids are then injected into a culture of living cells, which manufacture whole flu viruses containing the desired combination of genes.

Persistence Pays Off

Visiting Alaska in the summer of 1949, Swedish medical student Johan Hultin met Lutheran missionaries in Fairbanks who told him of the 1918 flu pandemic's toll on Inuit villages. One, a tiny settlement on the Seward Peninsula called Teller Mission, was all but wiped out in November 1918. Overwhelmed missionaries had to call in the U.S. Army to help bury 72 victims' bodies in a mass grave, which they marked by two crosses.

Haunted by the story, Hultin (*right, center* and *below*) headed to the University of Iowa to begin his doctoral studies in microbiology. There he kept thinking about the 1918 pandemic and wondering if the deadly virus that caused it could be retrieved for study from bodies that may have been preserved by the Alaskan permafrost. In the summer of 1951, Hultin convinced two Iowa faculty, a virologist and a pathologist, to visit the village, then called Brevig Mission. With permission from tribal elders, the scientists excavated the grave and obtained tissue specimens from what remained of several victims' lungs.

HULTIN in Brevig grave, 1951

Back in Iowa, the team tried and tried to grow live virus from the specimens but never could. In retrospect, that was perhaps just as well since biological containment equipment for dangerous pathogens did not exist at the time.

Hultin's disappointment led him to abandon his Ph.D. and become a pathologist instead. Retired and living in San Francisco in 1997, Hultin read our group's first published description of the 1918 genes we retrieved from autopsy specimens, and it rekindled his hope of finding the entire 1918 virus. He wrote to me, eager to try to procure new lung specimens from Brevig Mission for us to work with. He offered to leave immediately for Alaska, and I agreed.

At the same time, Hultin tracked down his 1951 expedition mates to ask if they had kept any of the original Brevig specimens. We reasoned that those tissue samples obtained just 33 years after the pandemic and then preserved might be in better condition than specimens taken later. As it turned out, one of Hultin's colleagues had kept the material in storage for years but finally deemed it useless and threw it out. He had disposed of the last specimens just the year before, in 1996.

Fortunately, Hultin once again got permission from the Brevig Mission Council to excavate the 1918 grave in August 1997. And this time he found the body of a young woman who had been obese in life. Hultin said later that he knew instantly her tissue samples would contain the 1918 virus—together with the cold temperature, her thick layer of fat had almost perfectly preserved her lungs. He was right, and her tissue provided us with the entire genome of the 1918 pandemic virus. *—J.K.T.*

