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**THE IMPORTANCE OF EPIDEMIO-SURVEILLANCE IN THE
PREVENTION, CONTROL AND ERADICATION OF MAJOR
VIRAL DISEASES OF PRIMATES.**

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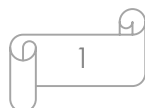
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INTRODUCTION TO VIRAL DISEASES OF PRIMATES

The infectious diseases of this large group of animals are as diverse as the groups of animals they affect. Only the most important zoonotic hazards in the primates will be considered. Discussion of the zoonotic diseases will be limited to the Virchow definition: animal diseases transmissible to man.

VIRAL DISEASES

Probably the most dangerous diseases, because they are so difficult to diagnose and treat, are those of viral origin. Many viral diseases, such as hepatitis or herpes B, can be transmitted from animal to man. A virus may be latent in one species of primate, with little or no disease, yet be fatal in another species of primate, including man.

Herpesvirus. Herpesviruses have been found in many different species of primates. Some herpesviruses can produce a highly fatal systemic disease.

Most primate herpes viruses are latent in one reservoir host species and fatal in another species. Overt disease in the host species rarely occurs other than as a mild skin lesion that is quickly self-limiting. The most important of the zoonotic diseases is herpes B virus or *Herpes simiae*.

Herpes simiae (herpes B) produces a mild disease in some species of monkeys that is analogous to the cold sores caused in humans by the virus *Herpes hominis* (simplex), to which B virus is immunologically related. In man, B virus can be fatal, causing an acute ascending myelitis. Of the 20 plus cases reported, only two patients have survived, and there is some question on the confirmation of B virus in those two. Thus, the virus has a possible mortality rate of 100 per cent in patients who develop clinical disease. Under natural conditions, the virus seems limited to the macaques, with both the rhesus and cynomolgus considered primary natural hosts; however, other macaque species are also incriminated from results of serologic testing.

As high as 25 per cent of macaques, both imported and domestically bred, have antibodies to herpes B virus in the U.S.A. A short incubation period of 4 to 10 days is required from initial exposure. As with *Herpes hominis*, recurrent infection can occur even in the presence of antibody; thus, all macaques at any time should be considered potential carriers. As with other herpes infections, viral shedding probably occurs only during periods of active lesions. The lesions in the primates can be difficult to detect because they are usually on the mucosa of the buccal cavity. There may be vesicles or ulcers around the lips and external nares, with an appearance very similar to the cold sore of man; however, the most common site is the tongue. The lesion resolves quickly and often goes unnoticed by the handler. A rate of 2 to 3 per cent has been reported for clinical evidence of lesions in the macaque at any one time.

The primary transmissions are from monkey bites and aerosolization of the virus. Most human infections have resulted from laboratory accidents and monkey bites; however, one case was thought to have been caused by droplet spread. The hazard to the practitioner and the owner makes it imperative that macaques not be kept as pets and

that the risk be explained to the owner. Any macaque being handled should be sedated with ketamine hydrochloride. Face masks and rubber gloves should be used to prevent possible spread.

Serologic testing is available from primate reference services to determine the presence of *Herpes simiae* and/or *H. hominis* antibody. An isolated animal found negative for *Herpes simiae* will remain negative unless brought into contact with a primate shedding the virus. The virus can also cause a fatal disease in the bonnet monkey (*M. radiata*).

Two other herpesviruses, *Herpesvirus saimiri* and *Herpesvirus ateles*, which are found in the squirrel and spider monkey, respectively, are oncogenic in other nonhuman primates, causing neoplasms of lymphoreticular origin upon injection. The incidence of antibody to *H. saimiri* in wild-trapped squirrel monkeys approaches 100 per cent; however, *H. saimiri* and *H. ateles* are not considered zoonotic hazards to human beings. A recent survey by NASA, using an indirect immunofluorescence test, showed no positive serologic response to *H. saimiri* in human beings frequently exposed to animals shedding the virus. Similar negative data exist for *H. ateles*. These negative findings are mentioned here because of the popularity of New World monkeys, especially squirrel monkeys, as pets.

