Zoonotic Diseases, the Global Ecosystem and the Human-Animal-Environment Interface

PEER REVIEWED

Living Communities and the Habitat

Man, as an individual and collective being, tends to see nature and the environment as something extraneous to himself, something to conquer and control and, if necessary, to defeat. Indigenous tribal cultures and post-modern science know better: what we call nature on this Earth is a living, pulsating, ever-changing, but persisting ecosystem – comprised of communities of beings living in their habitats. Resilience of the ecosystem relies on the delicate dynamic equilibrium between its components.

Five kingdoms of life inhabit this planet: Monera (bacteria), Protista, Fungi, Plantae and Animalia. Once adapted to the environment, they seek to thrive in their habitat; disruption of this habitat turns it again into mere environment, and the need to adapt to it again.

Microorganisms are sometimes seen as a 'plague', something filthy, invasive – against which we wage wars, and sometimes we lose. This adversarial language obscures the fact that most of the microbial world is either neutral toward, or supportive of, human wellbeing and survival. Indeed, we would not survive long without commensal microbes such as the beneficial strains of *Escherichia coli*. Any mature, sustainable, human ecology must come to terms with both the need for, and the needs of, the microbial species that help to make up the interdependent system of life on Earth. Humans and microbes are not 'at war'; rather, both parties are engaged in amoral, self-interested, co-evolutionary struggle.[1,2] Diseases can be caused by species from each of the five kingdoms, including man himself. Zoonotic agents belong to four kingdoms, and plants can serve as substrate or vehicle to the pathogens, much the same as the non-living objects, or fomites, do.

The Human-Animal-Environment Interface

Zoonoses occur at the human-animal-environment interface, within the context of ecosystems – from local to global. One of the basic epidemiological models of disease causation, *the epidemiological triad*, involves an agent, a *susceptible host* and an environment with conditions sufficient to enable pathology. Within this triad, we may find vectors that convey the agent to the host. Elimination of any of these elements may prevent disease. However, this is just the tip of the iceberg: causation of diseases is much more complex, and the *causal web* of many factors changes the probability of disease occurrence.[3,4]

The dynamic and complex nature of ecosystems, and the numerous transactions at the human-animal-environment interface, bring tension between the vulnerability and resilience of populations – human and animal. The web of causation of zoonotic diseases includes biologic, genetic, ecologic, climatic, anthropogenic and socioeconomic factors.[1,5,6] Migration towards urban areas, population density, lack of sanitation and basic hygiene premises, unemployment, lack of education, poverty, inequality, addiction and violence, are widely present in peri-urban slums, where more than 1 billion people live currently, and the number is expected to double in the next 25 years. Example: Leptospirosis became an urban health problem in slums. Even after controlling for environmental factors, differences in socioeconomic status contributed to the risk of *Leptospira* infection, indicating that effective prevention of leptospirosis may need to address the social factors that produce unequal health outcomes among slum residents, in addition to improving sanitation.[7]

The poor of the world live on less than $2 a day per person. The human poverty index uses indicators that capture non-financial elements of poverty, such as life expectancy, adult literacy, water quality, and children that are underweight. The map of human poverty where territories are re-sized according to the data (Figure 1), shows uneven distribution between regions and countries.

Figure 1 World map of human poverty - Worldmapper.org

Man has always been prone to infectious diseases. During the processes of human population dispersal around the world over the past 50,000–100,000 years, along with associated cultural evolution and inter-population contact and conflict, there have been several major transitions in the relationships of *Homo sapiens* with the natural world, animate and inanimate.[2] Since 10,000 years ago, when agriculture, livestock herding and domestication of animals commenced, three major transitions happened and each of these transitions has resulted in the emergence of new or unfamiliar infectious diseases:

- early agrarian-based settlements enabled sylvatic enzootic microbes to make contact with *Homo sapiens*;
- early Eurasian civilisations (such as the Greek and Roman empires, China and south Asia) came into military and commercial contact, ca. 3000-2000 years ago, swapping their dominant infections;
- European expansionism, over the past five centuries,

caused the transoceanic spread of often lethal infectious diseases. Conquest of the Americas by Spanish conquistadores brought the spread of measles, smallpox and influenza, which devastated the Amerindian populations; two centuries later, Captain Cook unwittingly repeated the decimation of indigenous peoples through syphilis, measles and tuberculosis in many of the Pacific islands.[1,2]

In the last decades, we are witnessing the *fourth major transition* in human-microbe-environment relationships, mainly due to the rapid changes in human demography, ecology and behaviour. These changes are closely connected with globalisation and the trends it brought, sometimes referred to as the 5 T's: trade, transport, travel, tourism and terrorism.

During the mid-twentieth century, the human achievements in public health brought a level of optimism: infectious diseases were in decline, due to the major sanitary, hygienic and medical achievements. Child mortality began to diminish, global life expectancy started to rise; international global financial aid stepped into the battle against poverty in the developing world; however, the resurgence of zoonotic diseases in the last three decades shattered the base for optimistic forecasts of the imminent demise of epidemics.