HULTIN in Brevig grave, 1997

MANUEL DA SILVA ROSA | ERIC J. STEELE

O MISTÉRIO COLOMBO REVELADO

Ruggero Marino

CRISTÓVÃO COLOMBO

O ÚLTIMO DOS TEMPLÁRIOS

OS SEGREDOS DO NAVEGADOR E DA DESCOBERTA DA AMÉRICA

O caso clínico de

EÇA DE QUEIRÓS

CONSIDERAÇÕES DE UM GASTRENTEROLOGISTA

Ireneu Cruz

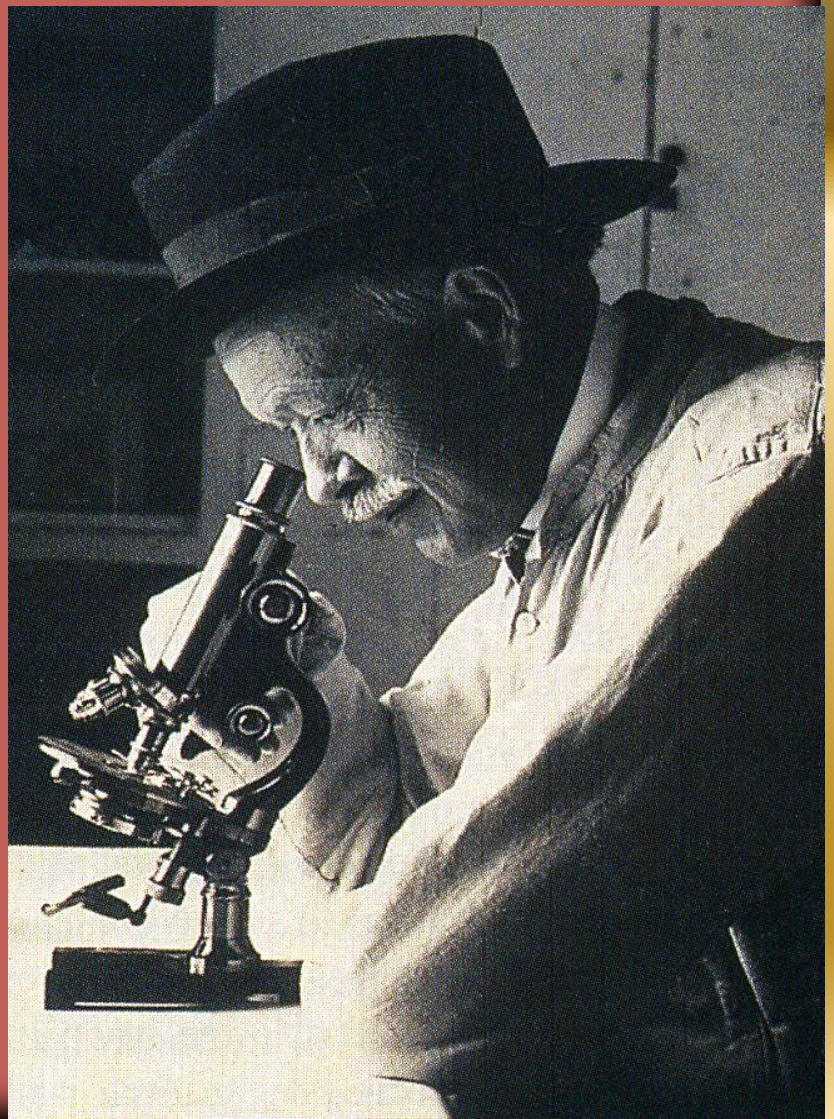
O HÁBITO DE BEBER NO CONTEXTO EXISTENCIAL E POÉTICO DE FERNANDO PESSOA

FRANCISCO MANUEL DA FONSECA FERREIRA

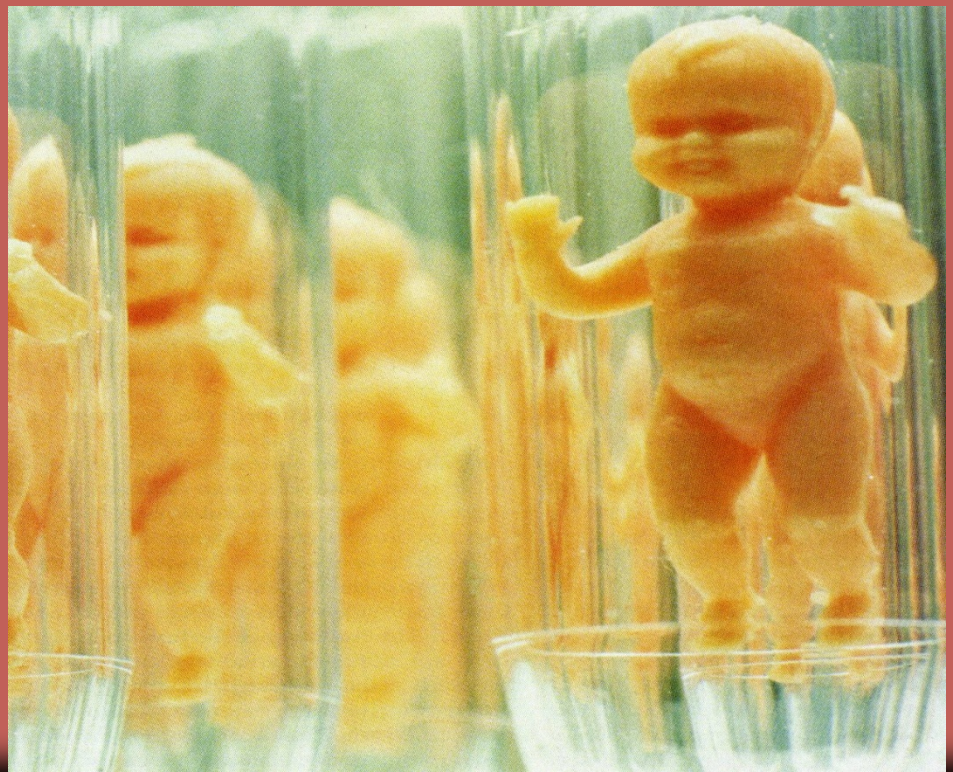
