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EMERGING INFECTIONS IN A WORLD OUT OF BALANCE

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Introduction

The world has become much more vulnerable to the widespread and even global spread of both new and old infectious diseases. Conditions conducive to the emergence and re-emergence of infectious diseases involve complex interplay between environmental, microbial and human behavioral and socio-economic factors. An emerging infection has been defined as a disease that comes to our attention because it involves a newly identified organism e.g. Human Immunodeficiency Virus (HIV), or a known organism that newly started to cause disease (e.g. microsporidia) or an organism whose transmission or virulence has increased, e.g. multidrug resistant tuberculosis (MDR TB), vancomycin resistant enterococci (VRE), methicillin resistant S.*aureus* (MRSA).

Shortly before the first cases of unexplained immunodeficiency among homosexual males were being recognized in the USA, the world health assembly announced that small pox has been eradicated throughout the world[1]. Moreover at that time there was wide spread optimism that many infectious diseases were under control, preventable or curable. The HIV epidemic, emergence antimicrobial resistance and the emergence of other infectious diseases all proved that this optimism was ill founded. Clearly, infectious diseases are among the most important issues facing medicine at the end of this century, just as they were at the end of the last century. The last 20 years have witnessed a rapid change in the spectrum of infectious diseases in both developing and developed countries and this currently threatens the health of populations throughout the world.

What I would like to address today is 'How changes in human behavior and the resulting new ecology have affected the spread of infectious diseases'. The human factors responsible for ecological changes include population growth, poverty, human migration caused by war, famine, geopolitical conditions, modern technology, rapid and creasing international travel and changing personal behavior.

Effect of war and urbanization

One such disease that resulted from war and urbanization is dengue haemorrhagic fever. Dengue virus is transmitted by the *Aedes aegypti* mosquitoes and humans are the intermediate hosts. The disease is caused by antigenically related but four distinct virus strains.

Dengue fever had been recognized for over 200 years. 'Denga' which means sudden overtaking by a spirit was the term used by East Africans to describe a mosquito carried disease that would abruptly overwhelm human beings producing severe headache, eye pain, and aching bones and joints. During the 18th and 19th centuries the disease occurred in intermittent epidemics affecting Asia and Americas occurring at intervals up to several decades. Spread was slow generally by ships carrying breeding mosquitoes and susceptible human hosts. As countries throughout the world conducted *Aedes aegypti* eradication campaigns during the early twentieth century to rid the earth of yellow fever another mosquito carried disease, dengue out breaks virtually ceased. A comfortable dengue silence set in during 1940s. In most cases dengue was not a life threatening ailment through it was certainly a miserable experience for the afflicted. The uncomplicated disease is a biphasic illness beginning abruptly 3 - 8 days after the bite of an infected mosquito characterized by fever and muscle pain. Improvement after several days is followed by reappearance of fever and sometimes a rash.

The clinical picture changed dramatically during and after World War II.

In 1953, the city of Manila reported an apparently new and more lethal form of dengue that caused haemorrhagic patches, skin of breakthrough bleeding shock and fever. Five years later a similar picture was seen in Bangkok causing 694 deaths. The medical records of people who suffered from the haerrtorrhagic form of the disease showed that nearly all victims had at sometime been exposed to another milder dengue infection due to a different strain.

The immune response to dengue infection plays an important role in determining the outcome and severity of infection. In most patients humoral and cellular responses result in recovery. However a subsequent infection with a different strain may result in severe disease due to immune pathologic disease mediated by the interaction of antibodies and T cells [2]. These complicated forms of dengue are known as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).

It was concluded by Thomas Monath, that the World War 2 was responsible for the emergence of haemorrhagic dengue in Asia[3]. Massive human migrations, serial bomb campaigns, densely populated refugees camps and wartime disruption of all mosquito control efforts allowed for an unprecedented surge in the *Aedes aegypti* population. The mosquitoes were able to use bomb craters filled with water as breeding sites and to draw blood from millions of human victims of war whose homes were destroyed and no longer provided protection from the hungry insects. Multiple dengue serotypes were geographically shuttled by viraemic troops and refugees. Therefore areas which for centuries had only a single strain of dengue infecting its human and insect population were over run by all four dengue types.

