Conservation Medicine –

New Health Concept and Inter-Discipline

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From SARS to Bird Flu

- **SARS，为祸源头在哪里？** 作者:张树义 来源:科学时报
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俗话说，他山之石，可以攻玉；前事不忘，后事之师。最近，全球被SARS搞得鸡犬不宁，人们都在问：这个造成“非典”的“坏小子”——冠状病毒变种，究竟从哪里来？对这个问题，目前自然是不敢贸然回答，但参考一下最近几十年爆发的几场病毒性流行疫病，我们也许会看到一点蛛丝马迹。

ＳＡＲＳ，源自何方？

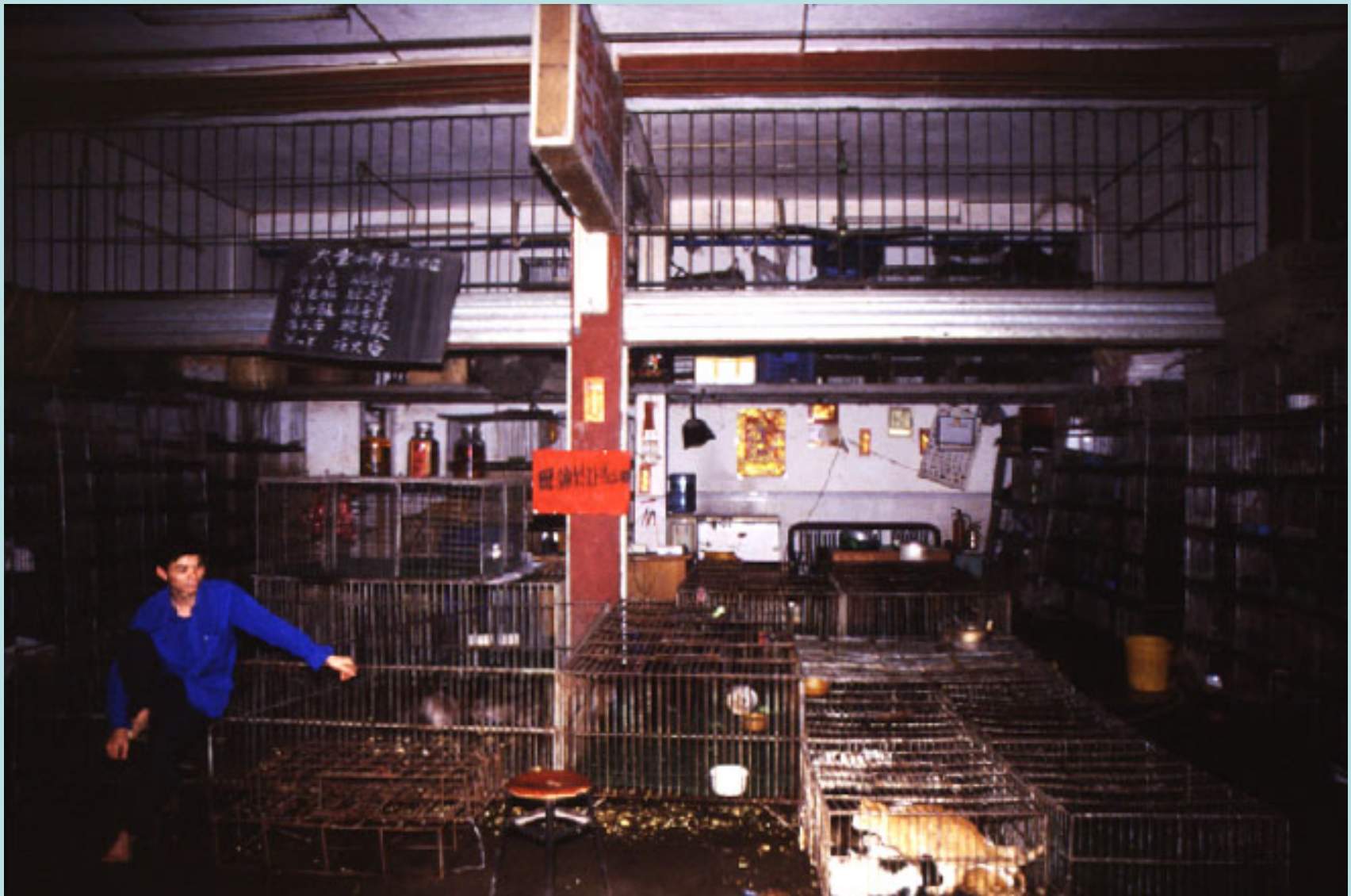
这里需要再次重申：目前绝不敢贸然说造成ＳＡＲＳ的冠状病毒变种来自何方。但如果它真是来自动物，也只有两种可能：一是来自饲养的动物，发生了变异；二是来自野生动物，这种野生动物可能原本与人类根本不发生关系。如果是后者，那么可以说，ＳＡＲＳ是来自人类自身的行为。

首先，病毒的爆发可能与自然环境的骤变有关，尼巴病毒的泛滥是前车之鉴。目前，在我国华南地区，一种果蝠——棕果蝠的数量很庞大，而且与人类发生密切的直接接触。１９９９年，在广西的一个洞穴，我们就观察到数千只棕果蝠。种群庞大的棕果蝠每年吃掉大量的龙眼和荔枝等栽培水果，也把我们带到了一个暴露于人兽共患病病毒的状态。不难想象，被棕果蝠接触过的水果有可能再被人吃到。但这也不能归罪于这些动物，因为它们在自然状态下栖息的原始森林已不存在，它们已经没有或者很少有属于自己的生存空间。我国曾有过个别关于棕果蝠病原学的研究工作，从血清内分离到乙型脑炎病毒，说明它们至少对乙脑病毒在自然界的贮存和扩散方面起作用。

其次，病毒的爆发可能与人类吃野生动物或其它类似的活动有关，埃博拉和艾滋病毒的爆发就是例子。迄今为止，人们普遍认为，埃博拉这种恶性传染病在刚果多次爆发的主要原因与当地居民习惯食用野生动物、特别是灵长类动物有关。在此次ＳＡＲＳ率先爆发的地区，吃“野味”是人们常见的和“高档”的事情。我们最近几年在该地区考察时，就发现不少当地人吃果蝠，甚至吃小蝙蝠。当然，鲜活的“猴头”早已是一道名菜了。除此之外，果子狸、穿山甲等其它兽类也被大吃特吃，尽管果子狸有如下症状的狸温热：突然高烧，３－５天后降至常温；有明显的呼吸道症状，剧烈喷嚏，鼻孔流出液样分泌物，并伴有眼结膜炎、咽喉炎；病狸烦燥不安，尖叫不停，最后出现严重的脱水或衰竭死亡。

一次次的病毒爆发反反复复地告诫人们：维护自然、尊重自然界中的其它生命，就是保护人类自身。这真的不只是一句口号！

Guangzhou Xinyuan wildlife market (2003)



Guan Y, BJ Zheng, YQ He, XL Liu, ZX Zhuang, CL Cheung, SW Luo, PH Li, LJ Zhang, YJ Guan, KM Butt, KL Wong, KW Chan, W Lim, KF Shortridge, KY Yuen, JSM Peiris, LLM Poon. **(2003). Isolation and Characterization of Viruses Related to the SARS Coronavirus from Animals in Southern China. Science. 302(5643): 276-278**

He JF, Peng GW, Min J, Yu DW, Liang WJ, **Zhang SY ...Zhao GP (2004)** Molecular evolution of the SARS-coronavirus during the course of the SARS epidemic in China. ***Science*** 303: 1666-1669.

Molecular Evolution of the SARS Coronavirus During the Course of the SARS Epidemic in China

The Chinese SARS Molecular Epidemiology Consortium*

Sixty-one SARS coronavirus genomic sequences derived from the early, middle, and late phases of the severe acute respiratory syndrome (SARS) epidemic were analyzed together with two viral sequences from palm civets. Genotypes characteristic of each phase were discovered, and the earliest genotypes were similar to the animal SARS-like coronaviruses. Major deletions were observed in the Orf8 region of the genome, both at the start and the end of the epidemic. The neutral mutation rate of the viral genome was constant but the amino acid substitution rate of the coding sequences slowed during the course of the epidemic. The spike protein showed the strongest initial responses to positive selection pressures, followed by subsequent purifying selection and eventual stabilization.

Severe acute respiratory syndrome (SARS) first emerged in Guangdong Province, China. Subsequently, the SARS coronavirus (SARS-CoV) was identified as the causative agent (*1*–*5*). It remains a challenge to establish the relationship between observed genomic variations and the biology of SARS (*4*–*8*). Recent molecular epidemiological studies have identified characteristic variant sequences in SARS-CoV for tracking disease transmission (*7*, *9*–*11*). Evidence suggests that SARS-CoV emerged from nonhuman sources (*8*, *12*). In this study, we sought epidemiological and genetic evidence for viral adaptation to human beings through molecular investigations of the characteristic viral lineages found in China (*13*).

On the basis of epidemiological investigations (*14*), we divided the course of the epidemic into early, middle, and late phases (Fig. 1). The early phase is defined as the period from the first emergence of SARS to the first documented superspreader event (SSE) (*13*). The middle phase refers to the ensuing events up to the first cluster of SARS cases in a hotel (Hotel M) in Hong Kong (*15*). Cases following this cluster fall into the late phase.

The early phase was initially characterized by a series of seemingly independent cases. Eleven index cases that had arisen locally in the absence of any contact history were identified from different geographical locations within Guangdong Province (fig. S1). This phenomenon was observed from the retrospectively identified SARS index patient from the city of Foshan (onset date, 16 November 2002) (*13*) through to an index patient from the city of Dongguan (onset date, 10 March 2003). All of these cases were confined to regions directly west of Guangzhou, the capital city of Guangdong Province, and to the city of Shenzhen in the south, with no cases being reported to the north or east of Guangzhou (Fig. 1) (fig. S1). This region, the Pearl River Delta, has enjoyed rapid economic development since the late 1970s, leading to the adoption of culinary habits requiring exotic animals. Seven of these 11 cases had documented contact with wild animals. In contrast to the apparently independent seeding of the earliest cases, the rest of the epidemic was characterized by SSEs and clusters of cases that were epidemiologically linked (Fig. 1) (fig. S1) (*10*, *11*, *13*, *15*, *16*).

The first major SARS outbreak occurred in a hospital, HZS-2, in the city of Guangzhou, beginning on 31 January 2003 where an SSE was identified to be associated with more than 130 primary and secondary infections, of which 106 were hospital-acquired cases. Doctor A, a nephrologist who worked in this hospital, visited Hong Kong and stayed in Hotel M on 21 February 2003. Other visitors to the hotel later became infected with SARS-CoV (*13*, *15*). This led to the transmission of SARS to Vietnam, Canada, Singapore, and the United States (*17*) with two further SSEs in Hong Kong, each resulting in the virus being transmitted to >100 contacts (*10*, *16*).

Genomic sequence data for SARS-CoV were largely derived from isolates linked to the Hotel M cluster (*6*), hence they were predominantly from the late phase of the epidemic. We determined 29 SARS-CoV genomic sequences obtained from 22 patients from Guangdong Province with disease onset dates in all three phases of the epidemic, and from two patients from the late phase in Hong Kong. To eliminate mutational noise, we assumed that sequence variants associated with common ancestry, but not arising in cell culture, should be seen in multiple isolates (*7*). Meanwhile, critical genomic variations or complete genome sequences of certain virus isolates were verified by sequencing the reverse transcription polymerase chain reaction (RT-PCR) products derived directly from patient specimens (*14*). The genomic sequences obtained were compared with 32 human SARS-CoV sequences and two SARS-like coronavirus sequences from Himalayan palm civets (*Paguma larvata*) available at GenBank as of the end of September 2003 (Fig. 2).