Prémio **Bial** 1994

Charles Nicolle, Prémio Nóbel da Medicina, 1928

- **"… irão haver sempre novas doenças. É uma fatalidade. Uma outra fatalidade, é o facto de nós não sermos imediatamente capazes de determinar a sua etiologia. Devemo-nos pois resignar com a ignorância perante os primeiros casos. Eles serão, pelo desconhecimento, encarados como uma doença já conhecida …" sic.**



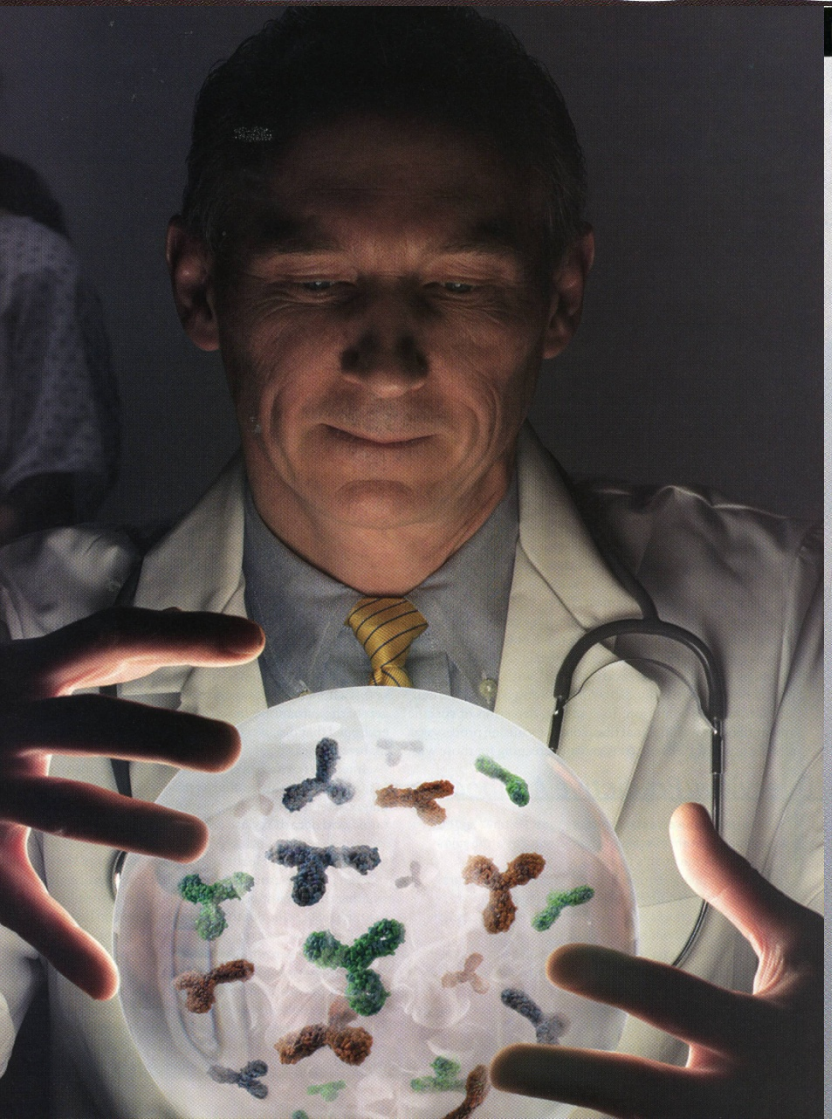
Qual será afinal o próximo objectivo da Ciência Médica ?...



Will you get sick?