Persistence of many neglected endemic diseases became aggravated by emerging infectious diseases (EIDs), at the rate of one per year. EIDs appear newly in populations, or have existed previously, but show a sudden increase in incidence or geographic range, or both. They may emerge exclusively in human or in animal populations; nevertheless, 75 % of EIDs are zoonotic. Some remain sporadic or endemic and many occur as outbreaks.[8,9]

Of 1415 human pathogens, 217 are viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths. Out of these, 868 (61 %) are zoonotic and 175 pathogenic species are associated with diseases considered to be 'emerging'. Of the emerging pathogens, 132 (75 %) are zoonotic, and overall, zoonotic pathogens are twice as likely to be associated with emerging diseases than non-zoonotic pathogens.[10]

A Closer Look at Zoonotic Diseases

In colloquial language, zoonoses are mentioned as infectious diseases common to humans and non-human animals. According to the WHO, any disease or infection that is naturally transmissible from vertebrate animals to humans and vice-versa is classified as a zoonosis[11]. The majority of these transmissions originate in animals, though increasing numbers of reports indicate that humans are transmitting pathogens to animals[12]. While some authors hold the term zoonosis synonymous with animal-to-human transmission, other terms were used to define the source of infection and the direction of transmission:

- **Anthropozoonoses**: zoonoses maintained in nature by animals and transmissible to humans; (e.g. rabies, brucellosis).
- *Zooanthroponoses*: zoonoses maintained by humans but transmissible to other vertebrates (e.g., amebiasis to dogs, tuberculosis).

Many scientists used these terms in the reverse sense or indiscriminately[13], and the joint WHO/FAO expert committee on zoonoses decided to abandon these two terms and recommended "zoonoses" as "diseases and infections which are naturally transmitted between vertebrate animals and man".

Most human pathogens are present in animal reservoirs, or once originated in animals, even if they became human-specific (e.g. HIV). Wolfe *et al*.[14] defined five stages in the evolutionary transformation of an animal pathogen into a specialised pathogen of humans:

- Stage I - pathogens exclusively infecting animals,
- Stage II - pathogens that can transmit from animals to humans to cause 'primary' infections but do not exhibit human-to-human ('secondary') transmission (e.g. anthrax and tularemia bacilli, and Nipah, rabies and West Nile viruses),
- Stage III - pathogens spill over into human populations from animal reservoirs and can cause limited cycles of human-to-human transmission that stutter to extinction (e.g. Ebola, Marburg, monkey pox viruses and *Leishmania infantum*),
- Stage IV - pathogens persist in animal reservoirs but can cause self-sustaining chains of transmission in human populations (e.g. *Yersinia pestis* plague and pandemic influenza).
- Stage V - pathogens exclusively infect humans (e.g. the agents causing falciparum malaria, measles, mumps, rubella, smallpox and syphilis).

The zoonotic component in this classification is presented through stages II to IV. Lloyd *et al*.[15] proposed the adaptation of this model, making the distinction between stages II-IV using the *basic reproduction number* - R_0, which is the expected number of secondary cases produced by a typical infectious individual in a wholly susceptible population. R_0 enables us to distinguish stages II–IV on dynamical grounds since it provides quantitative demarcation between pathogens capable of sustained transmission among humans (those with $R_0>1$) from those doomed to stutter to local extinction ($R_0<1$) or those with no onward transmission ($R_0=0$).

Cross-species spillover transmission is the defining characteristic of a zoonosis. The factors influencing the force of infection from animals to humans show three distinct components: the prevalence of infection in the animal reservoir, the rate at which humans come into contact with these animals, and the probability that humans become infected when contact occurs. These components are each influenced by diverse properties of natural, agricultural and human systems, with important differences driven by the pathogen's mode of transmission. Significant quantitative or qualitative differences may also arise between zoonoses that use wildlife rather than domesticated animals as reservoirs. [15]

Zoonotic Diseases according to the Ecosystem in which they Circulate:[13]

- **Synanthropic zoonoses** have an urban cycle and a source of infection from domestic or animals ecologically associated with humans (e.g. urban rabies, cat scratch disease, zoonotic ringworm).
- **Exoanthropic zoonoses** have a sylvatic (feral and wild) cycle in natural foci outside human habitats and the source of infection is animals that are not in close association with man (e.g. arboviroses, wildlife rabies, Lyme disease, and tularemia).
- Some zoonoses circulate in both urban and natural cycles (e.g., yellow fever and Chagas disease).

