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New and Re-emerging Viral Pathogens

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ABSTRACT. This manuscript aims to highlight a few of the new or re-emerging viruses that have made "news" recently. Of these are HIV, Hantavirus, monkeypox virus, dengue virus, influenza virus 1&5 NI, Kaposi's sarcoma-associated herpes virus (KSHV), Boma disease virus, Ebola virus, other haemorrhagic fever viruses, Al-Khorrna virus, hepatitis G virus, Calicivirus gastroenteritis, Enteroviral meningitis, Bovine prions and nvCJD. The advances in molecular techniques made it possible to detect new viruses. The new molecular tools for the identification of unculturable viruses are discussed.

Keywords: HIV, Hantaviruses, monkeypox virus, dengue virus, Influenza virus 1&5 N1.

Introduction

Over the past few years several viruses have been newly discovered. In addition, some already-known viruses have re-emerged either with the same or with a new disease picture. Both types of viruses have had an unexpected and significant impact on human illness. This presentation aims to highlight a few of the new or re-emerging viruses that have made "news" recently.

I. arv. Discussion of new viral pathogens can be most appropriately started with HIV. This virus, completely unknown until 1991 has dominated the medical scene over the last 16 years. By now it has killed more than 8.8 million people and infected more than 30 million. By July 1996 there were more than 22.6 million individuals in the world living with HIV/AIDSll}. *(This figure has recently been revised to'30.6 million people who are HIV positive by the end of* 1997; *the total of infected people since the beginning of the epidemic could thus number* 40 *million by the year 2000. The number of new infections for 1997, calculated to be* 3.5 *million, was underestimated originally)*[2].

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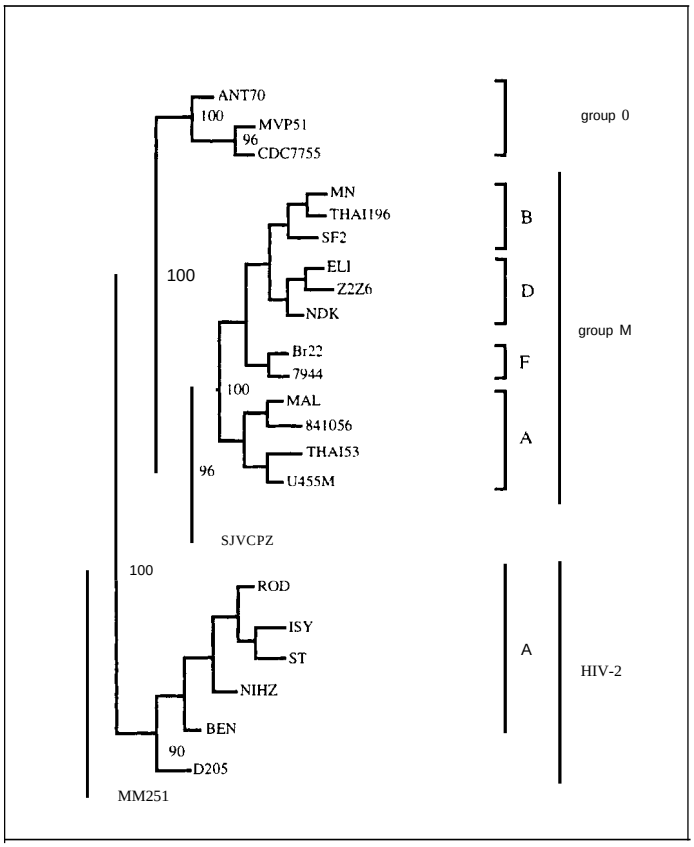
The most acceptable theory for the origin of HIV-I is based on transmission from a primate source, most likely the chimpanzee. Evidence for this comes from the isolation of closely-related chimpanzee virus, designated Simian Immunodeficiency Virus-chimpanzee (SIV_{cpz}). The chimpanzee appears to be the natural host for this virus as it does not get any disease despite long-term infection by the virus. SIV_{epz} genome is more closely related in nucleotide sequence to human group M HIV isolates (i.e., subtypes A-I) than are HIV-2 isolates or the group 0 isolates (Fig. 1). Similarly, HIV-2 is now assumed to have been transmitted to humans from the Sooty Mangabay Monkey (SIV_{smm}) because of close 'sequence relatedness between HIV-2 and SIV smm isolated from this animal (isolate MM251; Fig. I). The exact methods of transmission are not known, but are assumed to have occurred in the African jungle where there are ample opportunities for contact between these primates and man.