The dissemination of virus and vector was enhanced after the war by rapid population growth and urbanization. Asian cities were characterized by poor sanitation, the necessity for domestic water storage, crowded unhygienic living conditions creating conditions favoring breeding of *Aedes* mosquito species. Thus the system necessary for the creation of DHF and DSS was in place. This new dengue disease paradigm spread through South East Asia and at present the virus is endemic in and around major cites of Myanmar, Thailand, Vietnam, India and Sri Lanka. Dengue arrives each year shortly after the onset of every rainy season.

The incidence of dengue/DHF/DSS in Sri Lanka[4]

	DHF	Case Fatality rate %
1960	Number of cases	
1965.	2 deaths	
1966	13 cases/ 5 deaths	
1967	29 cases / 8 deaths	
1969 - 1976	No cases	
1977 - 1982	1 - 4 cases	
1982 - 1989	No records are available	
1990	1350cases / 54 deaths	4.0
1991	1048 cases / 31 deaths	3.0
1992	656 cases / 15 deaths	2.3
1993	756 cases / 7 deaths	0.9
1994	582 cases /7 deaths	1.2
1995	440 cases / 11 deaths	2.5
1996	1294 cases / 54 deaths	4.2
1997	980 cases / 17 deaths	1.7
1998	1275 cases / 8 deaths	0.6
1999	1699 cases /14 deaths	0.82

Since 1990 this is an annual phenomenon in Sri Lanka. The ability to control dengue by reduction of vectors seems increasingly remote. Efforts to develop effective vaccines are underway. However the immuno - pathogenesis of DHF demands that the protective immunity to all four serotypes be elicited simultaneously. Posing a formedable challenged to vaccine develoment.

Bioterrorism

In an era where war and violence are the rule of the day one needs to be concerned of bioterrorism. Bioterrorism is the deliberate use of pathogenic microorganisms and / or their products for the destruction of human, animal or plant life. The use of biological weapons probably started in the 1960's with a few isolated events and threats of use. In the 1970's and 1980's American groups such as RISE used agents of typhoid fever and dysentery. Red Army Fraction planned the use of botulinum toxin against West German officials. Rajneeshee cult in India used *Salmonella typhimurium.*

More recently the Japanese Aum Shinrikyo attempted the use of biological agents such as anthrak spores, botulinum toxin, Ebola virus and chemical agents such as hydrogen cyanide[5].

According to the United Nations Special Commission reports, Iraq is believed to have preserved biological weapons between 1991 and 1995. Some 380,000 liters of botulinum toxin, 84,000 liters of anthrax spores and 3400 liters of Clostridium perfringens spores had been in store. In 1990, 25 SCUD/ Al- Hussein missiles with biological weapon warheads were ready for use. As shown above, the scale of the problem could range from one isolated event to the involvement of many nations.

The motivation for such' attacks is varied. Promoting separatist and pseudopatriotic objectives, revengeful destruction of human life, apocalyptic prophecy, mimicking God and creating chaos were motivations for some of the groups mentioned above.

Traditional agents of bioterrorism [6]

Bacteria	Viruses	Toxins
Bacillus anthracis	Small pox	Botulinum toxin
Brucella suis	Viral encephalitis	Staphylococcal enterotoxin
Coxiella burnetti	Ebola, Marburg	Ricin
Francisella tularensis		
Yersinia pestis		

Biological weapons are considered more lethal than chemical weapons and could be as or even more destructive than nuclear weapons. Human effects can vary from temporary incapacitation to rapid death and could affect a few persons to thousands. In 1970 a WHO expert committee estimated that 50 kg of anthrax pores released by an aircraft over an urban population of 5 million would kill 100,000 without prompt treatment[7]. Since aerosols are colorless and odorless unaided detection by man is impossible.

The Effect of Changing Behavioral Patterns on Sexually Transmitted Diseases (STD)

The last 20 years have witnessed striking changes in the ST patterns. Despite its recent emergence, AIDS is shifting to affect new populations. In the United States AIDS spread first among predominantly white homosexual men, but AIDS incidence in this population began to plateau by the early 1990's. The second wave of the AIDS epidemic emerged among injecting drug users and was concentrated among racial and ethnic minority populations. At least since 1989, an increase occurred among heterosexuals and the majority occurred among women.