Only two major genotypes predominated during the early phase of the epidemic. Five isolates were found to contain a 29-nucleotide (nt) sequence that is absent in most of the publicly available SARS-CoV

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naviruses isolated from farmed civets in Hubei Province, China (*19*). It is thus interesting to note that both sequences of the early phase were identified from other mammalian hosts. They provided a link to support the notion that early human infection of SARS-CoV may have originated from wild animals (*8*, *12*).

In contrast to the early phase, a SARS-CoV sequence with the 29-nt deletion was observed during the middle phase that dominated the viral population for the rest of the epidemic (*4*, *5*, *7*). Although this shift in genome size might be due to chance, deletion

deletion rates in this region. Whether such hairpin structures actually play a role in regulating either RNA replication or mRNA transcription in SARS-CoV is a subject for future studies.

Besides the deletion variants, 299 single-nucleotide variations (SNVs) were detected among the 63 sequences. Eighty-five of these variant loci were seen in more than one of the human SARS-CoV sequences. Among them, 52 were predicted to cause amino acid changes (nonsynonymous variations) (table S2). When the epidemiologically determined transmission paths and SNV genotype data

BJ03, traceable to Guangdong. The transition between the characteristic motifs of the early and middle phases represented a G→T transversion at nucleotide residue 23,823 and is predicted to cause an Asp → Tyr change at amino acid residue 778 of the spike (S) protein (fig. S4).

An additional A→G transition at nucleotide 21,721 (Fig. 2) (fig. S4) was identified in one isolate from a secondarily infected patient from Hospital HZS-2 with disease onset on 7 February 2003 (HZS2-Fc) (Fig. 2). This sequence was additionally confirmed by direct sequencing of the RT-PCR product from

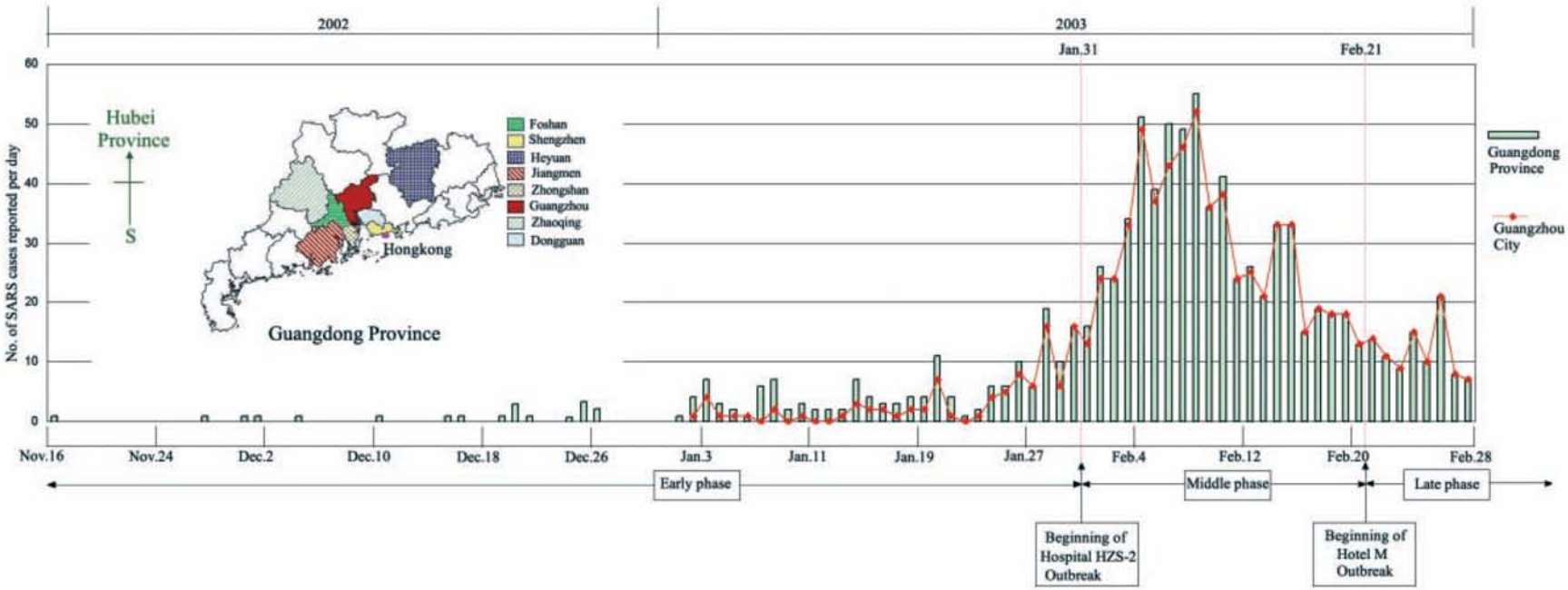

Fig. 1. The triphasic SARS epidemic in Guangdong Province, China. Shown are daily numbers of SARS cases reported in Guangdong Province, in particular the city of Guangzhou. The early, middle, and late phases of the epidemic are defined in the text. The map shows the geographical distribution of cases belonging to the early phase by administrative districts of Guangdong Province. The detailed data for individual cities are presented in fig. S1.

the S protein (Thr^{244} → Ile), and Orf8a tissue tropism (*24*). We noticed that the neu-

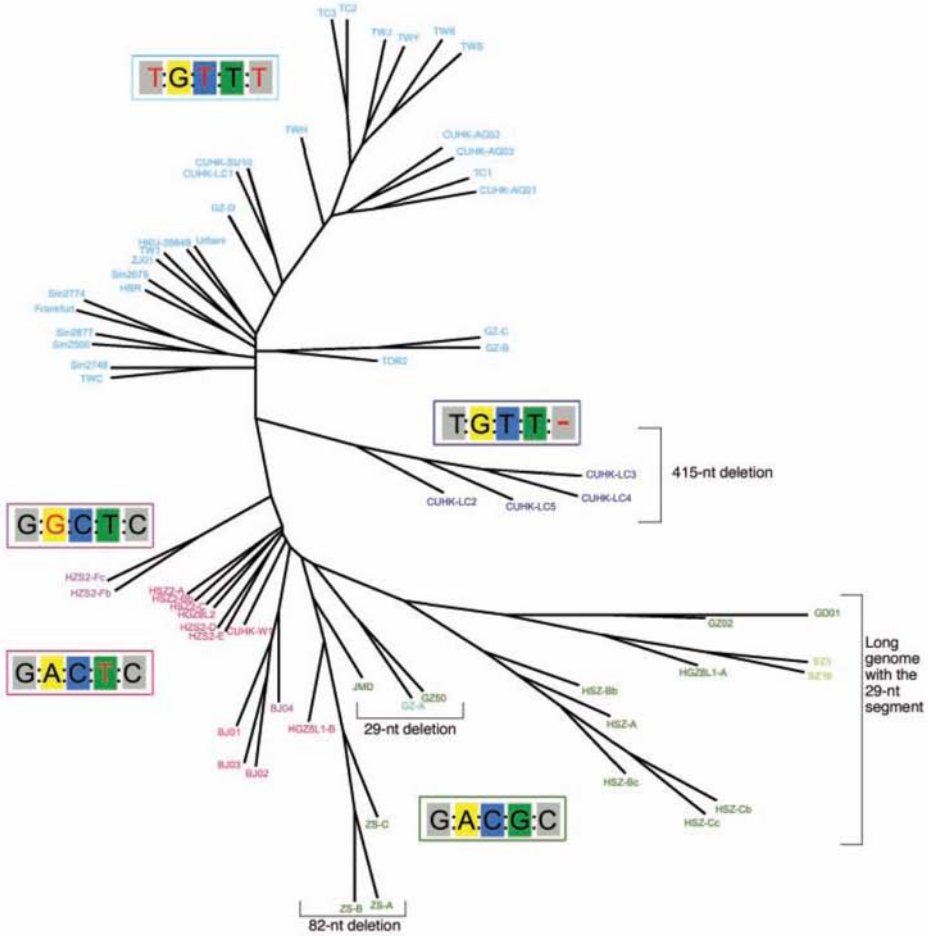

Fig. 2. Genotype clustering of SARS-CoV during the course of the epidemic. An unrooted phylogenetic tree of SARS-CoV is constructed from 61 human SARS-CoV genomes and two SARS-like coronavirus sequences from palm civets. Only those variant sequences (including deletions) that were present in at least two independent samples were used for tree construction (table S2). The map distance between individual sequences represents the extent of genotypic difference. The 5-nt motifs (see text) that characterized the phylogenetically related genotypes are boxed. The genomic sequences are named in concordance with their GenBank nomenclature and are represented in different colors according to the genotype clusters determined by our scoring method (table S2). Genotypes with major deletions are marked specifically (see text). All other genotypes (unmarked) had the 29-nt deletion. This 29-nt deletion was specifically marked for three genotypes, namely GZ-A, JMD, and GZ50, to indicate their special clustering within the early-phase isolates.

the rates of nonsynonymous to synonymous changes (Ka/Ks) for the S gene sequences were always greater than 1, indicating an overall positive selection pressure. However, pairwise analysis of the Ka/Ks for the genotypes in each epidemic group (fig. S6) (*14*) shows that the average Ka/Ks for the early phase was significantly larger than that for the middle phase, which in turn was significantly larger than the ratio for the late phase, which in fact was significantly less than 1 (table S3). These data indicate that the S gene showed the strongest positive selection pressures initially, with subsequent purifying selections and eventual stabilization. For Orf1a, we observed a pattern similar to that for the S gene (table S3). In contrast, Orf1b (nt coordinate: 13,398 to 21,485) seems to be undergoing purifying selection during the whole course of the epidemic. Indeed, it is the most conserved genomic region of SARS-CoV (*7*).

Our analysis thus suggests that adaptive pressures operated on the SARS-CoV genome but stabilized during the late phase of the epidemic with the emergence of a predominant genotype. Alternatively, sampling bias for cases related to SSEs (*28*) may distort the data. We believe that such a sampling strategy may be justifiable from a public health perspective, as the viral genotypes associated with the SSEs are the most epidemiologically important. However, to explore the possibility of bias, we estimated the date for the most recent common ancestor of the samples available. On the basis of the observed neutral mutation rate, this date was estimated to lie in mid-November 2002 (95% confidence interval: early June 2002 and late December 2002) (*14*). This result is consistent with the onset date of 16 November 2002 for the earliest index patient from Foshan (*13*) and supports the finding that the genotypes we studied from the early, middle, and late phases represent different stages of evolution of the same viral lineage. This is further evident from the remarkable correlation between the molecular clustering and epidemi-

Civet farms

Li WD, Shi ZL, Yu M, Ren WZ, Smith C, Epstein J, Wang HZ, Crameri G, Hu ZH, Zhang HJ, Zhang JH, McEachern J, Field H, Daszak P, Eaton BT, **Zhang SY,** Wang LF（**2005**）. Bats are natural reservoirs of SARS-like coronaviruses. ***Science*** 310：676-679.（co-corresponding author）

Bats Are Natural Reservoirs of SARS-Like Coronaviruses

Wendong Li,[1,2] Zhengli Shi,[2*] Meng Yu,[3] Wuze Ren,[2] Craig Smith,[4] Jonathan H. Epstein,[5] Hanzhong Wang,[2] Gary Crameri,[3] Zhihong Hu,[2] Huajun Zhang,[2] Jianhong Zhang,[2] Jennifer McEachern,[3] Hume Field,[4] Peter Daszak,[5] Bryan T. Eaton,[3] Shuyi Zhang,[1,6*] Lin-Fa Wang[3*]

Severe acute respiratory syndrome (SARS) emerged in 2002 to 2003 in southern China. The origin of its etiological agent, the SARS coronavirus (SARS-CoV), remains elusive. Here we report that species of bats are a natural host of coronaviruses closely related to those responsible for the SARS outbreak. These viruses, termed SARS-like coronaviruses (SL-CoVs), display greater genetic variation than SARS-CoV isolated from humans or from civets. The human and civet isolates of SARS-CoV nestle phylogenetically within the spectrum of SL-CoVs, indicating that the virus responsible for the SARS outbreak was a member of this coronavirus group.