Fie. I Phylogenetic relationship between various human and primate HIV isolates (adapted from ref. [3]).

It is important to emphasize that 90% of HIV-infected people now live in developing countries where most HIV patients receive little care. Despite the huge publicity that AIDS has taken, many developing countries have not yet seen the full brunt of the epidemicl!',

New aspects in the HIV epidemic include the emergence of multiple serologic variants, such as group 0 viruses. This group was first detected in the Cameroon and the Gabon but has now been reported fromseveral countries including the U.S.A.[3]. The emergence of group 0 variants has caused a significant diagnostic problem in several hospitals and blood transfusion centers as these variants were not detectable by some of the most commonly used HIV screening kits. The total number of recognized HIV variant subtypes (clades) has now reached seventeen: nine HIV-1 clades A-I, three group O clades, and five HIV-2 clades. The fact that the HI genome consists of two identical RNA strands (i.e. a diploid genome) has now been implicated in increasing the frequency of recombination in this virus, thereby increasing the chance of emergence of variants including drug-resistant ones[4].

Drug resistance, together with the high cost of anti-HIV drug regimens, constitute serious obstacles to widespread use of the recent, more effective anti-HIV drugs, and emphasize the point that chemotherapy is unlikely to offer practical solutions for the majority of patients in developing countries.

Progress in HIV vaccine development remains slow despite the multitude of approaches considered or attempted. Excitement about the live-attenuated Simian Immunodeficiency Vaccine (SIV), composed of deletion mutants in the "nef" gene (delta-net), was dampened by the recent cautionary notes that such mutants were found capable of causing diseases in infant and adult animals"". Such results must also lead to caution against attempt to vaccinate human volunteers with such live attenuated vaccines. Work on multiple deletion mutants (e.g., delta-4 SIV) will be awaited in the future.

II. Hantaviruses: Hantavirus disease (hemorrhagic fever, hemorrhagic fever with renal syndrome, nephropathia epidemica) has been known for many years in southeast Asia and in the Scandinavian countries, but these viruses emerged with a new disease picture in 1993 when they were associated with the previously-unknown hantavirus pulmonary syndrome (HPS) in the U.S. There are at least 14 known hantaviruses, but the number could rise up to 22. These viruses have a worldwide distribution (Table 1)[6]. Hantaviruses are primarily rodent-borne. They are transmitted by inhalation of virus-contaminated aerosols of rodent secreta.

A large number, approximately 150,000 - 200,OOO.cases of hemorrhagic fever with renal syndrome (HFRS) are reported each year from various countries, especially China, Russia, and Korea. HFRS can be mild, moderate, or severe with mortality ranging from less than 0.1% in the case of the Puumala (PUU) virus to 5-100/0 in the case of the HTN virus. The disease is manifested as sudden, intense headache, fever, chills, hemorrhage, rash, extreme albuminurea, and hypotension.

So far, more than 250 cases of HPS have been reported from North and South America. The 1993 HPS outbreak in the U.S.A. resulted in 174 cases and 75 deaths (43%). In HPS, capillary' leakage is exclusively localized to the lungs, Death occurs from shock and cardiac complications. An outbreak in Argentina in 1996 resulted in 20 cases and 50% mortality including three doctors and one hospital receptionist. Person-to-person transmission was strongly suggested".

TABLE 1. Worldwide distribution of hantaviruses (adapted from ref. [6]).

Species	Symbol	Distribution
Hantaan	HTN	China, Russia, Korea
Taiwan	-	Taiwan
Dobrava	DaB	Balkans
Seoul	SEa	Worldwide
Puumala	PUU	Europe, Russia, Scandanavia
Thailand	Thai	Thailand
Prospect Hill	PH	U.S.A., Canada
Khabarovsk	KHB	Russia
Thottapalayam	TPM	india
Tula	TUL	Europe
Sin Nombre	SN	U.S.A., Canada,Mexico
New York	NY	U.S.A.
Black Creek Canal	BCC	U.S.A.
EI Moro Canyon	EMC	U.S.A
Bayou	BAY	U.S.A.
Others:		
Andes	AND	Argentina

Although renal involvement was rare in the early cases of HPS, a new variety has been observed in which renal involvement is commonly associated with the pulmonary syndrome.