Zoonotic Diseases have Different Routes of Transmission:
Zoonoses may be transmitted by **direct contact** between the infected animal and man (rabies), or **indirectly** through contact with contaminated objects or surfaces (fomites); some zoonotic diseases may be transmitted **orally**, by ingestion of food or water contaminated with a pathogen (echinococcosis, leptospirosis, cryptosporidiosis). This typically occurs from fecal contamination from unwashed hands or soil contact. Diseases can be transmitted through **aerosol** by fluids aerosolised from an animal to a person (e.g., sneezing or cough) and examples are influenza, Hantavirus, Q fever and plague; *vector-borne* diseases are transmitted by *arthropod vectors*: fleas (plague), mosquitoes (malaria, dengue fever, Chikungunya, West Nile fever), *ticks* (Lyme disease, Crimean-Congo fever, Q fever), *triatomine bugs* (Chagas disease) and sandflies (Leishmaniasis).

Mapping the Burden of Zoonotic Diseases
Zoonoses are present worldwide, however distribution of the determinants, and of the prevalence and incidence of zoonotic diseases, is not uniform. Figure 2 shows the map of human deaths due to the infectious and parasitic diseases; even the brief glance at Figures 1 and 2 indicates association and correlation between human poverty and deaths.

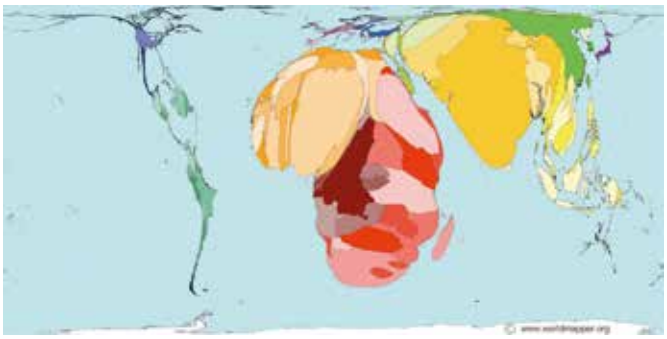

Figure 2 - Human deaths due to infectious and parasitic diseases - Worldmapper.org

What is the global impact of zoonotic diseases in terms of morbidity and mortality? Together, 56 zoonoses are responsible for an estimated 2.7 million human deaths and around 2.5 billion cases of human illness a year. The top-ranked 13 zoonoses caused 2.2 million human deaths and 2.4 billion cases of illness.[8]

The Global Burden of Disease (GBD) 2010 study shows that the leading causes of death are shifting to non-communicable diseases. In many countries, non-communicable diseases account for the majority of disability adjusted life years (DALY) = years of life lost due to premature mortality (YLL) + years lived with disability (YLD). In most countries outside of sub-Saharan Africa, non-communicable diseases caused 50 % or more of all healthy years lost, or DALYs. In Australia, Japan, and richer countries in Western Europe and North America, the percentage was greater than 80 % .[16]

Using GBD presents some challenges when it comes to estimating the burden of zoonotic diseases:

- **Firstly**, zoonoses (especially in poor countries) are widely unreported, and under-reporting is relatively greater for zoonoses than for non-zoonotic diseases of comparable prevalence. As the GBD report is based on national information for levels of mortality and cause of illness, this under-reporting is reflected in the GBD.
- **Secondly**, several zoonoses with considerable burdens are not included in the GBD assessment. For example, rabies, echinococcosis, cysticercosis, leptospirosis and brucellosis.
- **Thirdly**, the GBD is organised around diseases and not pathogens or transmission pathways. For example, diarrheal diseases, among the highest causes of morbidity and mortality in poor countries, comprise one category. Although the majority of important diarrheal pathogens are zoonotic, it is not currently possible to identify the zoonotic component of diarrheal disease from GBD figures.[8]

For zoonoses recorded in the GBD, 68 % of the burden is made up of just 13 countries: India (>7.5 billion DALY), Nigeria (2.3 billion DALY), followed in descending order by Congo DR, China, Ethiopia, Bangladesh, Pakistan, Afghanistan, Angola, Brazil, Indonesia, Niger and Tanzania. The last five countries each report approximately 500 million DALY due to zoonoses.

Global Problems Require Global Solutions

Prevention is better than cure, but the fight against zoonoses requires the whole range of available weapons: establishing surveillance networks on national, regional and global levels; using zoonotic disease reporting systems, which exist, although many zoonotic diseases remain undetected and under-reported on the local level; making vaccines accessible to every country directly, or stored in regional vaccine banks; focusing on those zoonotic diseases for which there is no vaccine, so research and development should be facilitated and translation to production accelerated. Bacterial zoonoses are fought with antibiotics, but the upsurge in antimicrobial resistance is a threat to animal and human health. Responsible use of antibiotics, by qualified professionals, is of critical importance; neglected tropical diseases are not exclusively tropical any more, due to the global transport of people and goods, and due to climate change - so why leave them neglected?

Sustainable control and eradication of zoonotic diseases could be achieved if all of society collaborates and unites its resources. The world needs 'One Health' – a collaborative, international, cross-sectoral, multidisciplinary mechanism to address threats and reduce risks of detrimental infectious diseases at the animal-human-ecosystem interface (FAO). The tripartite collaboration of the WHO, FAO and OIE, and the partnership of other international organisations, is necessary for attainment of the noble vision of the healthier world, thriving communities and the wellbeing of all.

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