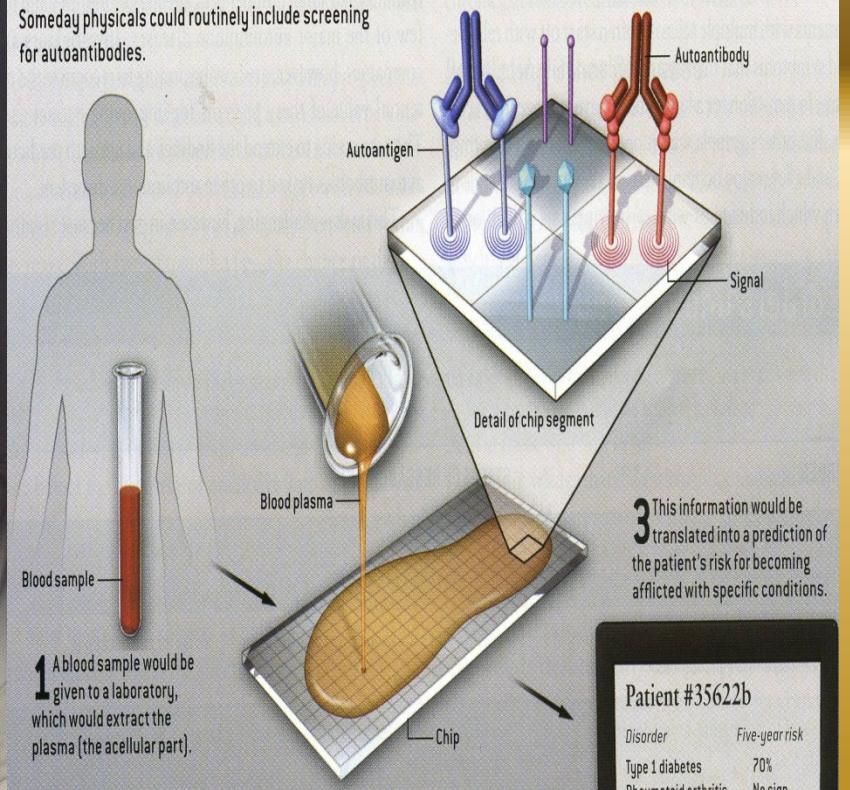
Antibodies could foretell the future of your health

Predicting Disease



CHECKUPS OF THE FUTURE

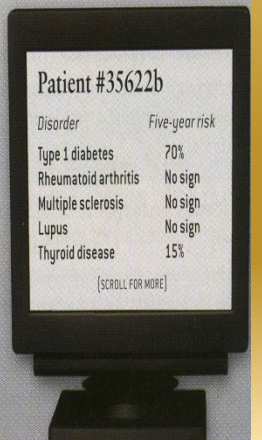
Someday physicals could routinely include screening for autoantibodies.