III. Monkeypox Virus: Several poxviruses are known to infect man (Table 2). Monkeypox virus can be transmitted from monkeys to humans, causing an illness almost identical to smallpox. Only a few cases of monkeypox have been recorded previously in several African countries. In Zaire, for example, 37 cases were recorded between 1981 and 1986. While 'transmission from animals to man is routine, person-to-person transmission was considered inefficient. Therefore, there was not much concern about widespread transmission of the disease among humans.

In 1996. a new outbreak occurred in Zaire causing 92 cases with three deaths. Not only was this the largest outbreak of monkeypox ever seen in humans, but the rate of person-to-person transmission.calculated to be 73%, was much higher than the *300/0* expected on the basis of previous cases.

Besides its ability to cause a smallpox-like disease in man, another major reason for concern about the monkeypox virus is that this virus, unlike the smallpox virus, has an animal reservoir. Animals known to act as reservoir for the virus not only include monkeys but also rats and squirrels.

TABLE 2. Poxviruses that can cause disease in man.

Species	Disease in Humans
Variola	smallpox, eradicated
Monkeypox	smallpox-like
Vaccinia	localized lesions. congenital vaccinia
Cowpox	localized pustular lesions
Buffalopox	localized pustular lesions
Orf	localized nodular skin lesions
Bovine papular stomatosis	localized nodular skin lesions
Tanapox	localized nodular skin lesions
Yabapox	localized nodular skin lesions
Molluscum contagiosum	many nodular skin lesions

Initial fears that the monkeypox virus has mutated into a more virulent form were partially alleviated when genetic analysis of one of the 1996 isolates was found to be similar to previous viruses. However, the possibility that the virus has become more efficient in human-to-human transmission remains worrying.

While monkeypox can be prevented by the same vaccine (vaccinia) used so successfully against smallpox, a complication had arisen from the fact that this vaccine can cause disease and death among people with HIV, which is a common situation in central Africa, including Zaire. These people may require a more attenuated vaccine, known as MVA. However, the extent of protection achievable by this vaccine against monkeypox remains to be shown. Continued surveillance over the next few years will prove or refute the ability of the monkeypox virus for increased transmission among humans[81.

IV. Dengue Viruses: Despite the recognition of dengue fever for over 200 years and the significant effects that dengue viruses have had on large areas of the. world, there is not enough appreciation of the impact of dengue virus disease. In the 1950's dengue fever (DF) and dengue hemorrhagic fever (DHF) were considered by some to be the most important cause of childhood morbidity and mortality in southeast Asia. It is currently estimated that 2.5 million people are at risk of dengue and that 60 million cases occur every year resulting in about 30,000 deaths, making dengue one of the main causes of viral morbidity in the world[9].

There has been a dramatic resurgence of dengue over the past 15 years[IO-14]. Examples of some recent epidemics are listed in Table 3, the most significant being in Latin America.

In 1994, dengue was reported for the first time in Jeddah, Saudi Arabia. Infection was confirmed in 294 out of 540 suspected cases *(540/0).* There were two deaths. Virus cul-

ture was positive in 182 cases *(330/0)* (56 DEN-] and 126 DEN-2), they are confirmed by detection of anti-dengue IgM using ELISA. *(In* 1997 *additional few dengue cases, including Den-3 virus, were detected).* It should be noted that repeat infections by different dengue virus serotypes (immune enhancement) are considered to be the mechanism of pathogenesis for the more dangerous *dengue hemorrhagic fever* which this region has largely, so far, escaped. Despite availability of vaccines for some dengue virus serotypes, the problem of the likely role of enhanced immunity in pathogenesis complicates the use of such vaccines until protection by these vaccines is assured.

TABLE 3. Examples of recent dengue epidemics.