Severe acute respiratory syndrome (SARS) was caused by a newly emerged coronavirus, now known as SARS coronavirus (SARS-CoV) (*1*, *2*). In spite of the early success of etiological studies and molecular characterization of this virus (*3*, *4*), efforts to identify the origin of SARS-CoV have been less successful. Without knowledge of the reservoir host distribution and transmission routes of SARS-CoV, it will be difficult to prevent and control future outbreaks of SARS.

Studies conducted previously on animals sampled from live animal markets in Guangdong, China, indicated that masked palm civets (*Paguma larvata*) and two other species had been infected by SARS-CoV (*5*). This led to a large-scale culling of civets to prevent further SARS outbreaks. However, subsequent studies have revealed no widespread infection in wild or farmed civets (*6*, *7*). Experimental infection of civets with two different human isolates of SARS-CoV resulted in overt clinical symptoms, rendering them unlikely to be the natural reservoir hosts (*8*). These data suggest that although *P. larvata* may have been the source of the human infection that precipitated the SARS outbreak, infection in this and other common species in animal markets was more likely a reflection of an "artificial" market cycle in naïve species than an indication of the natural reservoir of the virus.

Bats are reservoir hosts of several zoonotic viruses, including the Hendra and Nipah viruses, which have recently emerged in Australia and East Asia, respectively (*9*–*11*). Bats may be persistently infected with many viruses but rarely display clinical symptoms (*12*). These characteristics and the increasing presence of bats and bat products in food and traditional medicine markets in southern China and elsewhere in Asia (*13*) led us to survey bats in the search for the natural reservoir of SARS-CoV.

In this study, conducted from March to December of 2004, we sampled 408 bats representing nine species, six genera, and three families from four locations in China (Guangdong, Guangxi, Hubei, and Tianjin) after trapping them in their native habitat (Table 1). Blood, fecal, and throat swabs were collected; serum samples and cDNA from fecal or throat samples were independently analyzed, double-blind, with different methods in our laboratories in Wuhan and Geelong (*14*).

Among six genera of bat species surveyed (*Rousettus*, *Cynopterus*, *Myotis*, *Rhinolophus*, *Nyctalus*, and *Miniopterus*), three communal, cave-dwelling species from the genus *Rhinolophus* (horseshoe bats) in the family *Rhinolophidae* demonstrated a high SARS-CoV antibody prevalence: 13 out of 46 bats (28%) in *R. pearsoni* from Guangxi, 2 out of 6 bats (33%) in *R. pussilus* from Guangxi, and 5 out of 7 bats (71%) in *R. macrotis* from Hubei. The high seroprevalence and wide distribution of seropositive bats is expected for a wildlife reservoir host for a pathogen (*15*).

The serological findings were corroborated by poylmerase chain reaction (PCR) analyses with primer pairs derived from the nucleocapsid (N) and polymerase (P) genes (table S1). Five fecal samples tested positive, all of them from the genus *Rhinolophus*: three in *R. pearsoni* from Guangxi and one each in *R. macrotis* and *R. ferrumequinum*, respectively, from Hubei. No virus was isolated from an inoculation of Vero E6 cells with fecal swabs of PCR-positive samples.

A complete genome sequence was determined directly from PCR products from one of the fecal samples (sample Rp3) that contained relatively high levels of genetic material. The genome organization of this virus (Fig. 1), tentatively named SARS-like coronavirus isolate Rp3 (SL-CoV Rp3), was essentially identical to that of SARS-CoV, with the exception of three regions (Fig. 1, shaded boxes). The overall nucleotide sequence identity between SL-CoV Rp3 and SARS-CoV Tor2 was 92% and increased to ~94% when the three variable regions were excluded. The variable regions are located at the 5′ end of the S gene (equivalent to the S1 coding region of coronavirus S protein) and the region immediately upstream of the N gene. These regions have been identified as "high mutation" regions among different SARS-CoVs (*5*, *16*, *17*). The region upstream of the N gene is known to be prone to deletions of various sizes (*5*, *16*, *18*).

Predicted protein products from each gene or putative open reading frame (ORF) of SL-CoV Rp3 and SARS-CoV Tor2 were com-

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Rhinolophus

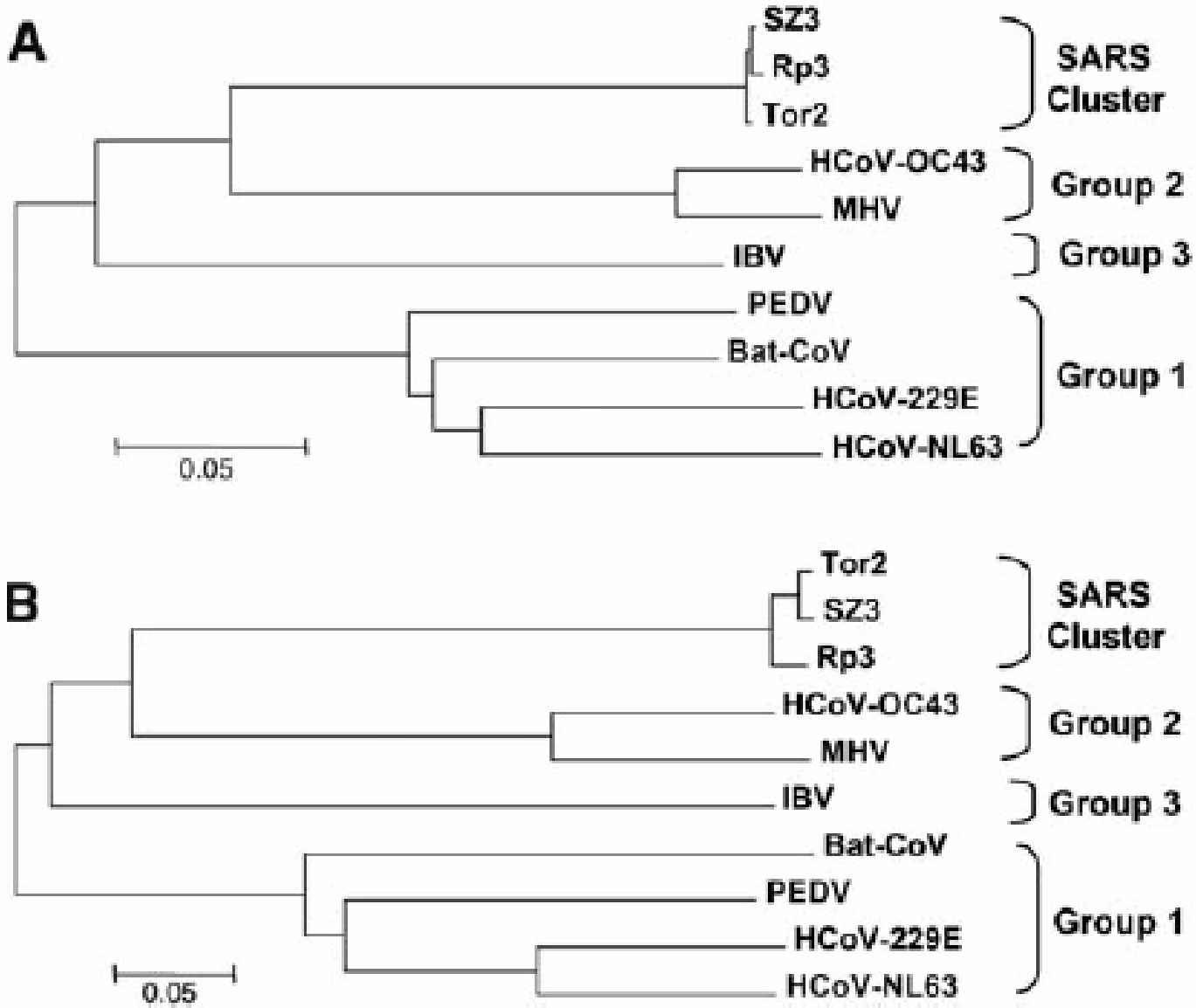
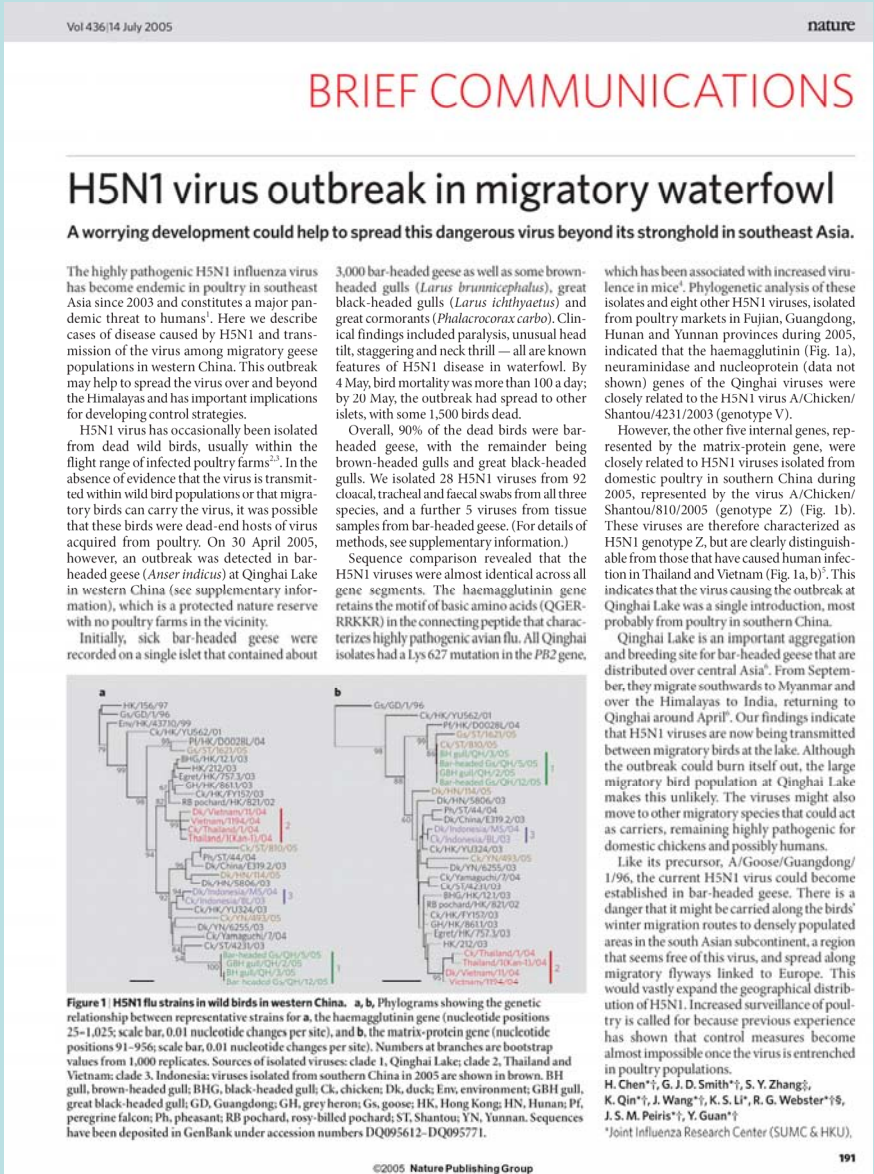


Fig. 2. Phylogenetic trees. (A) and (B) are trees based on deduced amino acid sequences of the same regions in P1b and S, respectively, as used by Poon *et al.* (*7*) for bat-CoV. Tor2 and SZ3, SARS-CoV strains Tor2 and SZ3; Rp3, SL-CoV Rp3; HCoV, human coronavirus; MHV, mouse hepatitis virus; PEDV, porcine epidemic diarrhea virus; IBV, avian infectious bronchitis virus.