Changes in sexual behaviors have been one of the primary engines driving changing patterns of STDs, including HIV infection. Steady decreases in the age of first sexual intercourse and concomitant increases in premarital sexual activity have been documented. Younger cohorts report multiple sexual partners compared to older groups. In part this may be due to the combined effect of trends toward younger age of coital debut and older age at first marriage. In addition these increases are greater in women living in poverty. Both commercial sex and specific sexual practices such as anal intercourse, intercourse during menses, or dry sex have also been linked to increased risk of STD's However not much data are available on these sexual behaviors [8.] Other health related behaviors, such as contraceptive use, and circumcision may influence STD patterns more broadly. Correct and consistent condom use and male circumcision both decrease risk of STD's. Oral contraceptive pill use on the other hand may augment the risk of chlamydial and gonococcal cervicitis probably due to hormonal changes. Intra uterine device (IUD) use has been linked with increased risk of pelvic inflammatory disease (PID) and this may also increase the risk of STD by reducing the likelihood of condom use.

Over the past 25 years, dramatic changes in substance use behaviors reinforced the impact of changes in sexual behaviors on STD and HIV patterns. Drug use promotes anonymous sex and exchange of sex for drugs and money. Both drug and alcohol use may also impair ability to practice safe sex. More broadly the socio-cultural macro-environment forces the shape of many of the sexual, substance abuse and health related behaviors. Factors such as poverty, low status of women, social upheaval, urbanization and geographic mobility promote risk behaviors, because they destabilize the social norms by increasing inequality,

anonymity and marginalization. These factors often foster in environments with fragile public health infrastructures thereby, resulting in communities with high STD prevalence.

Effect of Deforestation, Reforestation and Irrigation

All over the world humans driven by needs that ranged from the search for wood with or which to heat their stoves to the desire for exotic locales for golf courses were encroaching into ecological niches that had not previously been significant parts of the Homo sapiens habitat. No place was too remote or exotic for intrepid adventurers, tourists and developers. When ecospheres are stressed, certain species of flora and fauna that were best suited to adapt to the changed conditions would quickly dominate, often at the expense of less flexible competitors. The net result would be a marked decline in diversity. As a result both deforestation and reforestation could therefore give rise to imbalance between flora, fauna and microbes and new disease phenomena would emerge Such was the case with Japanese encephalitis *(JE)* out breaks that emerged in Sri Lanka in 1985 and Lyme disease that occurred in North America.

Effect of Changing Ecospheres in the Development of Japanese Encephalitis (JE)

The JE virus was first isolated in Sri Lanka in 1968 and did not constitute a serious hazard to human health until major epidemics occurred in 1980's [9]. The JE virus is transmitted by zoophilc mosquito vectors belonging to the genus Culex and consequently wild and domestic animals are the principal hosts. Man is considered to be a dead end host due to short duration of viraemia and the relative preference of vector mosquitoes for animals over man. Pigs, cattle and birds are the most important hosts for maintenance, amplification and spread of the virus and they remain asymptomatic. The first two major epidemics of JE occurred in 1985 and 1987 in the low country dry zone rice growing areas in the north central and western provinces.

The reasons for the emergence of epidemic JE in the north central province remain to be fully explained. However it is noteworthy that over the last two decades there has been a major expansion of irrigated rice cultivation in the affected area. More recently there has been an increase in peri-domestic pig husbandry carried out by rice farmers as a means of supplementing their income. It was postulated that, the migration of farmers from highland regions into newly irrigated farmlands brought many susceptible persons into an area of transmission resulted in out breaks. In addition extreme political unrest during 1988 resulted in the countrywide breakdown of irrigation system management. Irrigation water releases for rice cultivation in the Anuradhapura district was sporadic and uncoordinated which resulted in a non-synchronous rice cultivation season. The clogged canals and decaying vegetation favored the breeding of the *Culex* mosquito species[10]. The outbreaks were quite dramatic and placed a significant burden on the health care system. Mass immunization and mosquito control measures were instituted in response to these outbreaks and are being continued.

Cases, Deaths and Case Fatality Rate of Japanese Encephalitis (1985 - 1998) [4]

Year	Cases	Deaths	Case fatality Rate %
1986	345	48	12.9
1987	168	36	21.4
1988	421	98	23.2
1989	220	43	19.5
1990	387	43	11.1
1991	325	25	7.6
1992	291	27	6.9
1993	289	52	17.9
1994	230	41	17.8
1995	173	32	18.4
1996	307	44	14.3
1997	164	19	11.6
1998	122	3	2.5

The Lyme disease, which occurred in North America, is characterized by chronic skin, nervous system and joint abnormalities. The ubiquitous northeastern mouse *Peromyscus leucopus* is the natural reservoir of B*orrelia burgdoferi* bacterium that caused the Lyme disease. The tick *Ixodes dammini,* lived on the rodent blood. The deer grazed through these areas picking up ticks, which bile feeding on deer blood, passed on the bacteria.