Poxviruses. Poxviruses cause foul diseases in nonhuman primates. All four viruses are infective to man, although the incidence of human infection for these viruses is low; monkeypox is the most frequent. Monkeypox is serologically related to smallpox in man, so a smallpox vaccination will prevent human development of monkeypox. Recent surveys on purported "smallpox" outbreaks in Africa show that many of these cases were monkeypox in unvaccinated individuals. The virus is found in both New and Old World monkeys and apes with epithelial papular and vesicular lesions. Protection is achieved through vaccination of animal and owner.

Benign epidermal monkeypox (BEMP) is known as "Tana pox" in the human being. It was first recognized in 1965 in African children. The reservoir hosts are macaques; New World primates are not infected. Clinical signs are crusty elevations of the skin of the face, digits, and perineum. Lesions usually regress in 3 to 6 weeks with no scarring. Immunity following infection in the nonhuman primate lasts about 6 months.

Yaba virus infection is a rare disease of macaques, patas, baboon, and man. The squirrel monkey and marmoset are resistant. Clinical lesions are found as dermal tumors of the face, which regress spontaneously in 2 to 3 weeks for up to 4 months. The virus, which is arthropod-borne, is seen only in newly imported macaques.

Molloscum contagiosum is seen only in chimpanzees and man as a small, domelike waxy papule on the face and eyelids. The disease regresses spontaneously and is mildly contagious from animal to man.

Measles (Rubeola). Measles is the most frequently reported viral disease of nonhuman primates. In the wild, its incidence among them is almost nonexistent; infection comes from exposure to infected children during trapping. Upon infection, the primate sheds the virus and can reinfect man. Measles is a highly infectious exanthematous viral disease of children that causes a similar maculopapular rash in most nonhuman primate species. Vaccination with 1/2 ml of an attenuated live virus is protective for man and other primates. The disease in marmosets, tamarins, and owl monkeys is usually fatal.

Rabies. Nonhuman primates are as susceptible to rabies as human beings. Modified live vaccines for dogs and cats can cause rabies in the nonhuman primate. Only killed vaccines or vaccines suitable for man must be used in nonhuman primates. Primates housed in rabies-endemic areas are potentially at risk for indigenous wildlife and should be vaccinated. Symptoms in the primate, as in man, are hydrophobia and paralysis. The furious form is not usually seen in the nonhuman primate. Because of the seriousness of this disease, the risk should be minimized by isolation, environmental control, and a pre-exposure immunization program for animals in an endemic area.

Marburg Virus. Although the vervet, or African green monkey, is rare as a pet, the potential health hazard to human beings of this disease requires its mention. Marburg virus was first reported in human beings in Europe in 1967. Of the 31 cases in those outbreaks, 7 were fatal. Twenty-five of these cases were found in laboratory personnel exposed to African green tissue culture. No cases were reported in personnel handling the live African green monkey. The latest reports were of 300 fatalities in Sudan and Zaire (1976), caused by an unconfirmed but morphologically indistinguishable virus, and 3 confirmed cases in Kenya (1980). The reservoir host has never been determined; however, the virus is virulent experimentally for vervet, rhesus, and squirrel monkeys. In man there is a 4- to 9-day incubation period, accompanied by fever, weight loss, vomiting, and diarrhea after 3 to 4 days. In nonhuman primates, death occurs in 6 to 9 days with no signs until the day of death. Considering the potential danger all African green monkeys should be handled as if infected.

Viral Hepatitis. The virus of human infectious hepatitis (hepatitis A) can infect the chimpanzee, patas, woolly monkey (*Lagothrix* spp.), gorilla, cebus, aotus, and some tamarins. Infection in the primate is usually inapparent; however, the animal can carry the virus and be infective to man. Several outbreaks have been reported in primate handlers in research facilities. The disease in primate handlers appears to be related to handling recently shipped animals; the virus is probably spread shortly after exposure, antibodies develop, and the animals then become immune to reinfection. Because chimpanzees have not been imported as pets for many years, the few pet chimpanzees encountered probably present no danger of hepatitis. However, the chimpanzee is susceptible to disease from infected persons. Vaccines are being developed, but they are not recommended for routine primate vaccination (Renquist and Whitney, 1987).