Country	Year	No. of Cases	Outcome
Latin America	95 - 96	500,000 cases	11,000 DHF
Mexico-Texas	95 - 96	-	-
French Guiana	92	3,000	6 deaths
Djibouti	91 - 92	12,000	-
Germany (imported)	-	several hundred	-
Saudi Arabia (Jeddah)	94	540	2 deaths

V. Influenza Virus U5 N1: In May 1997, a new influenza virus, type A H5 NI, was isolated from a fatal case of influenza associated with Reye's Syndrome in a three-year- old boy in Hong Kong. Between March and May, several thousands of chickens in Hong Kong farms were killed by a virus belonging to the same type (H5 N1)[15]. Previously, only types Hl NI, H2 N2, or H3 N2 viruses were known to infect humans. Animal types ranged up to H13 and N8. While some animal viruses (e.g., A1seal/Mass/80/ H7 N7) have infected man before, only minor illness has resulted and human-to-human transmission did not occur. Although concern was mostly expressed about transmission of the virus to people closely exposed to chickens, human-to-human transmission was reported from the first case mentioned above to a healthcare worker who was in close contact. *(By the end of* 1997 *the number of human cases in Hong Kong had arisen to 22 with four deaths. Authorities in Hong Kong started to kill all the chicken population in the city as well as some other bird species (about* 1.3 *million birds). [15]*

The spread of a completely new type of influenza such as this one would be expected to have drastic consequences as no humans are known to carry immunity against this type. The appearance of even "human" types of the influenza virus, such as H3 N2 in 1968 has resulted in 45,500 fatalities all over the world. The next few months will indicate how efficiently the new H5 N1 virus can be transmitted among humans and whether the control efforts taken by the Hong Kong authorities are successful in aborting as potentially very serious pandemic. Any indication of a possible pandemic should call for the quick production of millions of doses of vaccine for use in the most susceptible individuals, especially the elderly and the very young. - - - -

VI. Kaposi Sarcoma-Associated Herpes Virus (KSHV) (Human Herpes Virus 8): For several years some scientists argued that AIDS-associated Kaposi's Sarcoma (KS) was most likely caused by an infectious agent separate from HIV because it occurred much more commonly (approximately 20 times more) in gay and bisexual men than in hemophiliac, heterosexual, or pediatric AIDS patients. Alternative explanations (e.g., nitrite inhalation among homosexuals) could not be ruled out. In 1994, herpesvirus-like DNA sequences were identified in AIDS-associated KS tissues suggesting the presence of a new herpesvirus' 16]. This was done with polymerase chain reaction (PCR) technique using a procedure called representational difference analysis (RDA) (see section on molecular tools below).

Much work done during the last few years has confirmed the presence of KSHV and strongly suggested its causation of KS. Thus, KSHV-DNA is detected in all KS including classical, AIDS-associated, and iatrogenic types.

KSHV can now be cultured. Sequencing of the KSHV genome has demonstrated its relatedness to the gamma herpesviruses, Epstein-Barr Virus (EBV) and Herpevirus Saimiri[17]. Antibodies to this virus are detectable mainly in KS patients or in those at risk of developing KS. Serologic assays suggest that infection with KSHV is not ubiquitous because seropositivity is limited to a small proportion of the population[18].

KSHV has also been etiologically linked to multicentric Castleman's disease, a polyclonal lyrnphoproliferation associated with prominent vascularity and with primary effusion lymphoma (body-cavity-based-lymphoma). KSHV DNA was also detected in bone marrow dendritic cells in multiple myeloma patients. In addition, KSHV encodes a homologue of interleukin-6 (IL-6) which may playa role in induction or promotion of growth of myeloma cells; however, serologic studies did not support the association between KSHV and multiple myeloma.

KSHV also encodes two chemokine-like proteins (vMIP-I and vMIP-II). These proteins are highly angiogenic in the chick embryos, which suggests that they may playa pathogenic role in KS[19]. Interestingly, these chemokines have an inhibitory effect on HIV attachment to CR3 and, to a lesser extent, CCR5 receptors. CCR3 is one of the main receptors for HIV-1 entry into microglia. This has led to the suggestion that patients with KS may be less likely to develop HIV-related dernentias! 19].