The Lyme disease resulted from deforestation of the northeastern territory, which was carried out in order to supply wood and fuel for the housing construction in the western territory and for the North Americas iron industry[11]. The old forests with tall oaks never returned but were replaced by scrub bush, meadows and non shade trees and the deer, voles, squirrels and birds unchallenged by predators. The new ecology was filled with insects and rent vectors. The deer carried the ticks as they made long foraging journeys through woodlands in to sub urban areas as there were no predators to keep the deer population on check There sheer numbers were great enough to force the animals to venture boldly for food into suburban front yards to nibble at cultivated land. This in turn guaranteed that three more species; humans, canines and felines would come into contact with the ticks and the *B. burgdoferi* bacteria they carried. Most Lyme sufferers live in wooded areas, which are inhabited by small animals.

Effect of Travel

The dramatic increase in worldwide movement of people and goods is the driving force behind globalization of disease. A jet plane boarded by a person harboring a life threatening microbe or cargo carried inside brings infectious agents into new ecologic settings. The current volume and speed of travel is unprecedented in history. It is now thought that any place in the world can be reached from any other within 36 hours. This time is shorter than the incubation period of almost all infectious diseases, which makes the usefulness of a quarantine officer standing at every port of entry ready to bar any ill appearing arriving passenger, much less relevant than in the past. Worldwide statistics on travelers indicate that 1.4 million individuals cross international borders per day. The travelers could be refugees, displaced persons, new immigrants or tourists[12].

Few habitats on the globe remain truly isolated and untouched as tourists and other travelers penetrate into most remote and previously inaccessible areas in their search for new vistas, business or recreation. New infections may arise in areas frequented by tourists and these may provide the first evidence for a new disease agent. Travelers often visit areas where the spectrum of infectious diseases includes agents that are non-endemic for their homeland. During travel such persons can get exposed to these illnesses and transport them home, contributing to potential global spread. They may also bring disease vectors with them and expand their range. Also travelers often engage in activities that increase their risk for disease exposure such as outdoor activities during adventure travel.

Common travel associated diseases[13] with a wide distribution are malaria, dengue, yellow fever. Schistosomiasis (Mali, Malawi), leptospirosis (tropical countries), cyclosporiasis, bartonellosis (Peru, Ecuador), avian influenza H5NI (Hong Kong), enterovirus- associated disease (Malaysia) are diseases that have a focal distribution but the latter two have the potential for explosive outbreaks.

'THIRDWORLDIZATION' (the interaction of poverty, poor housing and social despair with disease)

Effect of third worldization on the unchecked emergence of diseases is characteristic especially in the African, Southeast Asian and Eastern European countries when HIV hit the poor third world countries the effect was disastrous. It is making the worlds poorest nations, much, much poorer. After years of struggle to rise above the third world status, these nations are slipping backward.

When the African nations are considered, they entered the AIDS era already severely impoverished. At the same time a host of new microbes had successfully emerged and swept across the continent, such as drug-resistant malaria, drug-resistant tuberculosis, urbanized yellow fever, waves of measles epidemics to name a few. Also the hardest hit in Africa was the well-educated urban elite. They had attended universities abroad and acquired skills that could be used to navigate the country out of the post-colonial stagnation in to prosperity and infra-structural order. They were also among the few Africans who possess disposable incomes and could afford to indulge in the carefree nightlife of cities. The other factor was the familial nature of the epidemic, which led to wiping off of whole families and consequently whole villages. Direct AIDS costs,

i.e. drugs, hospitalization, health care personnel were lower compared to more affluent countries. Nonetheless indirect AIDS costs are more important than direct costs because AIDS strike people in their productive years.