Recent HIV infection or divergent HIV or **simian immunodeficiency virus (SIV)** strains may be responsible for Western blot-indeterminate results on 70 serum samples from Zairian hospital employees that were reactive in an enzyme immunoassay. Using universal polymerase chain reaction HIV-1, HIV-2, and SIV primers, we detected 1 (1.4%) HIV-1 sequence. Except for 1 sample, no molecular evidence for unusual HIV- or SIV-like strains in this sampling was found. HIV-1 and HIV-2 are believed to be the result of cross-species transmission from simian immunodeficiency virus (SIV)-infected chimpanzees and sooty mangabeys, respectively, which represent 2 (SIVcpz and SIVsm) of the 6 major lentiviral phylogenetic lineages. No evidence exists that SIV strains from the remaining nonhuman primate lineages have infected humans, although many grow in

human cells in vitro as do SIVcpz and SIVsm. Since humans are exposed to a plethora of primate lentiviruses through blood or body fluids during hunting, butchering, eating bushmeat, and keeping primates as pets, the potential exists for zoonotic transmission of diverse primate lentiviruses in many parts of sub-Saharan Africa, including the Congo River basin. This potential is supported by the identification of a Cameroonian man whose HIV serologic results were indeterminate but whose serum specimen reacted strongly and exclusively with an SIVmnd V3 loop peptide. An even more compelling case for cross-species exposure is the recent finding of a Cameroonian man who may have been exposed to a colobus SIV, as indicated by a strong humoral (env IDR and V3) and a weak cellular (gag) immune response. Although SIV sequences were not identified in either case, the findings suggest that humans are probably exposed to different simian retroviruses that can establish new infections in humans.

Nonhuman primates infected with SIV from the currently recognized lineages can harbor antibodies that serologically cross-react with some HIV-1 or HIV-2 antigens. In many cases, HIV Western blots (WBs) with indeterminate profiles of SIV-infected monkeys resemble those of HIV enzyme immunoassay (EIA)-positive, WB-indeterminate human sera from Africa. In general, such indeterminate African sera demonstrate a broad range of reactivity to HIV-1 proteins, in contrast to predominant p24 reactivity in WB-indeterminate sera from persons in the United States. These data suggest that the WB-indeterminate patterns in HIV EIA-reactive sera from persons living in Africa may reflect more than just a recent HIV infection or an infection with a highly divergent HIV-1 strain; they may reflect either cross-reactivity with unknown pathogens of African origin or exposure to new HIV- or SIV-like strains (Schaefer *et.al*, 2005).

Sentinel Surveillance

In tropical lowland forests, which contain the greatest biodiversity of terrestrial habitats (Turner, 1996), exist rarely seen or unknown pathogens with the potential to enter human populations. These pathogens may affect residents of and visitors to forested regions (Meslin, 1992) and act as the source of introduction of infectious agents to distant susceptible populations. Increasing human contact with forested systems almost certainly leads to a corresponding increase in the emergence of infections in the human population. Nevertheless, predicting which pathogens humans may encounter and be susceptible to remains a methodologic challenge.

Surveillance methods for predicting emerging pathogens include surveillance of vectors or forest-dwelling human populations and wildlife epidemiology (epidemiologic study of infections in wild populations) (Grenfell, 1995). These approaches have limitations. While vector sampling may prove the easiest method for widespread surveillance, the pathogens identified from vectors may be difficult or impossible to culture. Even when successful, vector sampling is likely to identify a range of pathogens, only some of which may infect humans. Studies of human populations, while providing

valuable information, are limited to regions in which forest-dwelling human populations exist.

Epidemiologic research among free-ranging primate populations has the potential to predict which pathogens might enter human populations as contact with forested regions increases. In addition to their physiologic similarities to humans, primates have other characteristics that contribute to their accumulation of infectious agents. Primates live primarily in forested environments; in general, they have large bodies and live in large groups characteristics that may attract vectors. Furthermore, dependence on fruit, a characteristic of most primates, requires mobility (both terrestrially and arboreally), a trait that may increase exposure to pathogens (Freeland, 1976; Loehle, 1995).