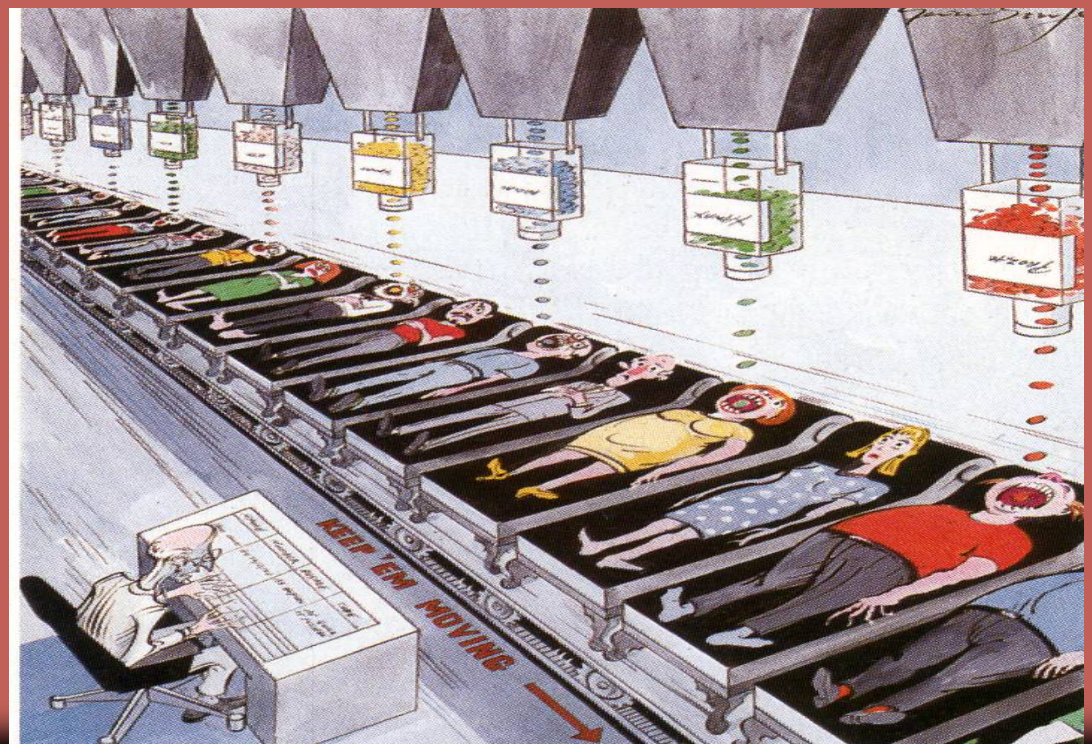
1 A blood sample would be given to a laboratory, which would extract the plasma (the acellular part).

2 The plasma would be washed over a chip containing an array of autoantigens—molecules known to be capable of eliciting autoimmune reactions—at known positions. Any autoantibodies in the blood would bind to the autoantigens, triggering signals indicating the identity and quantity of the bound autoantibodies.

3 This information would be translated into a prediction of the patient's risk for becoming afflicted with specific conditions.



E qual será então a ambição última da Espécie Humana ?...