Though in some parts of Africa women were less valuable than local livestock, they raise crops and children, the Africa's future. When husbands contract HIV in cities and passed it on to wives AIDS appeared in rural settings. If the husband died, his property would revert not to his wife but to his relatives. Thus one of the few survival options available to widows was prostitution and the cycle would repeat. Hope had to rest with the children of Africa. But studies revealed that many orphans died shortly after demise of their mothers due to failure to thrive rather than AIDS. Many were not vaccinated against childhood diseases and most were malnourished. A similar picture is taking shape in Asia. In some Indian states 50% of commercial sex workers are HIV positive at present.

Russia provides a classic example of 'thirdworldization'. Several hospital outbreaks of HIV were reported due to shortage of sterile syringes: The nation needed 3 billion syringes, but was manufacturing 30 million annually and importing none. Simple mathematics indicated .that the average syringe was being used 100 times. The result was widespread public panic and a sharp decline ill willingness to under go invasive medical procedures. Dentists, vaccinators noted a drop in attendance. Perhaps the most striking example of Russian thirdworldization was the 1993 outbreaks of Diphtheria in St Petersburg and Moscow [14]. A hallmark of the old Soviet Union had been its tremendous success in universal vaccination and resultant decline in the incidence of measles, whooping cough, polio and diphtheria.

Disease rates in Russia[15]

Disease	1993(rate per 100,000)	% increase from 1990
Measles	30	282
Diphtheria	1.9	163
Syphilis	9.5	136
Typhoid	0.2	82
Gonorrheal	77.4	60
Tuberculosis	13.6	24
Whooping cough	5.9	16

Effect of human behavior on development of drug resistant microbes

This presentation would be incomplete if I do not speak at least a few words on the emergence of drug resistant microbes. The mutability of bacteria coupled with their ability to pass around and share genetic material, which is the single most important factor, seems to leave Homo sapiens at a loss.

Long before Homo sapiens discovered the chemicals, yeasts, fungi, and rival bacteria had been making antibiotics against rival species to ensure that their niches are not invaded. The rivals had long since evolved to rapidly mutate to withstand to such chemical attacks and the cycle would repeat countless times over the millennia. Humans simply accelerated the natural process by exposing billions of microbes at a time to a particular drug or drugs.

The present status

Despite the development of new antibiotics staphylococcal infections remain potentially lethal. By 1982, fewer than 10% of all clinical staphylococcal cases could be cured with penicillin compared to 100 cure rates in 1952. Most strains of the bacterium accomplished this feat of penicillin resistance by absorbing the beta-lactamase plasmid in to their DNA that was passed from one generation to the next. Fortunately alternate drugs existed that did not use the beta lactam mechanism so clinicians were not alarmed. The treatment was switched to cloxacillin. But in the early 1980's cloxacillin resistant outbreaks were reported from all over the world, and more often from burn units, neonatal wards, ICU's and from settings where immunocompromised patients were treated. The alternative drug available for treatment of cloxacillin resistant strains was vancomycin, However by 1999 vancomycin resistant Staphylococci were reported from Japan

for the first time and effective new drugs are not available yet and therefore we are back in the 1930's with regard to staphylococci. The resistance probably was acquired from genes of vancomycin resistant enterococci in the human gastrointestinal tract.

Switching from inexpensive penicillin to cloxacillin increased the cost by about ten folds. Changing to vancomycin meant turning to one of the most expensive antibiotics in the market. It is a burden to wealthy countries but not prohibitive. The increased cost was beyond the reach of the poorer nations rendering some of the staphylococcal infections untreatable. The once penicillin sensitive *pneumocot,US,* the causative agent of lobar pneumonia and meningitis has evolved to become multiply drug resistant microbe in response to antibiotic pressure. *Streptococcus pneumoniae* is not efficient at absorbing plasmids, but it is a voracious DNA scavenger. At present it is sensitive to vancomycin, but it is only a matter of time.

Group A *Streptococcus* is one of the organisms that has remained susceptible to penicillin. However it has reappeared in the 1980's s a virulent bacterium causing toxic shock and narcotizing fasciitis. This affects people of all ages without any clear pattern of host vulnerability. The organism shows decreased susceptibility to penicillin, thus much higher doses are required for treatment and might be still fatal if treatment is not timely. In addition to penicillin tolerance this organism shows resistance to commonly used oral antibiotics such as erythromycin and cotrimoxazole in a substantial proportion. These are only three examples of emerging drug resistant bacteria.