Chen H., Smith G. J. D., **Zhang SY**., Qin K., Wang J., Li K. S., Webster R. G., Peiris J. S. M. and **Guan Y**. (**2005**) Avian flu: H5N1 virus outbreak in migratory waterfowl. *Nature* 436: 191-192.



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BRIEF COMMUNICATIONS

H5N1 virus outbreak in migratory waterfowl

A worrying development could help to spread this dangerous virus beyond its stronghold in southeast Asia.

The highly pathogenic H5N1 influenza virus has become endemic in poultry in southeast Asia since 2003 and constitutes a major pandemic threat to humans[1]. Here we describe cases of disease caused by H5N1 and transmission of the virus among migratory geese populations in western China. This outbreak may help to spread the virus over and beyond the Himalayas and has important implications for developing control strategies.

H5N1 virus has occasionally been isolated from dead wild birds, usually within the flight range of infected poultry farms[2,3]. In the absence of evidence that the virus is transmitted within wild bird populations or that migratory birds can carry the virus, it was possible that these birds were dead-end hosts of virus acquired from poultry. On 30 April 2005, however, an outbreak was detected in bar-headed geese (*Anser indicus*) at Qinghai Lake in western China (see supplementary information), which is a protected nature reserve with no poultry farms in the vicinity.

Initially, sick bar-headed geese were recorded on a single islet that contained about 3,000 bar-headed geese as well as some brown-headed gulls (*Larus brunnicephalus*), great black-headed gulls (*Larus ichthyaetus*) and great cormorants (*Phalacrocorax carbo*). Clinical findings included paralysis, unusual head tilt, staggering and neck thrill — all are known features of H5N1 disease in waterfowl. By 4 May, bird mortality was more than 100 a day; by 20 May, the outbreak had spread to other islets, with some 1,500 birds dead.

Overall, 90% of the dead birds were bar-headed geese, with the remainder being brown-headed gulls and great black-headed gulls. We isolated 28 H5N1 viruses from 92 cloacal, tracheal and faecal swabs from all three species, and a further 5 viruses from tissue samples from bar-headed geese. (For details of methods, see supplementary information.)

Sequence comparison revealed that the H5N1 viruses were almost identical across all gene segments. The haemagglutinin gene retains the motif of basic amino acids (QGERRRKKR) in the connecting peptide that characterizes highly pathogenic avian flu. All Qinghai isolates had a Lys 627 mutation in the *PB2* gene, which has been associated with increased virulence in mice[4]. Phylogenetic analysis of these isolates and eight other H5N1 viruses, isolated from poultry markets in Fujian, Guangdong, Hunan and Yunnan provinces during 2005, indicated that the haemagglutinin (Fig. 1a), neuraminidase and nucleoprotein (data not shown) genes of the Qinghai viruses were closely related to the H5N1 virus A/Chicken/Shantou/4231/2003 (genotype V).

However, the other five internal genes, represented by the matrix-protein gene, were closely related to H5N1 viruses isolated from domestic poultry in southern China during 2005, represented by the virus A/Chicken/Shantou/810/2005 (genotype Z) (Fig. 1b). These viruses are therefore characterized as H5N1 genotype Z, but are clearly distinguishable from those that have caused human infection in Thailand and Vietnam (Fig. 1a, b)[5]. This indicates that the virus causing the outbreak at Qinghai Lake was a single introduction, most probably from poultry in southern China.

Qinghai Lake is an important aggregation and breeding site for bar-headed geese that are distributed over central Asia[6]. From September, they migrate southwards to Myanmar and over the Himalayas to India, returning to Qinghai around April[6]. Our findings indicate that H5N1 viruses are now being transmitted between migratory birds at the lake. Although the outbreak could burn itself out, the large migratory bird population at Qinghai Lake makes this unlikely. The viruses might also move to other migratory species that could act as carriers, remaining highly pathogenic for domestic chickens and possibly humans.

Like its precursor, A/Goose/Guangdong/1/96, the current H5N1 virus could become established in bar-headed geese. There is a danger that it might be carried along the birds' winter migration routes to densely populated areas in the south Asian subcontinent, a region that seems free of this virus, and spread along migratory flyways linked to Europe. This would vastly expand the geographical distribution of H5N1. Increased surveillance of poultry is called for because previous experience has shown that control measures become almost impossible once the virus is entrenched in poultry populations.

H. Chen*†, G. J. D. Smith*†, S. Y. Zhang‡, K. Qin*†, J. Wang*†, K. S. Li*, R. G. Webster*†§, J. S. M. Peiris*†, Y. Guan*†
*Joint Influenza Research Center (SUMC & HKU).

Figure 1 | H5N1 flu strains in wild birds in western China. **a, b,** Phylograms showing the genetic relationship between representative strains for **a,** the haemagglutinin gene (nucleotide positions 25–1,025; scale bar, 0.01 nucleotide changes per site), and **b,** the matrix-protein gene (nucleotide positions 91–956; scale bar, 0.01 nucleotide changes per site). Numbers at branches are bootstrap values from 1,000 replicates. Sources of isolated viruses: clade 1, Qinghai Lake; clade 2, Thailand and Vietnam; clade 3, Indonesia: viruses isolated from southern China in 2005 are shown in brown. BH gull, brown-headed gull; BHG, black-headed gull; Ck, chicken; Dk, duck; Env, environment; GBH gull, great black-headed gull; GD, Guangdong; GH, grey heron; Gs, goose; HK, Hong Kong; HN, Hunan; Pf, peregrine falcon; Ph, pheasant; RB pochard, rosy-billed pochard; ST, Shantou; YN, Yunnan. Sequences have been deposited in GenBank under accession numbers DQ095612–DQ095771.

- **There is a danger that H5N1 might be carried along the birds' winter migration routes to Europe.**
- **14 July, 2005,**

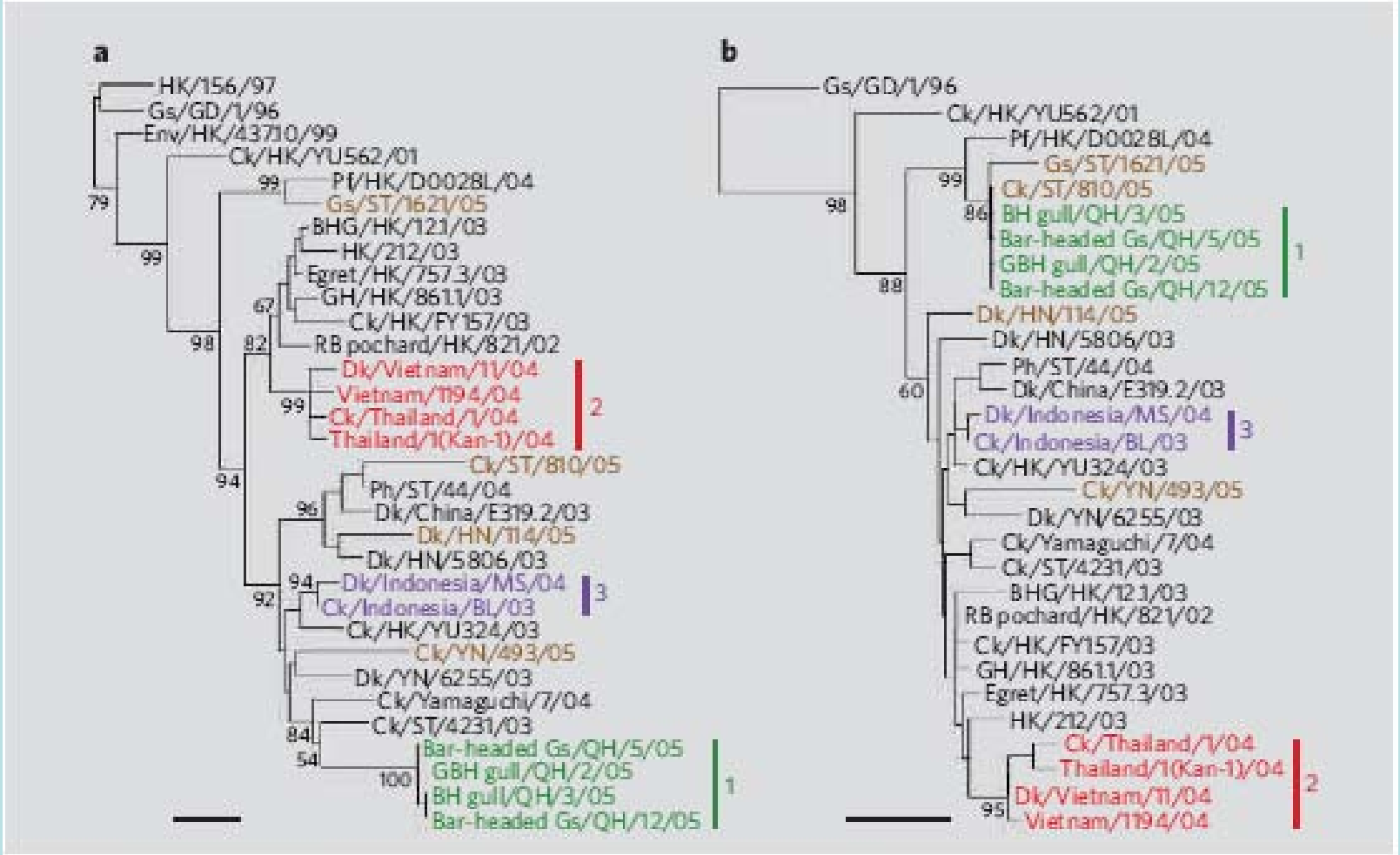


Figure 1 | H5N1 flu strains in wild birds in western China. **a, b,** Phylograms showing the genetic relationship between representative strains for **a**, the haemagglutinin gene (nucleotide positions 25–1,025; scale bar, 0.01 nucleotide changes per site), and **b**, the matrix-protein gene (nucleotide positions 91–956; scale bar, 0.01 nucleotide changes per site). Numbers at branches are bootstrap values from 1,000 replicates. Sources of isolated viruses: clade 1, Qinghai Lake; clade 2, Thailand and Vietnam; clade 3, Indonesia; viruses isolated from southern China in 2005 are shown in brown. BH gull, brown-headed gull; BHG, black-headed gull; Ck, chicken; Dk, duck; Env, environment; GBH gull, great black-headed gull; GD, Guangdong; GH, grey heron; Gs, goose; HK, Hong Kong; HN, Hunan; Pf, peregrine falcon; Ph, pheasant; RB pochard, rosy-billed pochard; ST, Shantou; YN, Yunnan. Sequences have been deposited in GenBank under accession numbers DQ095612–DQ095771.