VII. Borna Disease Virus: Borna Disease Virus (BDV)[20] is a newly recognized virus classified under a new family (Bornaviridae) with a nonsegmented negative-strand RNA genome. The virus has been associated with Borna disease, recognized in 1895 in Borna, Germany, as a neurological disease of horses. A similar disease in horses has been known for over 200 years. The disease is also found in other animals including llamas, cats, and cattle and most likely includes all warm-blooded animals. BDV replicates in neurons at low levels without killing them. It persists in the nervous system despite a vigorous immune response. Extensive pathological changes in the brain may occur. There is a wide range of disease manifestation from asymptomatic infection to movement and behavioral disorders. These may include posture, ataxia, immobility, impaired excitation, aggressiveness, paralysis, vision disorder, and progressive blindness.

The resemblance between animal disease manifestations and some human neuro-psychiatric disorders and the broad host range and geographical distribution of the virus has prompted consideration that BDV might be involved in human psychiatric illness. Virus isolation from clinical cases has been unsuccessful because of low productivity. Serological assays of anti BDV antibodies in psychiatric patients gave varying results *(0.6 380/0* reactivity) as compared to 0.20% reactivity in controls. Detection of the viral RNA with the PCR gave higher positive results but also a wide range between *0.0-800/0* in psychiatric patients as compared to 0.0-14% in controls, respectively. Generally it was concluded that there is a higher incidence of BDV markers in patients than controls. However, no single neuro-phychiatric disease in man could be clearly associated with BDV infection.

VIII. Ebola Virus: The well-known Ebola outbreak which occurred in Kikwit, Zaire in 1995 caused an international scare and resulted in 315 cases and 244 *(770/0)* deaths. Two subsequent outbreaks occurred in the Gabon in 1996, one involving 37 cases with 21 deaths, the other 24 cases with 17 deaths. The Gabon viruses are more closely related to the Zaire viruses than to other Ebola virus isolates (i.e. Cot d'Ivoire, Sudan, or Reston (Philippines) isolates. Figure 2 shows the genetic relatedness between the various Ebola viruses isolated in recent years[21].

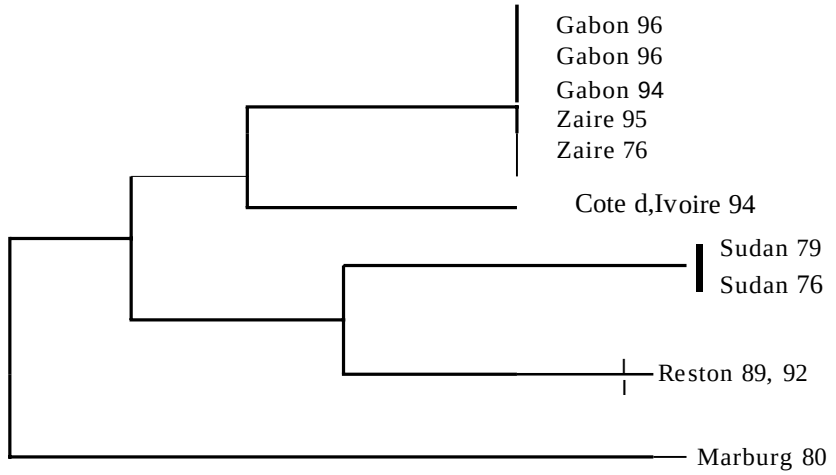


FIG. 2. The genetic relatedness between the various Ebola viruses isolated in recent years.

The natural reservoir of the Ebola viruses remains elusive. The primates from which disease has usually been transmitted to man are not considered to be the natural reservoir for these viruses because infection in these animals is quickly fatal. Recently, bats have been found to support virus replication under experimental conditions without getting the disease[22].

The potential danger of Ebola virus in our local setting, such as during Hajj, cannot be estimated. Air travel may allow for the introduction of virus for endemic areas. Per-

son-to-person transmission by close contact or by blood contamination, particularly in the health care setting, have been the main methods of transmission. This indicates that proper case recognition and containment and the enforcement of universal precautions in hospitals should be strongly emphasized during such major events.