How did this come about? What factors in human behavior contributed to this? Poor people all over the world were more likely to self-medicate, purchase antibiotics over the counter, borrow left oversee from relatives. Without consulting costly physicians, and certainly in the absence of expensive tests that could determine drug sensitivities of the bacterial strains with which they were infected, the world's poor were compelled to guess what drug might cure the disease that was ravaging their children or themselves. not long after the advent of antibiotics a radical change in veterinary and livestock practices took place. Expensive livestock lived longer when routine antibiotic dosing was given to chickens, cattle and dairy cows. The shelf life of meat, dairy products, eggs were extended through antibiotic treatment. As a result the number of drug resistant bacterial species increased.

This overuse and misuse of antibiotics guaranteed that a sizeable percentage of the human population are walking petri-dishes, providing ideal conditions for accelerated bacterial mutation, natural selection and evolution of resistant microbes. One must note that it is not only the bacteria that have acquired resistance to antimicrobials, but the viruses including herpes simplex virus, HIV and cytomegalovirus. The multi resistant *P. falciparum* species, which originated in the Thai-Cambodian border spread through out the world causing high mortality.

Antibiotic resistance in Sri Lanka

Organism	% Resistance
Methicillin resistant S. aureus	22-40[16]
Penicillin intermediate resistant pneumococci	41[17]
Erythromycin resistant S. *pyogenes*	25[18]
MDR tuberculsis	3[19]
Penicillin resistant *N gonorrhoeae*	69[20]
Ampicillin resistant *E. coli* in UTI	82[21]
Miconazole resistant C. *albicans*	42.8 [22]
Chloroquine resistant Malaria in endemic area	30[23]

Searching for Solutions

Many scientists struggled to understand and control microbial threats during post world war II era. Humanity's ancient enemies are after all microbes. They did not go away just because science invented drugs, antibiotics and vaccines. They did not disappear from the planet when Americans and Europeans cleared up their towns and cities in the post-industrial era. They certainly won't become extinct simply, because human beings choose to ignore their existence.

The lessons of history in the prevention of infectious diseases by immunization will not be particularly effective in the majority of cases in the absence of changes in human behavior and ecology. Syphilis for example is still rampant not withstanding availability of inexpensive and effective penicillin therapy. However effecting changes in human behavior and ecology may put rights of individual against the best interests of the society and one may face conflict of interest.

What are the options available to combat emerging infections?

1. Education of scientists in different disciplines

Emerging and re-emerging infections are attracting greater attention from the public health and medical communities. Microbiologists and Pathologists have an important role in the recognition, characterisation, diagnosis surveillance and research of emerging infectious diseases. This role is likely to increase in the coming years.

Microbiologists

Since the recognition less than 120 years ago that organisms visible only microscopically are capable of causing human diseases microbiologists have played a major role in identifying and characterizing the etiologic infectious agents and in elucidating the pathogenic mechanisms.

First microbiologists must educate themselves and their staff about emerging infectious diseases, including familiarity with the epidemiology. Diagnostic clinical laboratory personnel must be made part of public hea1th reporting. And they must have increased interaction with infectious disease clinicians, infection control practitioners and public health personnel.

Pathologists

Pathologists also have made important contributions to the understanding of infectious diseases. Despite significant achievements, pathology remains largely oriented toward neoplastic diseases and has not yet identified infectious disease diagnosis as an important component of anatomic pathology training and research, even in the face of the current the threats posed by microbial agents. A possible start to address these issues would be the development of formal training program infectious disease pathology as no such program exists in the world including USA.

Veterinarians

In the case of emerging infections involving free -ranging wildlife, the intrusion of urban and agricultural enterprises into wildlife habitats appears to be playing a major role in the exchange of infectious agents of domestic to wildlife species and vice-versa. It is important that the veterinary profession prepares itself to respond to the threatening challenges.

2. Improved laboratory services for accurate and rapid diagnosis

Diagnostic molecular methods have had a large effect on diagnosis and management of infectious diseases[24]. These tools have been developed in response to diagnostic methods that lack sensitivity, specificity, or rapid turnaround time, to assist with identification of agents that are difficult to cultivate or classify or as methods for assessing the effects of antiviral or antimicrobial agents in chronic infection. Molecular methods have also enabled microbiologists to define disease by the presence of virulence, toxin, or antimicrobial resistance genes and to identify potentially important clones of organisms responsible for outbreaks of infection. Early outcome-based studies suggest that molecular methods may provide substantial reductions in per patient costs. Nucleic acid diagnostic methods will continue to be used in infectious disease and microbiology, and increasingly appear to be complementary tools with important diagnostic, patient management, and health care cost benefits for the laboratory and health care systems.