SARS: bats/civet cats to humans

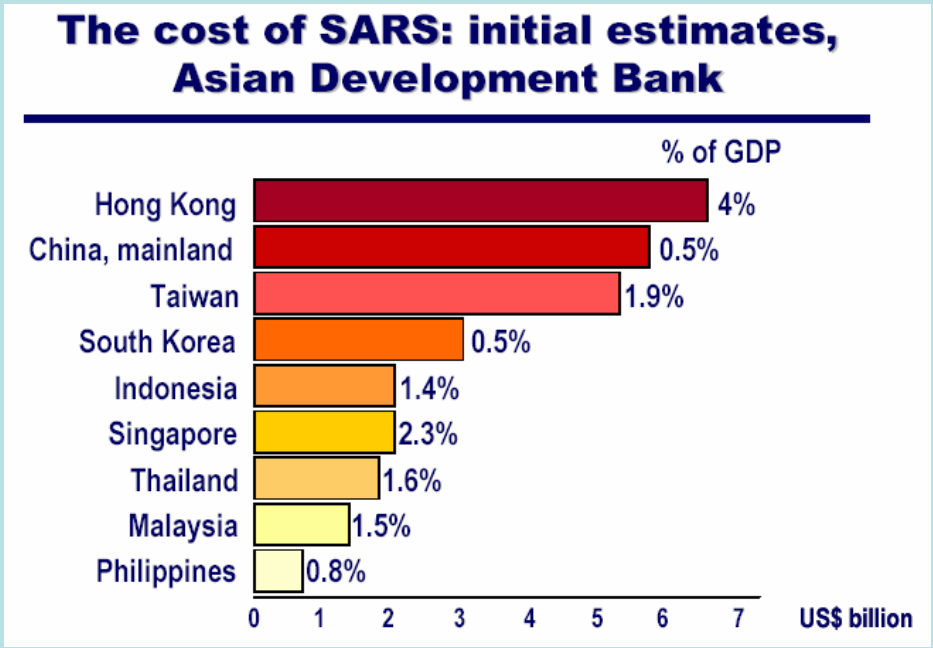
Bird flu: domestic/wild birds to humans

Zoonoses (zoonotic diseases): Diseases and infections which can be naturally transmitted between vertebrate animals and humans.

WHO: more than 30 new zoonotic diseases have emerged since the mid 1970s.

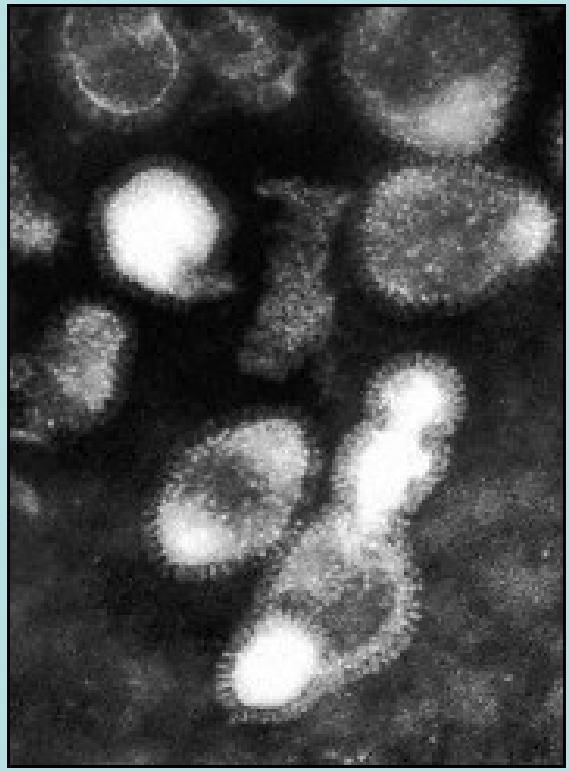
OIE (International Office of Epizootics): more than 150 zoonotic diseases

Cost of SARS



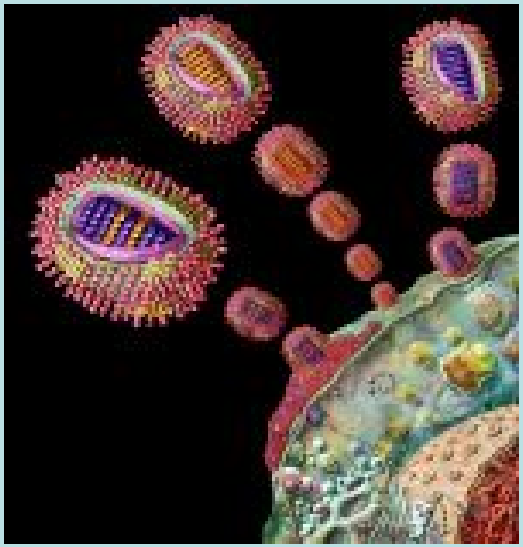
$30~150 billion

Cost of Avian flu



In the first two months: 100 million chickens died or were destroyed; 15 billions USD to control the H5N1

Some zoonotic diseases of last century

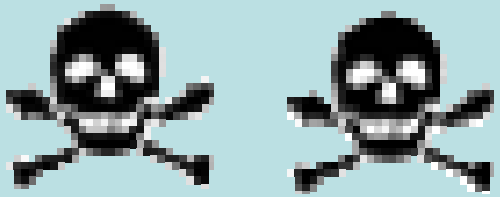


Flu virus

HIV virus

1918 Influenza, Dengue Hemorrhagic Fever, Ebola, HIV/AIDS, Bovine Spongiform Encephalopathy, Nipah, etc.

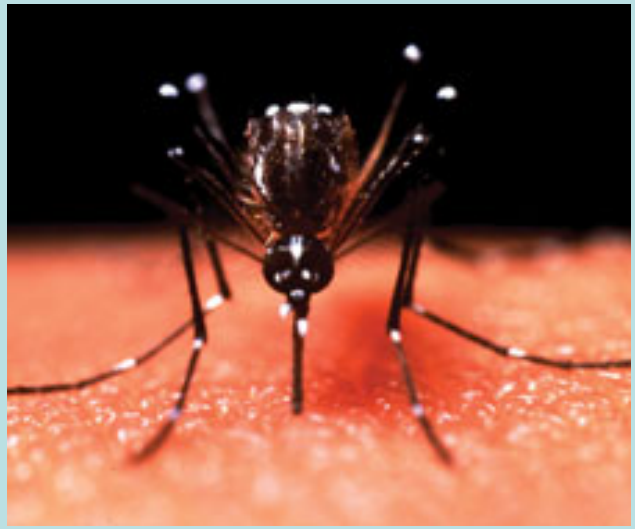
1918 Influenza (20~50 million deaths)



1918 Influenza: most deadly for people aged 20 to 40 year-old

An Emergency Hospital for Influenza Patients

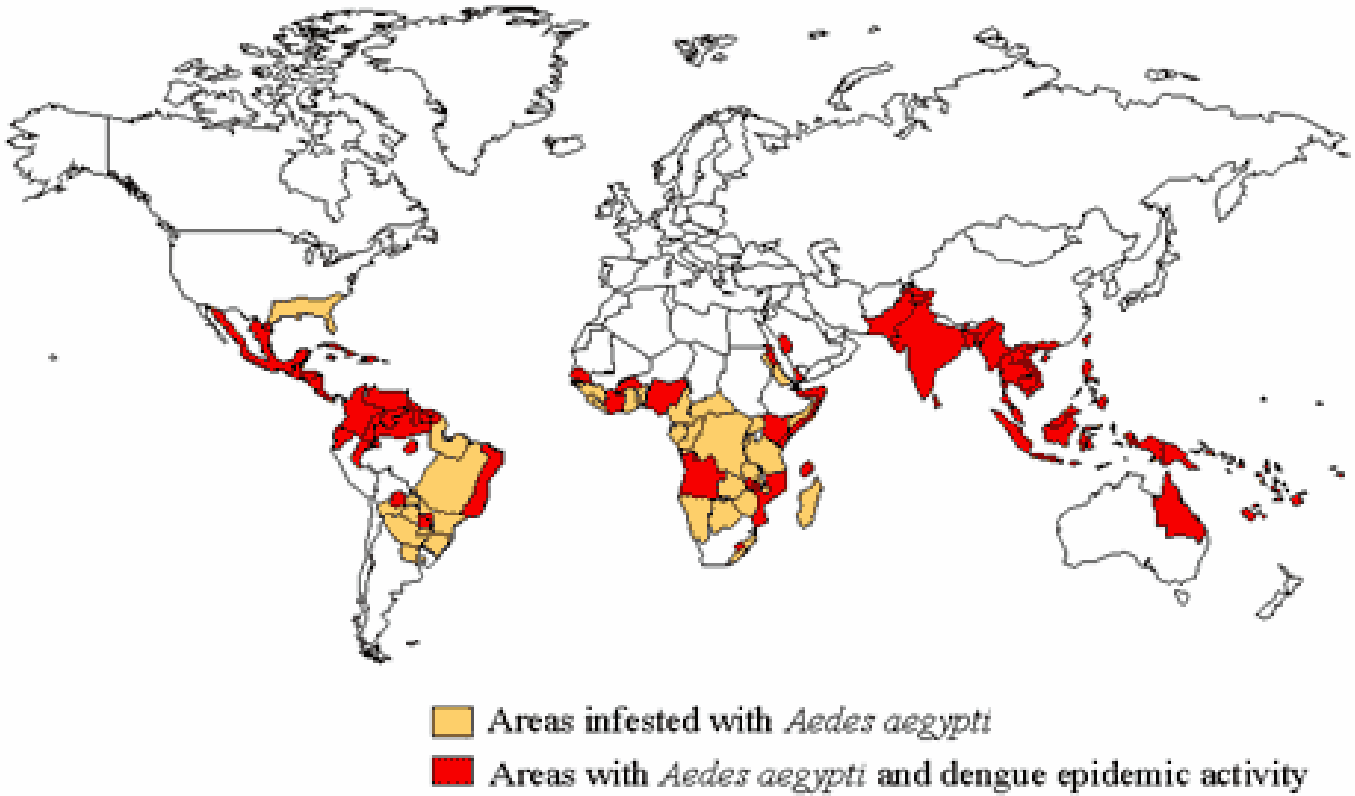
Dengue Hemorrhagic Fever



Aedes aegypti

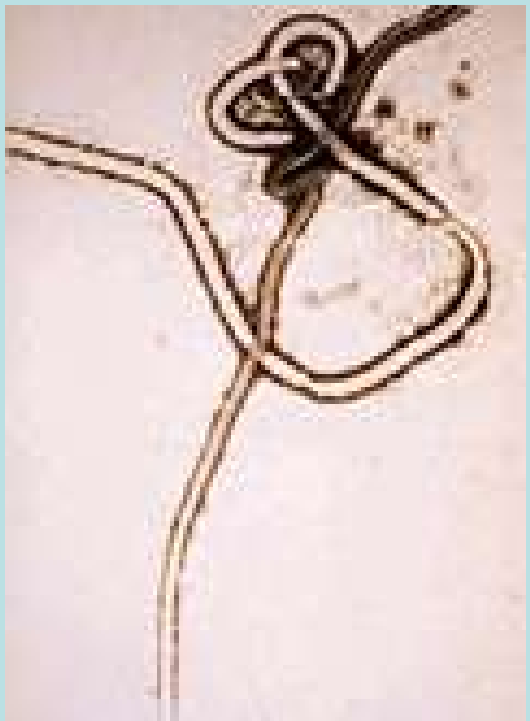
Dengue Hemorrhagic Fever / Flavivirus / Nonhuman primates