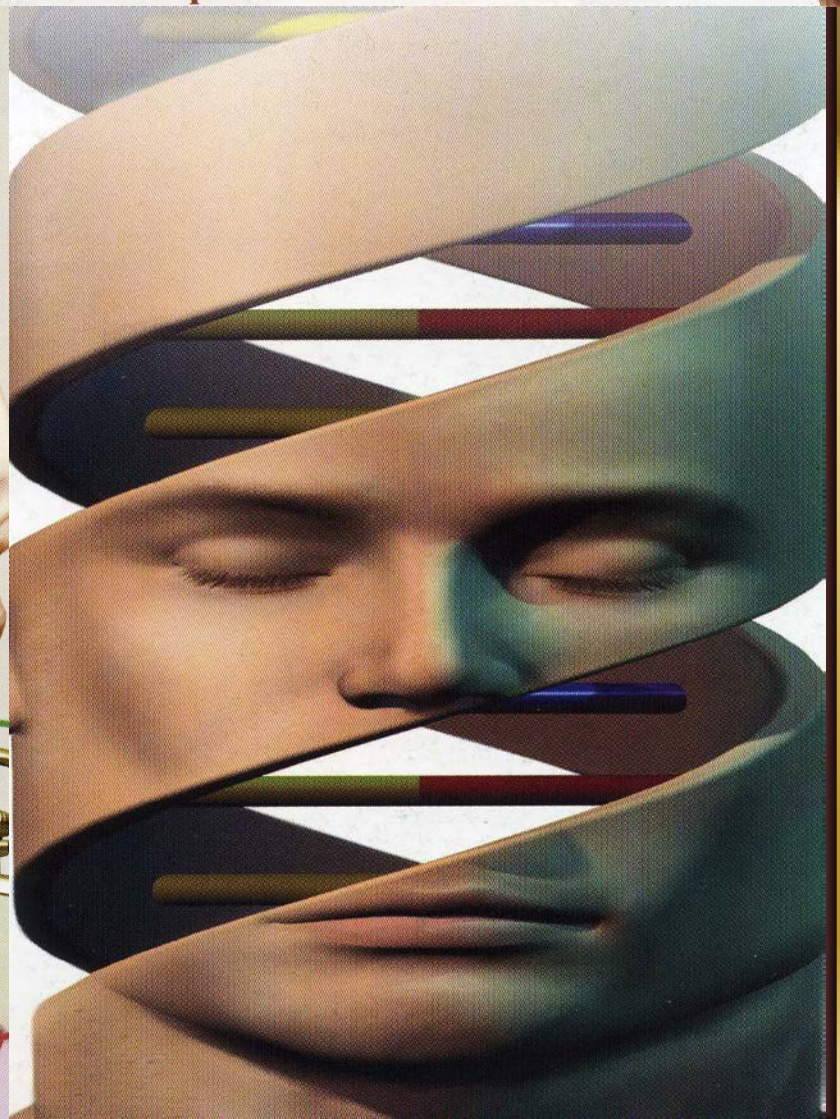


Can DNA Stop Time?

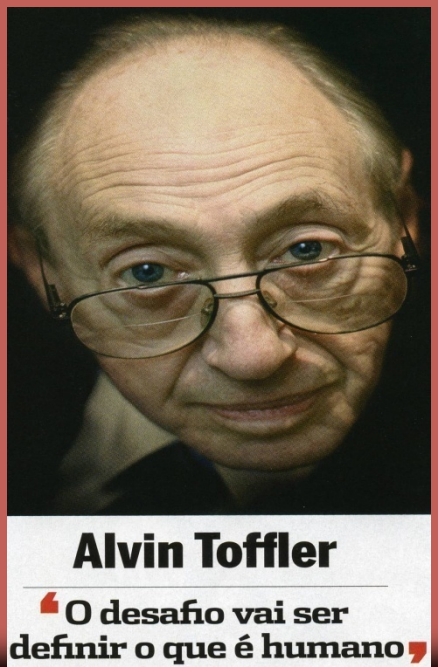
UNLOCKING THE SECRETS OF **LONGEVITY GENES**

Know Your DNA

Inexpensive **gene readers** will soon unlock the secrets in your personal double helix



E ainda: O que é que deu origem à VIDA, e qual será o "*destino*" do HOMEM ?...



Ceux que nous appelions des brutes eurent leur revanche quand Darwin nous prouva qu'ils étaient nos cousins.
George Bernard Shaw

Les derniers hominidés se sont-ils **croisés** ?

On ne peut pas l'écarter : l'hybridation, mécanisme réputé pour produire une descendance stérile, a pu être à l'œuvre dans l'évolution humaine. Des traces fossiles récemment découvertes le suggèrent même fortement.

Le fait que le cerveau humain soit l'objet neurologique le plus complexe de la planète ne signifie pas que l'homme soit l'être le plus complexe.
Stephen Jay Gould

L'apparition de l'homme était-elle inévitable ?

S'il était possible de remonter 500 millions d'années et de dérouler à nouveau la chaîne du vivant, l'évolution aurait-elle conduit à la même biodiversité ? Des êtres sociaux et intelligents comme *Homo sapiens* auraient-ils émergé ? La possibilité que l'évolution ait un sens demeure, encore aujourd'hui, âprement débattue.

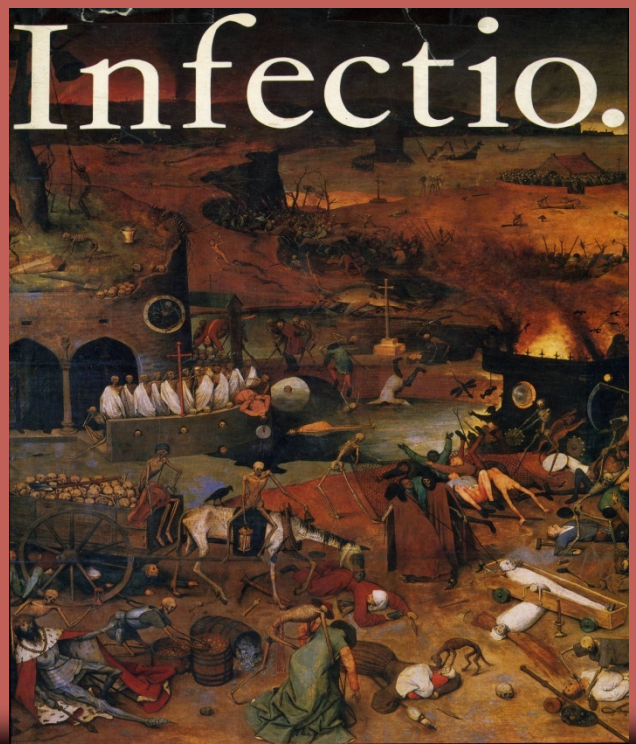
Des virus ont-ils inventé l'ADN ?