3. Reinstating autopsy medicine

The gradual decline of autopsy as an investigative tool has recently received much attention. The significance of providing pathology services, especially the autopsy, to patients with potentially hazardous communicable diseases is underestimated. The Under use of the autopsy has occurred in spite of literature documenting its value in diagnosing clinically occult or undetected infections. Therefore with the advent of the AIDS pandemic, and newly emergent and re-emergent infections, the necessity for autopsy based studies has never been greater.

4. Strategies to contain drug resistance

Education

Educating the health workers on the wiser use of antimicrobial drugs is imperative to halt the spread of resistance. Educating consumers and the community on the judicious use of antibiotics is also critical in tackling the problem of drug resistance. Irresponsible advertising sometimes persuade prescribers to dispense expensive second or third line drugs that should normally be kept in reserve. Both pharmaceutical companies and government should join forces to ensure that existing guidelines for responsible advertising and promotion are followed.

Antibiotic policies

The most intensive use of antibiotics occurs in hospitals where large number of sick people drives the emergence of drug resistance. Thus it is imperative that hospitals quickly develop and implement new policies ensuring wise use of antimicrobials, It is also important to monitor drug use and carryout resistance surveillance.

Regulated use of antibiotics in livestock.

The risk to public health with the use of antimicrobials in food animals has been acknowledged in many international meetings and forums. The experts and opinion leaders need to formulate realistic recommendations for the prudent use of antimicrobials in food animals. The recommendations include the obligatory prescriptions for all antimicrobials used in disease control in food animals, phasing out or termination of the use of antimicrobials for growth promotion, if the same agents are used in the treatment of humans, creation of national systems to monitor antimicrobial usage in food animals, preparation of guidelines on antimicrobial usage to veterinarians.

Increase research for new drugs and vaccines

Encouraging the research community to develop new compounds is essential, as even our best efforts will only slow the pace at which resistance emerges. Effective vaccination programmes will prevent people from getting sick in the first place and thus minimize the need for drugs, which in turn prevent selection of resistant microbes.

Reversal of antibiotic resistance by non-antibiotic antimicrobial agents

Uses of non antibiotic medicinal compounds which have antimicrobial properties for the treatment of troublesome antibiotic resistant infections are being researched on. Among Phenothiazines, thioridazine, is shown to inhibit the growth of multi drug resistant strains of M tuberculosis and enhance the activity of anti tuberculosis agents rifampin and streptomycin. Phenothiazines are not the only class of non-antibiotics that have antimicrobial activity. Therefore non-antibiotics have a potential role in the management of specific antibiotic-resistant infections for which current antibiotic therapy is ineffective[26].

5. Surveillance

In response to emerging infections many systems of surveillance have been initiated mostly in the USA.

Data Mining Surveillance System (DMSS):

DMSS available in the USA uses a large electronic health-care database for monitoring emerging infections arid antimicrobial resistance[27]. For example, information from DMSS can indicate potentially important shift in infection and antimicrobial resistance patterns in the intensive care units of a single health-care facility.

Electronic outbreak reporting

ProMED mail [28] Pro MED mail was established in 1994 by the Federation of American Scientists. This is subscribed for by over 14,000 in more than 150 countries. The ProMED mail reports are screened by specialists in infectious diseases and selected items are posted. The advantage of this system is that it does not face the bureaucratic processes inherent in official channels and are not constrained by politically motivated government embargoes. Reports appear faster than those coming through official channels.

APEC net work project [29]

The Asia Pacific Economic Co-operation (APEC) has undertaken an initiative in emerging infections. The APEC Emerging Infections Network project uses collaborative telecommunications tools such as e-mail

and a World Wide Web site to bridge the broad geographic expanse and diversity of APEC. Scientists and policymakers share information to effectively combat emerging infectious disease (EID) through surveillance, prevention, research, and control measures.

Emergency ID NET [30]

This is a sentinel system in operation as a network of academic emergency medicine departments that are systematically evaluating conditions that are likely to present in the emergency departments. eg. seizure in cysticercosis.