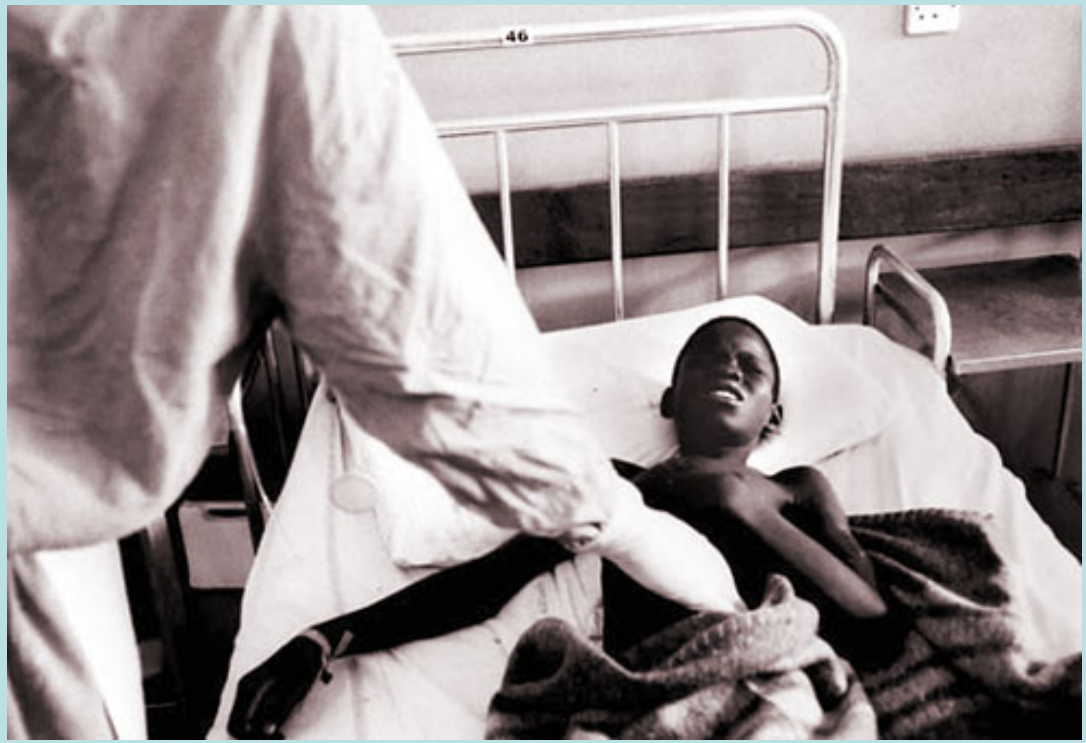
World Distribution of Dengue



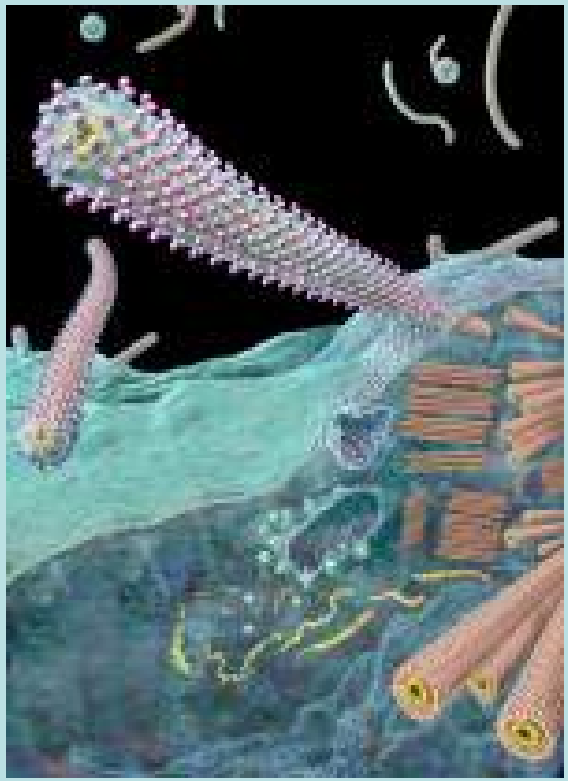
2.5 billion people live in areas at risk for dengue epidemic transmission

Ebola (1976~present)



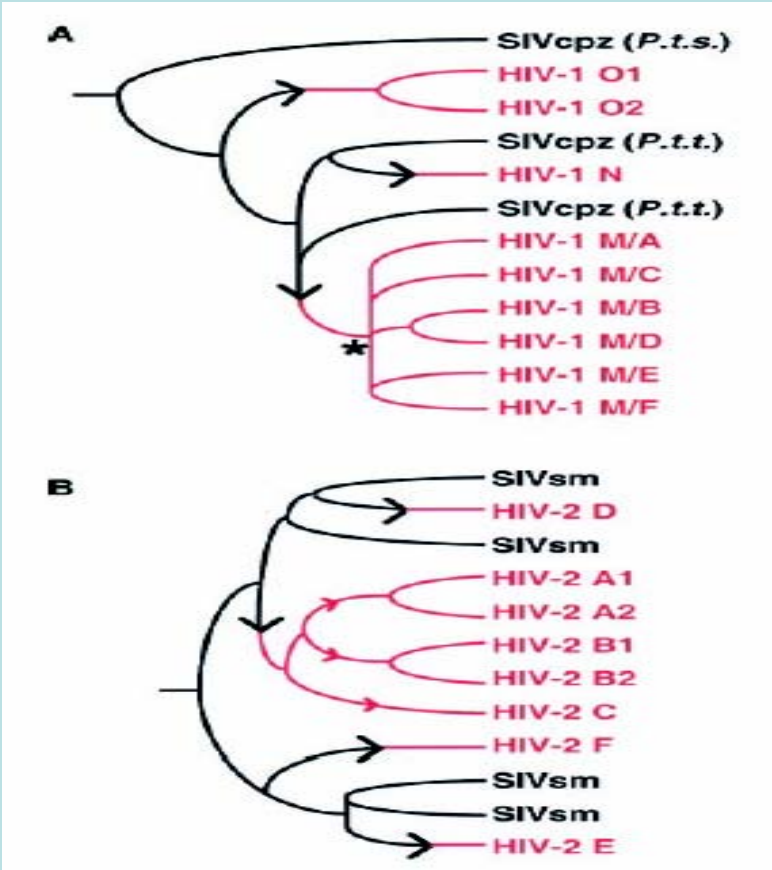


Ebola hemorrhagic fever - zoonotic

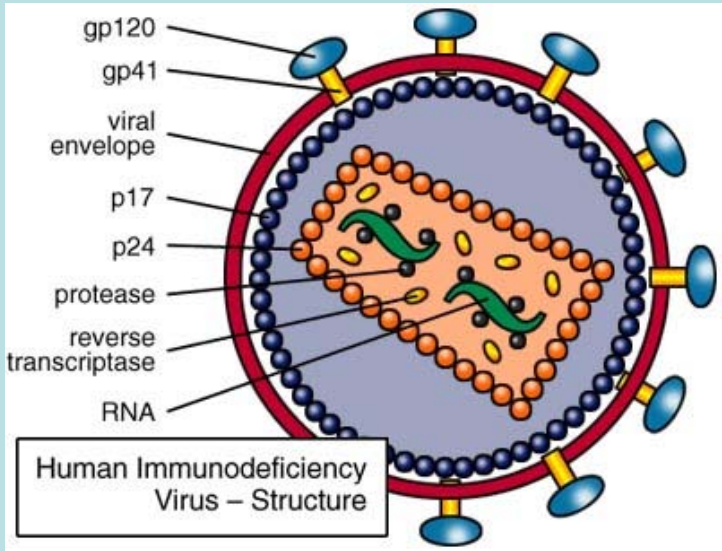


1,850 cases, over 1,200 deaths, WHO

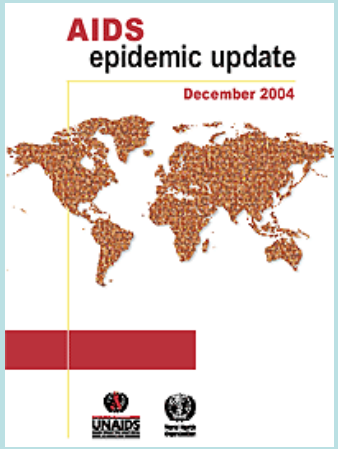
HIV/AIDS (1980-present)

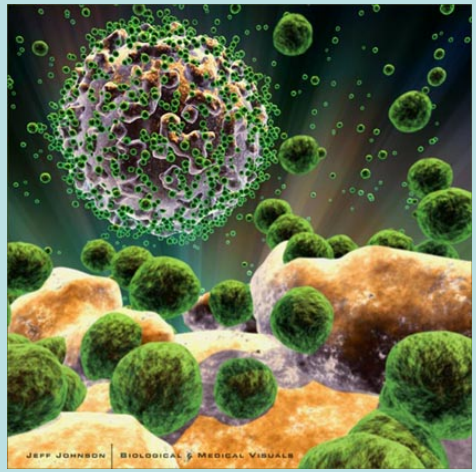


Hahn et al., Science, 2000



GLOBAL SUMMARY OF THE HIV/AIDS EPIDEMIC, DECEMBER 2004 (WHO)



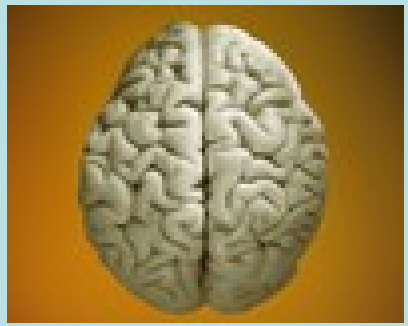


People living with HIV/AIDS in 2004 : 39.4 million

People newly infected with HIV in 2004 : 4.9 million

AIDS deaths in 2004 : 3.1 million

Bovine Spongiform Encephalopathy (BSE) (1986-2002)



Creutzfeldt-Jacob Disease (CJD), found in people

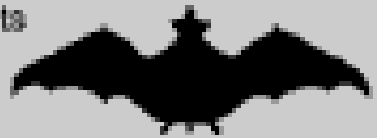
The costs of BSE

UK: by the 1990s, several billion dollars

USA: a single cow, more than 50 countries banning imports of American beef

POSSIBLE TRANSMISSION OF NIPAH VIRUS

Fruit bats



The only animal to be tested positive for Nipah. Also wildlife reservoir for Hendra in Australia