IX. Other Hemorrhagic Fever Viruses: There were recent outbreaks of hemorrhagic fevers caused by several viruses as follows:

- Yellow fever
  1988-1991 18735 cases 4522 deaths
- Lassa fever
  1996-1997 823 cases 153 deaths
- Several other hemorrhagic fever viruses in Latin America (e.g., Junin, Sabia, Machupo)

X. AI-Khorma Virus: a New Arbovirus (Flavivirus) from Saudi Arabia: A new tlavivirus was isolated from cases of hemorrhagic fever in the Mecca region in 1995[23]. This virus was found to be related to the tick-borne Kaysanur forest disease virus group. About ten cases were diagnosed by virus isolation or seroconversion. Six of the cases occurred in butchers, one of whom had possible exposure during the Hajj season. Some patients had encephalitis in addition to hemorrhagic manifestations. There were four deaths. The virus was named "Al-Khorrna" after a village in western Saudi Arabia where some of the specimens yielding virus isolates came. The principal mode of transmission was percutaneous from slaughtered livestock, but in one case drinking of raw camel milk was suspected. This outbreak and previous outbreaks of Congo-Crimean hemorrhagic fever emphasize the existence of arboviral zoonotic infections in Saudi Arabia.

XI. Hepatitis G Virus: Two new hepatitis viruses (HDV; GBV-V) were recently identified from the blood of chronic hepatitis or cryptogenic hepatitis patients. The two viruses are very similar and probably represent different isolates of the same virus, now called hepatitis G virus. This virus is similar to the flaviviruses and, especially, to hepatitis C virus. A new scheme of classification will place both of these viruses, together with similar primate viruses, under a new family, the Hepciviridae. It is now realized that HGV has a global distribution, that is transmitted by blood or blood products, and that it causes persistent infection. The prevalence of HGY RNA among blood donors in the U.S.A., Japan, and Europe was estimated to be about 1-2%. Higher rates are detected among blood donors in some countries or among hemodialysis patients or IV-drug abusers. Although HGV has been detected in acute or chronic hepatitis cases, frequently in association with hepatitis C, most HGV infections are subclinical and do not lead to disease. The pathogenic potential of this virus in humans thus remains to be assessed[24,25]. However, even if HGY does not turn out to be significantly associated with disease, it will still present blood transfusion centers with a problem, i.e., to screen or not to screen blood for this virus.

XII. Equine MorbjJjvirus: In]994 and 1995 outbreaks of equine morbillivirus affecting horses and humans occurred in Australia, as follows[26]:

		Infected	Dead
1st Outbreak	Horses	21	14
	Humans	2	1
2nd Outbreak	Horses	2	2
	Humans	1	1

Equine morbillivirus belongs to the family of paramyxoviruses. These were the first known human cases associated with infection by this virus. The genus Morbilivirus includes measles virus.. the canine distemper, and the rinderpest (cattle) viruses. Epizootics by dolphin and porpoises morbilliviruses occurred in the U.S.A. Atlantic coast in 1987 and 1993. Preliminary search resulted in the identification of bats as possible reservoirs for the equine morbillivirus.

XIII. Calicivirus Gastroenteritis: Several outbreaks of gastroenteritis associated with human caliciviruses were reported from the U.S.A. in the last few years[27]. Human caliciviruses have been classified into four genogroups: Norwalk virus (NY), Snow Mountain agent (SMA), Sapporo, and hepatitis E technique (HEY). Caliciviruses cannot yet be grown in tissue culture. Diagnosis is by ELISA using recombinant antigens or by detection of virus-specific sequences by PCR.

XIV. Enteroviral Meningitis: An increase in enteroviral meningitis among hospitalized children was recently noted abroad. In Riyadh, an apparent increase in enteroviral meningitis was also reported[28]. ,Thus, cases of aseptic meningitis increased ten-fold from a mean of 3.8 cases per month to more than 32 cases per month between January and July 1996. Of 285 cases of meningitis admitted to five government hospitals, aseptic meningitis was diagnosed in 184 (65%). Enteroviruses, including echoviruses 27,30 and 33 were isolated from ten patients.

XV. Bovine Prions and nvCJD: Despite not being viruses, prions are usually ineluded in the discussion of viral agents because of their small size and their intracellular multiplication. Bovine spongiform encephalopathy (BSE) appeared in the U.K. in 1986 and has since resulted in over 161,000 cases. In 1996, a new variant of Creutzfeldt Jakob (nvCJD) disease was noticed in the U.K. which differed from the classical CJD in that it affected younger patients, had a prolonged illness, and a different neuropathological picture[29,30]. So far, 20 cases of nvCJD have been reported in the U.K. and one case in France. NvCJD was originally linked to BSE on the basis of epidemiological studies. New evidence on the relationship of .nvCJD and BSE has now come from the observation that macaques inoculated with tissue from BSE animals get a disease with a similar pathology to human disease. Additionally, molecular markers in mice infected with nvCJD or BSE agents are similar.