This was inaugurated in 1995, when Centre for Disease Control (CDC), Atlanta entered into co-operative agreements with the infectious Diseases Society of America (IDSA) and Emergency departments of geographically diverse hospitals. Here data are collected during ED evaluation of patients with specific c1inical syndromes and electronically stored, transferred and analysed at a central receiving site. Each site has a designated emergency medicine investigator who establishes specific contacts with the hospital laboratory and local public health departments.

The preliminary results show that that this has a case finding sensitivity of 55% to 85%.

Geo Sentinel net work [I3]

Travel is a significant factor in the emergence and spread of infectious diseases as I mentioned earlier. Therefore surveillance of travellers may provide some unique benefit from a scientific perspective. Surveillance system such as the GeoSentinal network can be set up to use travellers as sentinels to detect new pathogens early enough to develop appropriate Public health responses to limit the dissemination of normal microbial threads. GeoSentinel is a consortium of 22 travel medicine clinics operated by members of the International Society of Travel Medicine and was developed in 1996. The basic surveillance tool is a one page faxable form linking geographic location, reference date and diagnosis. The current sample size is approximately 5000 travelers per year. Aggregated data are then available to link diagnoses or syndromes to dates and location. GeoSentinel then define a constellation of symptoms, signs, risk factors, geographic regions heralding the emergence of a new pathogen. It also monitors changing trends to known pathogens on a global scope and effect rapid international response by electronically disseminating out going alerts to all surveillance sites as well as to all ISTM member clinics in 55 countries. In addition these Travel medicine clinics will enable travelers to receive up to date information on epidemics of diseases and vaccinations and prophylaxis relevant diseases at the destination of travel.

6. Use of Medical geography to predict outbreaks [31]

Rift valley fever (RVF), a viral disease first described in Kenya in 1931, affects domestic animals and humans throughout sub-Saharan Africa and result in widespread livestock losses and frequent human mortality. All known Rift Valley fever virus outbreaks in East Africa from 1950 to May 1998, and probably earlier, followed periods of abnormally high rainfall. Such heavy rainfall floods mosquito breeding habitats which contain trans-ovarially-infected mosquito eggs. Vegetation responds to increased rainfal1 and can be easily measured by satellite. Analysis of rainfall records and Pacific and Indian Ocean sea surface temperature anomalies, coupled with satellite normalized difference vegetation index data, shows that prediction of Rift Valley fever outbreaks may be made up to 5 months in advance of outbreaks in East Africa. Concurrent near freal-time monitoring with satellite normalized difference vegetation data may identify actual affected areas.

7. In the event of an outbreak 'Preparedness'

A critical factor in the amplification of emerging' infections as a global health threat has been pervasive sense of complacency toward infectious diseases in general by health professionals and policymakers[32]. This attitude has led to serious breakdowns in public health surveillance systems, prevention programs and disease control efforts.

A survey by the WHO in 1993 demonstrated that virology laboratories around the world are not fully prepared to recognize emerging viruses or even known viral pathogens that do not commonly occur in their re-

spective geographic areas. The state health departments in many countries including Sri Lanka do not have a standard protocol to follow when faced with an outbreak of a new infectious disease. When a new infectious disease is detected in one hospital, it is important to increase awareness of possible future out breaks in other hospitals and ensure early communication with respective staff in those institutes.

There may be concerns over data ownership, intellectual property rights and publication credit. For effective collaboration and co-operation therefore, there should be assurances that these will be openly and fairly discussed at a later date. Communications with the media are equally important. A new infectious agent is bound to attract a great deal of media attention, and fears and anxieties may result in overly sensational and inaccurate reporting. Relative risks need to be conveyed to the public effectively, so that people will know how best to alter their behavior, life style or environment to prevent infection. Effective media management can also reduce public discrimination of people affected by the disease.

Until the pathogen is isolated, clinicians and epidemiologists practice a speculative science. A central laboratory will often be established to lead in the identification of the pathogen. The specimens should be collected and transferred to the designated laboratory, which has the required technology. In a public health crisis it is the usual practice to focus exclusively on the short-term issues that immediately confront them. Long term planning such as resource allocation, epidemiological monitoring and intervention, internal and public communication, for managing the out-break must be carried out simultaneously.

I wish to conclude my presentation with this verse from Arrowsmith by Sinclair Lewis

Germs come by stealth
And ruin Health,
So Listen, pard,
Just drop a card
To a man who'll clean up your yard And that
will hit the old germs hard

In Arrowsmith, Sinclair Lewis

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