Contamination of food and water supplies

Contamination of food/water supplies or direct contact

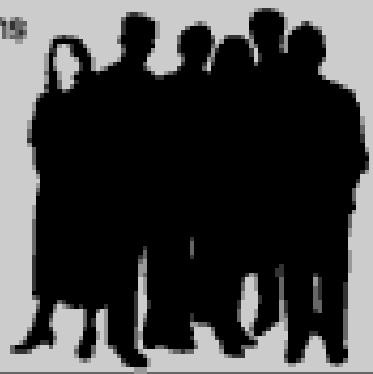
LEGEND

Speculated transmission

Known transmission

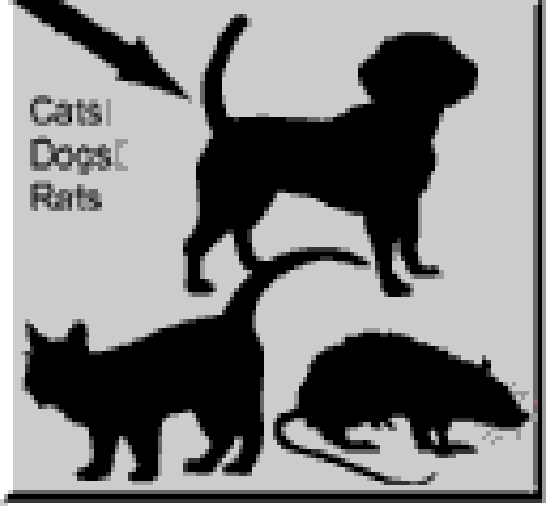
Pigs

Humans



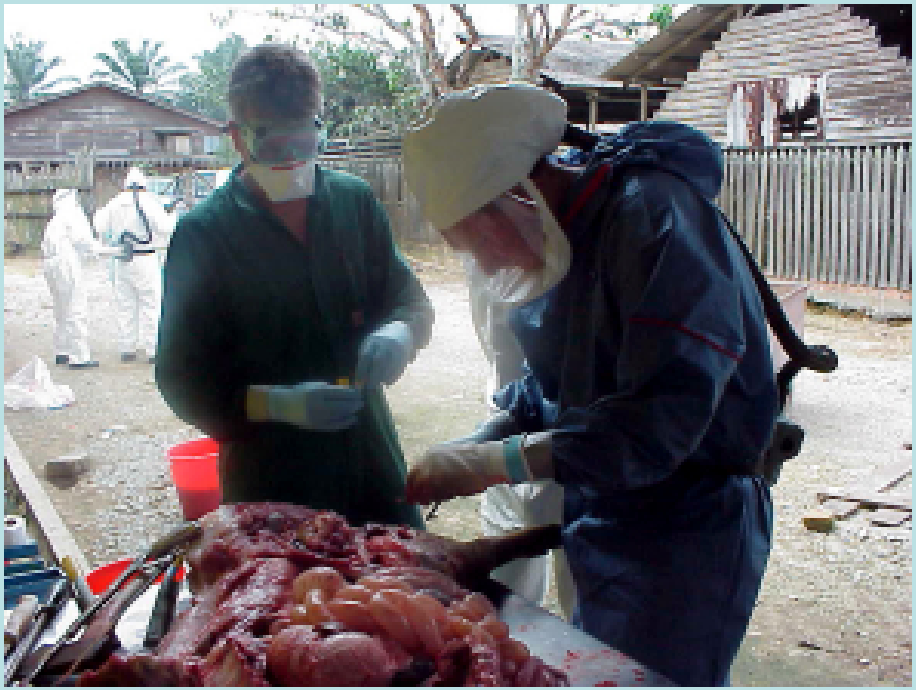
Horses

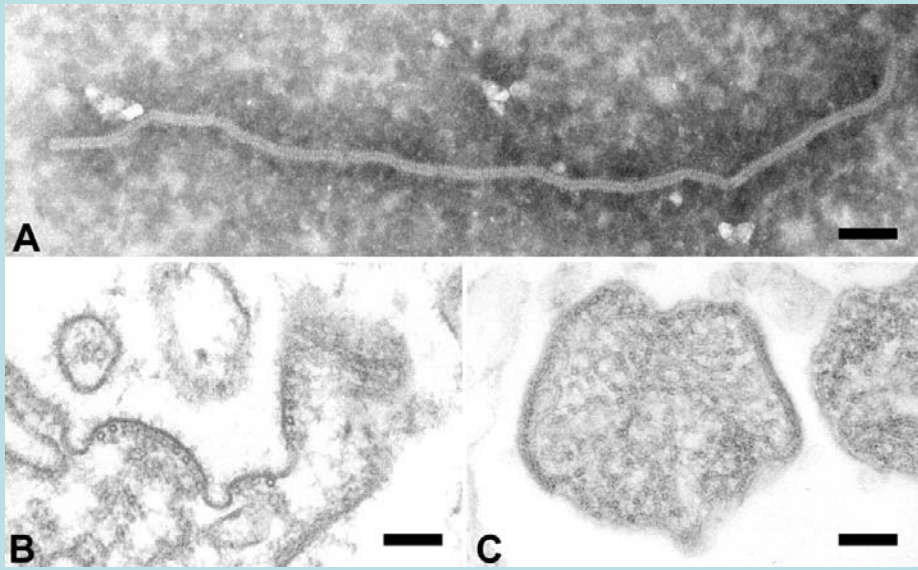
Cats
Dogs
Rats



Nipah/fruit bats

1998，Malaysia





105 deaths

Zoonoses : Increase globally

Why ?

SARS / Domestication of wild animals

Under suspicion. Civets were found to have t
virus, but they may not be the primary animal rese

Masked palm civets (*Paguma larvata*)

Avian influenza / High-density livestock rearing

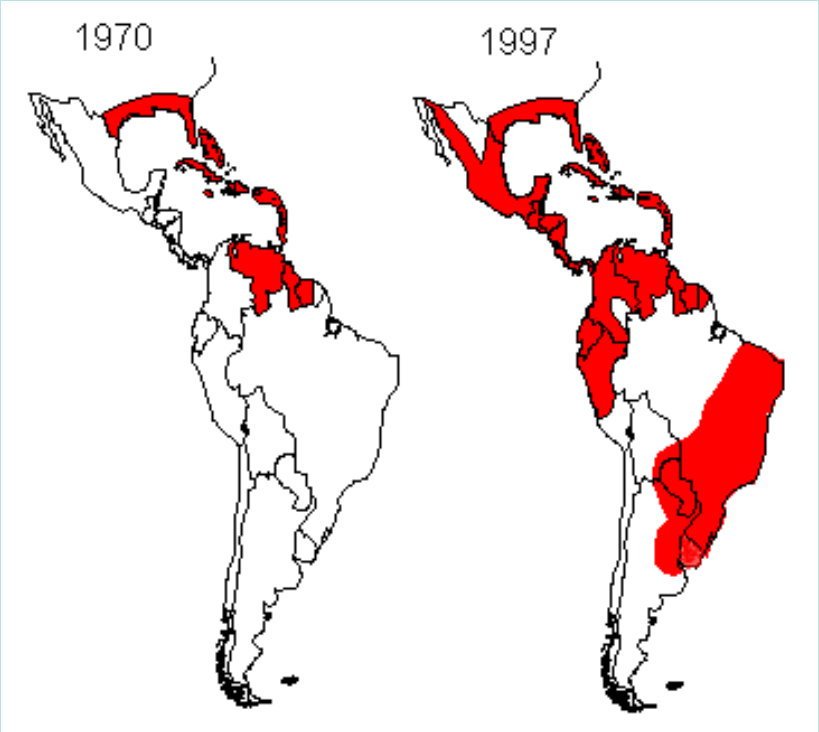
Bovine Spongiform Encephalopathy (BSE) (mad cow disease) / Unnatural feeding practices

Nipah / Deforestion

Ebola / Hunting and forest exploit

Field surveys have shown that the more local people hunted, the more likely they were to contract Ebola.