Patrick FORTERRE

Depuis leur découverte, les virus sont restés exclus de l'arbre de l'évolution. Aujourd'hui, de nombreux biologistes discutent ce fait, et donnent aux virus un rôle primordial dans les changements subis par nos cellules ancestrales.

VIRUS La fin de l'Homme ?

Notas Finais



“As Epidemias na História do Homem”

J-C. Sournia e J. Ruffie, 1984

- **“… doenças que não consideramos actualmente de origem infecciosa são-no talvez e, na ignorância que estamos acerca do seu determinismo, algumas que são presentemente endémicas, podem um dia vir a tornar-se epidémicas. Os progressos da ciência, particularmente da Medicina, foram tais desde há meio século que acreditámos possuir o domínio total da natureza que nos cerca. Nada há de mais falso. O Homem continua a ser tão frágil como foi, e a sua adaptação e defesa contra o meio muitas vezes agressivo que o cerca devem renovar-se incessantemente: ele deverá inventar sempre novas armas contra novos inimigos …” (sic)**

- **“… o nosso futuro não está numa imortalidade física, que no nosso estádio complexo de organização se situa fora das leis biológicas. Encontra-se numa sociedade acolhedora e fraterna, onde cada um teria o seu lugar até ao último dia e que seria capaz de trazer a todos, longe da angústia e da solidão demasiadas vezes quotidianas, uma velhice feliz e com uma vida que acabasse doce, pacífica e aceite …” (sic)**

Un lion mort ne vaut pas un moucheron qui respire.
Voltaire

De fausses bonnes raisons de mourir

- “… se nós não morresse-mos, a biosfera não o suportaria por muito tempo. E como é que as espécies iriam então passar a evoluir? A ideia que a senescência e a morte têm uma função biológica na própria vida continua válida …” (sic) *André Karlsfeld*
- “ a evolução e a imortalidade são conceitos incompatíveis. Se os organismos evoluem aperfeiçoando-se e renovando-se periodicamente, então a morte constitui um fenómeno tão necessário como a própria reprodução …” (sic) *Sir Franck Burnet* (Nóbel da Medicina, 1960)
- “… a morte é pois imposta a partir do interior do ser, como uma necessidade prescrita, desde a formação do ovo, como que através de um programa genético intrínseco à própria vida …” (sic) *François Jacob*

ENVIRONMENT

An Earth WITHOUT PEOPLE

A new way to examine humanity's impact on the environment is to consider how the world would fare if all the people disappeared

Interview with ALAN WEISMAN

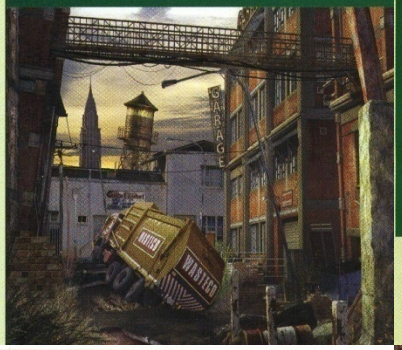
HUMANITY'S LONG FADE-OUT: A TIMELINE FOR THE FALL OF NEW YORK

2 DAYS AFTER THE DISAPPEARANCE OF HUMANS
Without constant pumping, New York City's subway system completely fills with water.

7 DAYS
Nuclear reactors burn or melt down as their water-cooling systems fail.

1 YEAR
Street pavements split and buckle as water in the cracks freezes and thaws.

2 TO 4 YEARS
In New York and other cities, cracked streets become covered with weeds and, later, colonizing trees whose roots upheave sidewalks and wreak havoc with already damaged sewers.