Despite the lack of organized attempts to document the distribution of pathogens in wild populations, recognized "die-offs" in wild primate populations have played an important role in identifying novel pathogens. In 1956, for example, a novel flavivirus was identified through the investigation of large-scale deaths of bonnet macaques (*Macaca radiata*) and hanuman langurs (*Presbytis entellus*) in the Kyanasur Forest of India (Barack, 1987) caused by Kyanasur Forest virus. More recently, in 1995, deaths in a chimpanzee population studied by Christoph Boesch in the Tãï Forest, Côte d'Ivoire, and a single human case following a necropsy led to the identification of a novel strain of Ebola virus (Morell, 1995; Le Guenno *et.al.*, 1995). The single human case in the Swiss researcher foreshadowed the localized mini-outbreak of Ebola hemorrhagic fever in Mayibout, a village in the northeast of Gabon in January 1996. The Gabon epidemic was linked to the handling, preparation, and consumption of a chimpanzee that had been found dead; 29 of 37 identified cases involved exposure to the dead chimpanzee (WHO, 1996). Close monitoring of such populations, as is being conducted in the Tãï Forest, has the potential to identify emergence-linked behavior, such as the consumption of specific plants or insects, which may lead to the still elusive reservoir of Ebola virus. Considering the exceptionally small percentage of wild primate populations under long-term study, these examples represent only the tip of the iceberg. More systematic monitoring of wild primate populations will likely provide a substantial payoff in our understanding, identification, and possible control of novel pathogens, both for humans and endangered primates.

Surveillance for certain types of human-nonhuman primate contact may be particularly useful. Hunting, which involves tracking, capturing, handling, transporting, preparing, and consuming meat, may play a particularly important role in pathogen exchange. In addition to the recent evidence of hunting-mediated Ebola transmission, the hunting of a red colobus (*Colobus pennanti oustaleti [=badius]*) has been implicated in a localized epidemic of monkeypox, an orthopoxvirus similar to smallpox, which continued for four generations of human-to-human contact (Jezek *et.al.*, 1986). Another example is the increased risk for feline plague among cats that hunt rodents (Eidson *et.al.*, 1988). Necropsies share many characteristics with hunting and are appropriately considered a high-risk activity.

Bites from wild primates may also play a role in the transmission of certain pathogens. For example, chimpanzee-to-human transmission of monkeypox occurred when a wild chimpanzee bit a 2-year-old girl (Mutombo *et.al.*, 1983). Further sampling demonstrated high prevalence in forest squirrel populations (up to 49% among *Funisciurus lemniscatus*)

(Fenner, 1993), underlining the need for comprehensive studies before determining the ultimate source and reservoir of pathogens. Bites and scratches have transmitted pathogens to laboratory workers. The transmission of B-virus, a herpesvirus infecting rhesus macaques (*Macaca mulatta*), has caused death in 18 of 24 known human cases (Palmer, 1987). Surveillance and education in human populations that hunt nonhuman primates, as well as follow-up of reported primate bites in nonlaboratory settings, may be indicated.

EPIDEMIOLOGICAL SURVEILLANCE

- _ Organizing surveillance networks.
- _ Surveillance strategies: epidemiology of priority diseases, sampling, domestic/wild animal interactions.
- _ Diagnosing parasitic, bacterial and viral diseases, managing laboratories.
- _ Sampling, setting up and managing relational databases, geographical information systems (GIS).
- _ Identifying and monitoring pathogens (molecular epidemiology) (www.euprim-net.eu/network/courses/downloads/presentations/course4/1aa_gillespie).

ONE EXAMPLE OF PRIMATE DISEASE SURVEILLANCE (CHIKUNGUNYA DISEASE SURVEILLANCE)

INTRODUCTION

Chikungunya is a viral disease. The illness was observed for the first time in 1952 in Tanzania. The name comes from the local dialect, Swahili which means "that which bend up" for stooped walk, reflecting the physic of a person suffering from the disease.