Dengue Fever / Climate change and mosquito distribution



Distribution of *Aedes aegypti* in the Americas in 1970, and in 1997

Emerging diseases

SARS : Domestication of wild animals

Avian influenza: unnatural livestock rearing

BSE: Unnatural feeding practices

Nipah: Deforestion

Ebola: Hunting and forest exploit

Dengue Fever: Climate change and mosquito distribution

Zoonotic diseases also kill wild animals

Chimpanzee

Gorilla

West Nile

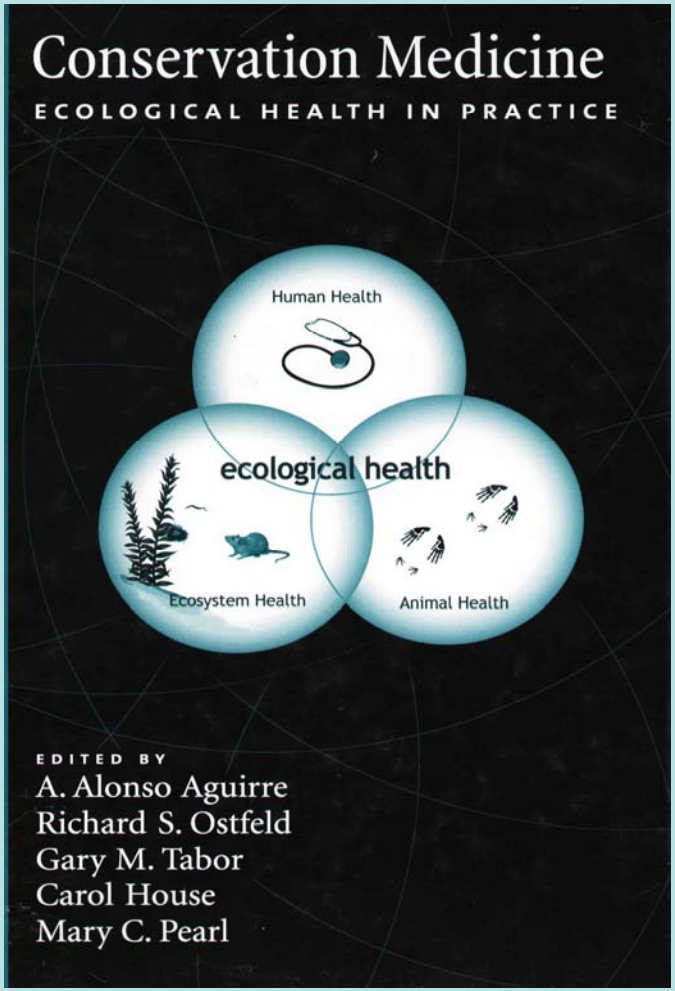
STELLER'S JAY

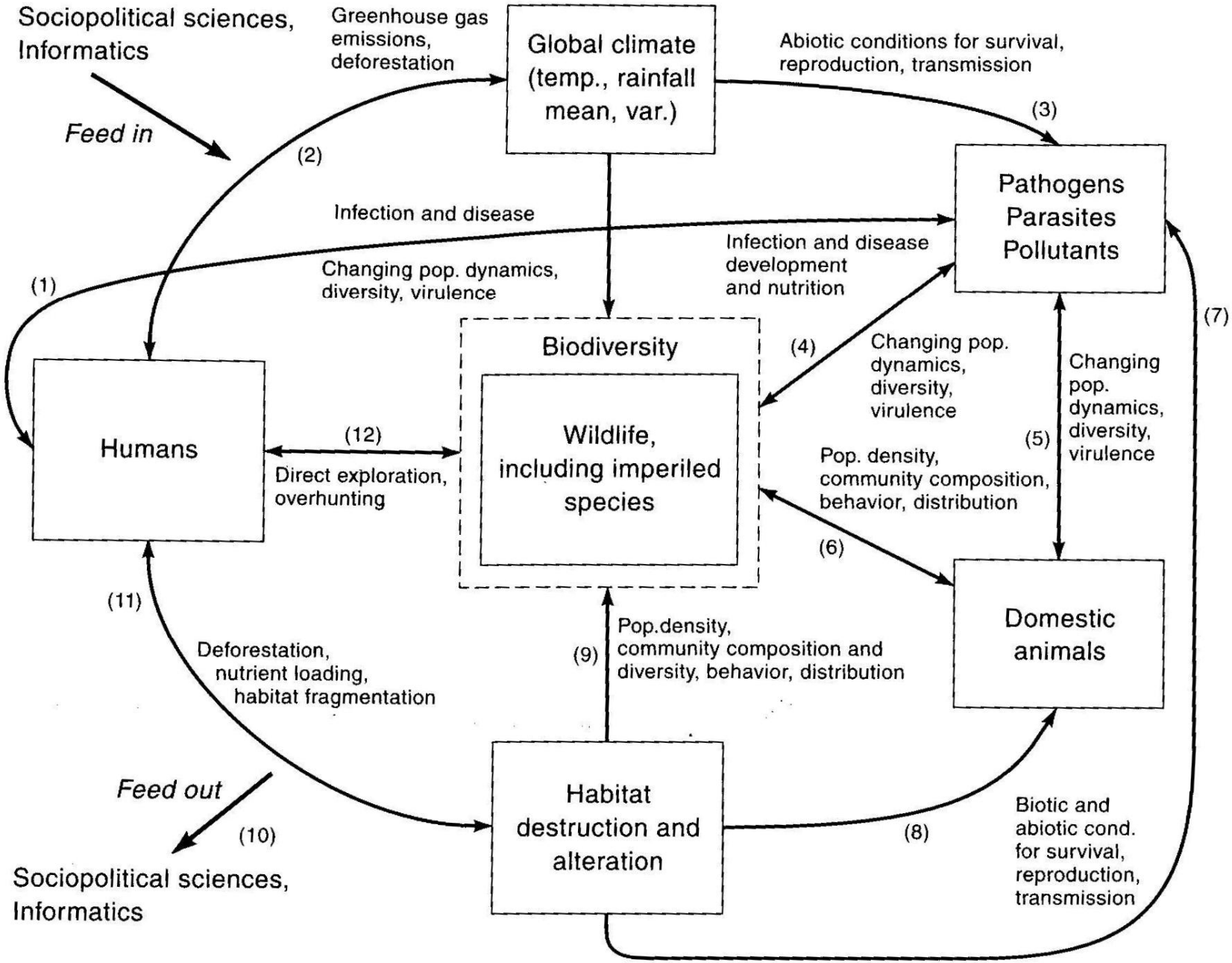
Micronesian kingfishers

West Nile virus is a mosquito-borne infection that can cause encephalitis

Birds of a few species develop extremely high levels of virus in their tissues and quickly die

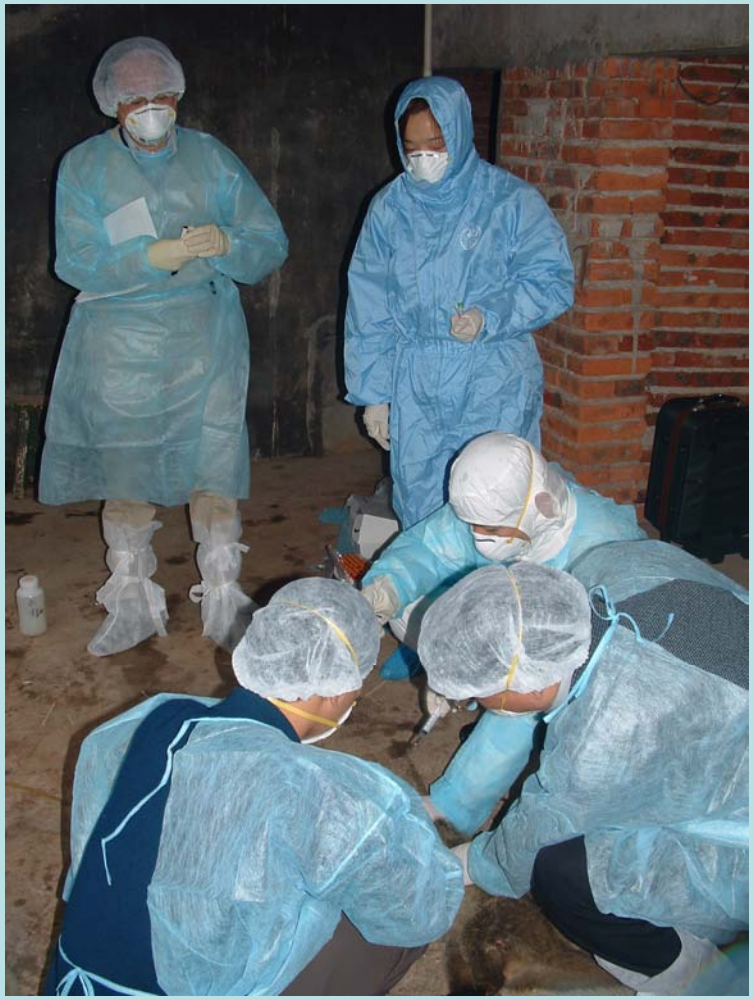
Conservation Medicine
– new concept and inter-discipline




Sociopolitical sciences, Informatics
Feed in
Greenhouse gas emissions, deforestation
(2)
Global climate (temp., rainfall mean, var.)
Abiotic conditions for survival, reproduction, transmission
(3)
Pathogens Parasites Pollutants
Infection and disease
(1)
Changing pop. dynamics, diversity, virulence
Infection and disease development and nutrition
(7)
Biodiversity
(4)
Changing pop. dynamics, diversity, virulence
Changing pop. dynamics, diversity, virulence
Humans
(12)
Direct exploration, overhunting
Wildlife, including imperiled species
(5)
Pop. density, community composition, behavior, distribution
(6)
Domestic animals
(11)
Deforestation, nutrient loading, habitat fragmentation
(9)
Pop.density, community composition and diversity, behavior, distribution
Feed out
(10)
Habitat destruction and alteration
(8)
Biotic and abiotic cond. for survival, reproduction, transmission
Sociopolitical sciences, Informatics

The Consortium for Conservation Medicine : Harvard Medical Schools Center for Health & the Global Environment, Tufts University School of Vet. Med. Center for Conservation Medicine, Johns Hopkins Bloomberg School of Public Health's Department of Environmental Health Sciences, USGS National Wildlife Health Center, and Environment, and Wildlife Trust.

Global cooperation to address zoonoses



Unity is strength

International Organizations/ National Governments/Political Awareness and Support

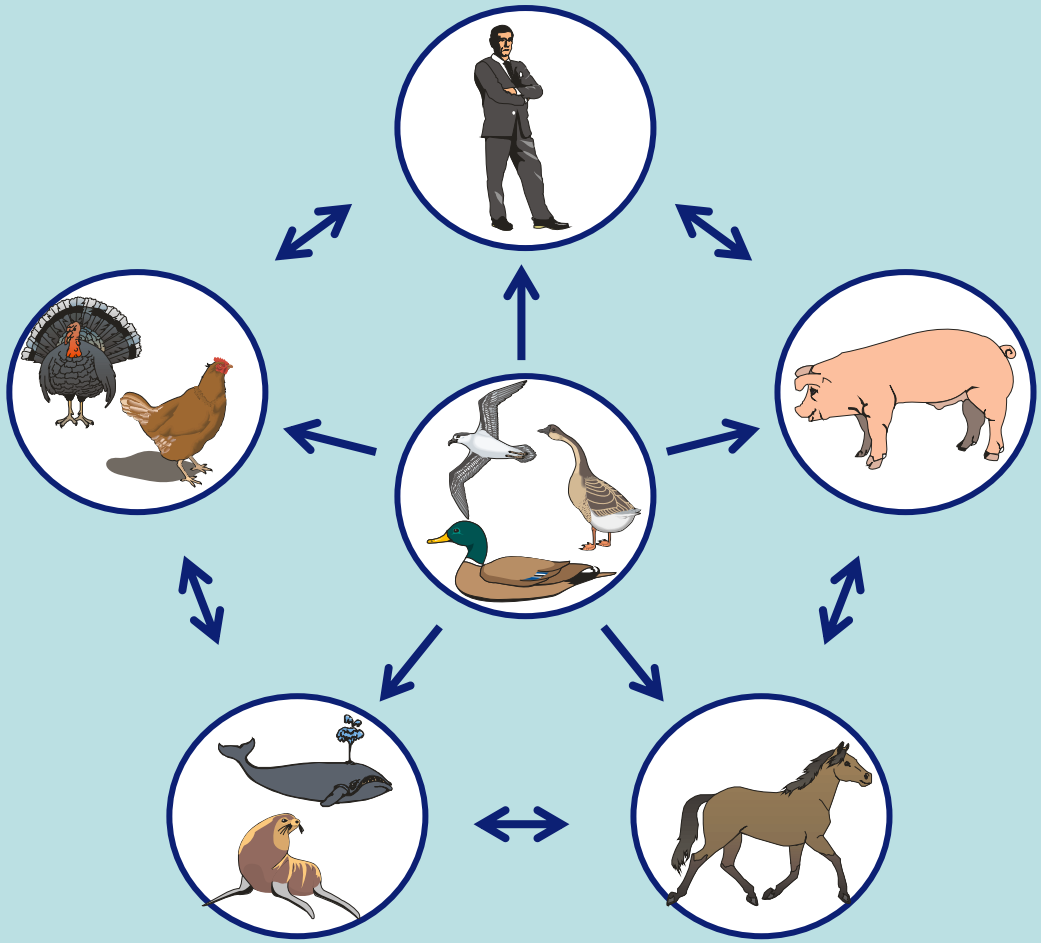
WHO, FAO, OIE, etc.

Experts

New tools and new mechanisr

Surveillance systems

Avian influenza-from birds to humans



2005

科学发展报告

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中国科学院

科学出版社
www.sciencep.com

的丧失引起的。③媒介传染生物与景观变化之间的关系。这里所说的景观变化就是指原始森林的砍伐和人工造林带来的森林的演替，这种变化使得病原体寻找新的自然宿主，从而有可能进一步感染给人。例如，狐蝠本来分布于原始热带雨林，但由于人类不断砍伐森林，它们飞到人类活动的地区，将尼帕病毒传播给家畜和人。④人兽共患疾病与野生动物保护之间的关系。一方面，动物携带的病原体和寄生虫会传染给人类，给人类健康构成威胁；另一面，野生动物的自然保护问题也成为人类共患疾病管理的挑战。西尼罗河病毒通过蚊虫叮咬传播，蔓延迅速。已知美国有150多种鸟类、15种哺乳动物和1种爬行动物已经感染上了这种病毒，对许多濒危野生动物的保护影响越来越大。与生态旅游相关，中非的山地大猩猩受到人类疾病的威胁，流行性感冒、麻疹和肺结核都给它们的种群带来巨大伤害。

在达尔文时代，自然科学与医药科学分道扬镳，就像进化树上的分支，朝各自的方向发展；现在，保护医学终于将二者重新聚在一起。我国是一个人口众多、健康水平相对低下、生态系统破坏严重的大国，尤其需要重视和尽快开展保护医学的研究。

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4 Burroughs T, Knobler S, Lederberg J. The emergence of zoonotic diseases: understanding the impact on animal and human health. Washington D C: National Academy Press, 2002, 1~157
5 Aguirre A A, Ostfeld R S, Tabor G M, et al. Conservation medicine: ecological health in practice. Oxford: Oxford University Press, 2002, 1~395

From Emerging Diseases to Conservation Medicine

Zhang Shuyi

Outbreaks of emerging diseases are mostly originated from wild or domestic animals, caused by diverse reasons such as wild animal hunting, domestication and eating of wild animals, deforestation, global climate change, factory farming etc. Conservation medicine is an emerging field that focuses on the intersection of the environment, human and non-human hosts, and pathogens. At its core, conservation medicine champions the integration of techniques and partnering of scientists from diverse disciplines.

Thank you!