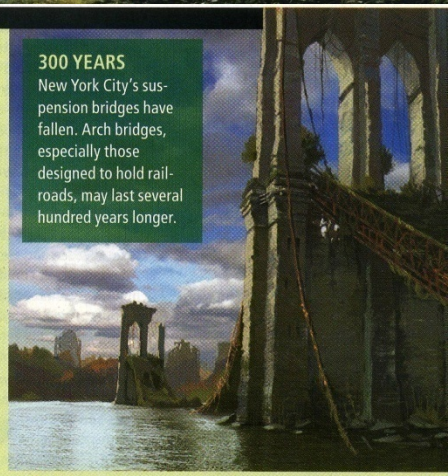
4 YEARS
Without heat, homes and office buildings fall victim to the freeze/thaw cycle and begin to crumble.

5 YEARS
Large parts of New York may be burned by now; a lightning strike on uncollected dead branches in Central Park could easily start a catastrophic fire.

20 YEARS
Dozens of streams and marshes form in Manhattan as collapsed streets fill with water.

100 YEARS
The roofs of nearly all houses have caved in, accelerating the deterioration of the structures.

300 YEARS
New York City's suspension bridges have fallen. Arch bridges, especially those designed to hold railroads, may last several hundred years longer.

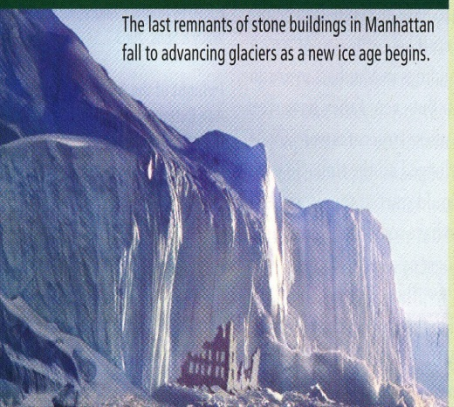


500 YEARS Mature forests cover the New York metropolitan area.

HUMANITY'S LONG FADE-OUT

5,000 YEARS
As the casings of nuclear warheads corrode, radioactive plutonium 239 is released into the environment.

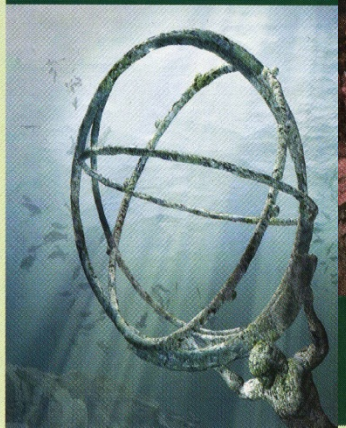
15,000+ YEARS
The last remnants of stone buildings in Manhattan fall to advancing glaciers as a new ice age begins.

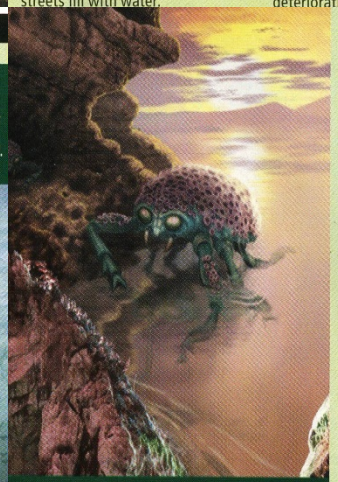


35,000 YEARS
Lead deposited in the soil from automobile emissions in the 20th century finally dissipates.

100,000 YEARS
The concentration of carbon dioxide in the atmosphere returns to preindustrial levels.

10 MILLION YEARS
Bronze sculptures, many of which still retain their original shape, survive as relics of the human age.





1 BILLION+ YEARS
As the sun brightens, the earth heats dramatically, but insects and other animals may adapt.

5 BILLION YEARS
The earth vaporizes as the dying sun expands and consumes all the inner planets.

TRILLIONS OF YEARS
Broadcasts of *The Twilight Zone* and other television shows, faint and fragmented, still travel outward through space.