EPIDEMIOLOGY

Chikungunya is caused by an Arbovirus, belongs to the genus *Alphavirus* under the *Togaviridae* family. The virus is transmitted to human by infected *Aedes* mosquitoes, *Aedes albopictus* in the rural area and *Aedes aegypti* in the urban area. The urban outbreaks are sporadic but explosive in nature. It then disappears and reappears at irregular intervals. In some parts of Africa, Chikungunya virus was isolated from zoophilic mosquitoes. It suggests that the virus circulates in rodents and cattle in the region. Virus was also obtained from a squirrel, chiroptera, and ticks (*Alectorobius sonrai*), as well as the presence of antibodies specific for Chikungunya virus in rodents and birds, support the assumption that secondary wild cycles exist in animals. The existence of such cycles could contribute to maintaining of the virus in an endemic region in Africa.

OBJECTIVES

1. To predict impending outbreak of Chikungunya in the future.
2. To estimate the magnitude of Chikungunya disease in the population.
3. To reduce *Aedes* mosquitoes density in the community.
4. To increase public support and community participation in the prevention and control of dengue.

CASE DEFINITION

Suspected Chikungunya disease

A case with sudden onset of high grade fever, polyarthritits and maculopapular rashes.

Confirmed Chikungunya (CHIK) disease

The above with laboratory confirmation of Chikungunya virus infection either;

♦ occurrence at same location and time as other confirmed cases of Chikungunya case;

OR

♦ detection of anti-CHIK-IgM antibody in serum , 2 fold rise of IgM;

OR

♦ detection of CHIK nucleic acids in serum by RT-PCR test;

OR

♦ isolation of Chikungunya virus.

NOTIFICATION OF CASES

Clinics and Hospital.

Chikungunya disease is not a notifiable disease. However medical practitioners is required to notify any case suspect or confirmed Chikungunya infection within 24 hours, as to reduce the morbidity and to curb Chikungunya outbreak. It is an administrative mandatory notification.

Laboratory

Any laboratory with a positive laboratory CHIK result should inform the nearest District Health Office for further investigation and field management.

PUBLIC HEALTH RESPONSE

Case management

Investigate the contacts of cases through active case detection. Search for unreported or

undiagnosed cases where the patient lived during the 2 weeks period prior to onset of notified case. Any new case* which fulfilled the clinical case definition detected during the ACD activities should be referred for further management.

Vector Control

The source of infection should be sought.

(a) House and Premise Inspection

House and premise in the area where patient lives should be inspected for potential mosquito breeding sites, to get the Aedes Index (normal < 1 %) and the Bruteau Index (normal < 5) of the area. The source reduction activities should be carried out to reduce breeding sites in all premises.

(b) Fogging

Fogging should be done in areas where the Chikungunya case is reported, after doing the Aedes survey. Activity should be targeted to Aedes mosquito i.e. it should be done at dawn and dusk time.

(c) Larviciding

Larviciding e.g. using temephos to destroy the larval stage of Aedes mosquito should be carried out to potential breeding sites that could not be destroyed.

Entomological surveillance

Adult mosquito and larval survey should be conducted in the area where patient lives. Larval survey for Chikungunya virus is important to evaluate the transovarian/ vertical transmission of the virus; even though at present moment there is no evidence of vertical transmission. Intermittent entomological study for Chikungunya virus in adult mosquitos and larvae should be carried out. It is especially important in area where the possibility of sustained transmission occurred in animal e.g. monkeys, as in Africa and areas with many foreign workers from endemic area of Chikungunya disease.

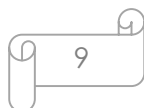
** a new case of Chikungunya virus infection is a case who fulfilled the case definition and manifest the symptoms for the first time.*

Community empowerment and mobilisation.

Exhibitions, dialogue sessions, demonstrations and distribution of pamphlets, posters should be enhanced; to inform the public about the disease and the prevention measures. Stress on treatment seeking behaviour of cases, eliminating the breeding sites and notification of cases by private clinic and head of community should be made. Interagency cooperation and community participation in keeping the environment free from mosquitos especially *Aedes* is also one component that should be enhanced.

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