The concept of "prions" as causes of infectious disease has gained wider acceptance recently with additional evidence from molecular techniques despite the fact that opposing views still remain. The recent awarding of the Noble prize to Dr. S. Prusiner indicates the extent of acceptance of this concept.

The occurrence of BSE and its possible transmission to humans show the tremendous impact that new infectious agents may have, even if the total number of human cases was small.

Why More Viruses are Discovered: There are several reasons why new viruses have been discovered recently. One is the advances in molecular techniques which made it possible to detect new agents that are not easily grown in tissue culture such as hepatitis C, hepatitis G, Hantaviruses, and Kaposi sarcoma herpes virus. Another factor is better awareness of the type of disease that viruses may be causing. A third factor is the establishment of sentinel reference labs to be continuously on the lookout for new viruses, such as in the case of the H5N1 influenza virus.

New Molecular Tools for the Identification of Unculturable Viruses: New molecular techniques that proved useful in the detection of new agents include!'!':

1. Representational difference analysis PCR.
   This technique is based on PCR enrichment of DNA fragments present in diseased tissue but absent from healthy tissues of the same patients. Only the infectious agent's sequences are intensified after host sequences are absorbed out. This technique was useful in the discovery of KSHV and hepatitis G (GBV-C) viruses.
2. Consesur PCR.
   This technique relies on the use of highly conserved DNA sequences, such as ribosomal'RNA gene sequences from known organisms, to amplify DNA from related organisms not yet discovered. Consensus PCR was useful in the discovery of hantavirus involvement in the 1993 U.S.A. outbreak of hantavirus pulmonary syndrome.
3. cDNA Screening.
   This technique was useful in the discovery of hepatitis C and hepatitis G viruses. It relies on the synthesis and detection of viral antigens made from cDNA isolated from infected tissue.

Control of Emerging Viral Pathogens: Several measures should be considered if the effect of new emerging infectious diseases are to be minimized. Such measures include:

1. Prompt diagnosis based on epidemiological suspicion, conventional laboratory techniques, and molecular techniques is essential.
2. Public health measures such as patient isolation, quarantine measures, and animal culling may be needed.
3. The technology for fast production of vaccines should be ready for the control of new reassortant viruses (e.g. H5N1) if they prove capable of efficient widespread transmission. In this regard, the new technology of DNA vaccines[32,33] may turn out to be very helpful.

International Conference of Emerging Infectious Diseases: In the above presentation I have, only selected some new viruses for illustration of the importance of new in-

fectious agents. Several bacterial, fungal, and parasitic agents which have not been addressed have also re-emerged in the past few years. A more comprehensive review of new infectious agents may be expected at the International Conference on Emerging Infectious Diseases to be held in Atlanta during 8-12 March 1998.

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إعـــادة انبثـاق وظهور فيـروسات مرضيـة جـــديدة

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II - **خلص.** لقـد اكـ - ـ ف ت في السنوات القليلة الماضيـة عـدة أنواع من الفيروسات - وبالإضـافة JI ذلك فإن بعض الفيـروسات المعروفة قد أعـادت انبثاقـها إما بنفس الصورة المرضية Ji بصورة ".ضية جديدة وكلاالنو عين من الفيروسات التي عادت للظهور Ji بدت جديدة مثل فيروس متلازمة العوز - المناعة المكتسبه وهانتافيرس (Hanta) وفيروس جدرى القرود وفيروس الدنجيج وفيـروس الإنفلونزا – والورم اللحـمى كـابوس المتـلازم لمرض نقص المناعـه المكتسـبـه (الإيدز) وفـيـروس ".ض بورنا Barna disease وفـيـروس إبولا وفيروسات الحمى النزفية الاخرى وفيروس الخرمه من المملكه العربية السعودية وفـيروس الكبـد الوبائي G وغـيـرها من الفيـروسات الجـديدة ويعزى مزيد من الإكتـشـافات الجـديدة في حقل الفيـروسات إلى التـقـدم العلمي خـاصـة في التقنيات الجزيئية.