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Veterinary public health and veterinary epidemiology: partner disciplines for the protection of humans from zoonotic diseases

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«Between animal and human medicine there is no dividing line – nor should there be. The object is different but the experience obtained constitutes the basis of all medicine.» Rudolf Virchow (1821–1902)

Historically, medicine for animals and humans was not separated. Medical practitioners treated animals as well as people. This approach is intuitive, since animals and humans share the same physiology and even a large number of common diseases (zoonoses). With the rapid increase of scientific knowledge and methodology in the last centuries, a trend towards specialization and separation of disciplines began. It started with separation into human and veterinary medicine and continued with splitting each discipline into sub-disciplines such as internal medicine, surgery or radiology. While this specialization enables in-depth expertise and research of high quality, it bears the danger that the connections between different areas of expertise within and between species are neglected. However, at all times there were scientists and medical practitioners who recognized the close interconnection between human and animal wellbeing, and who continued interdisciplinary work on improving the health of animals as well as humans. For example, the initiative for founding a Society of Swiss Veterinarians in 1813 came from one physician and two veterinarians. Modern disciplines which work at this intersection are veterinary epidemiology and veterinary public health. Within the Vetsuisse-Faculty, these disciplines at the two sites in Bern and Zürich are closely collaborating in veterinary education as well as in research.

1. Veterinary epidemiology

Epidemiology is the science that studies the patterns, causes, and effects of health and disease conditions in defined populations and is a cornerstone of (veterinary) public health. However, this is not just about groups of animals. By understanding the epidemiology of diseases, we can also make significant contributions to clinical studies such as the diagnosis and likely prognosis in individual animals presenting with disease. Our interests in public health are particularly focused on zoonoses. A zoonosis is a disease that can be transmitted from vertebrate animals to man. Of about 1500 known human pathogens (viruses, bacteria, parasites), approximately 61% are zoonotic. That means that most human infectious disease ultimately arise from an animal source. Transmissible diseases include well known medical conditions such as rabies, salmonella, the fox tapeworm and bird flu. But HIV/AIDs is believed to be originally of animal origin and made a jump from primates to humans several decades ago. In addition, EBOLA is thought to have an as yet unidentified animal source with epidemics occurring when the virus is given the opportunity to transmit between species. Thus, understanding patterns of animal diseases can also help us to understand risks to human health and to minimize these risks.

Mathematics and biostatistics are used extensively in veterinary epidemiology and it is important that veterinary students understand the basic concepts. In populations of animals, we need to be able to describe how much disease is present. This might be for example the proportion of animals (or prevalence) that is infected with a particular pathogen. Then, we apply biostatistics for analysis. For example, if we observe differences in the amount of disease between different populations, we need to know if this is a real difference or due to random chance. If there is a real difference, then we might investigate to see if those populations with higher amounts of disease have certain characteristics which are absent in populations with a lower disease prevalence. This can then help us to understand the possible causes of the disease and how best to design intervention to prevent the disease in the future. And with zoonoses, understanding these disease risks in animals helps us understand how to mitigate these diseases in humans.

The amount of disease in animal and human populations is not only dependent on the proportion of individuals infected, but also depends on the severity of the clinical effects, the duration of the disease and the mortality. In Zurich, we have a number of international collaborators, including the World Health Organization, with whom we have research programs to estimate the societal impact of zoonotic diseases. This helps us to answer questions whether common diseases of mild clinical signs and negligible mortality (e.g. the common cold) have a greater or lesser societal impact compared to more rare diseases that may have long term severe morbidity and

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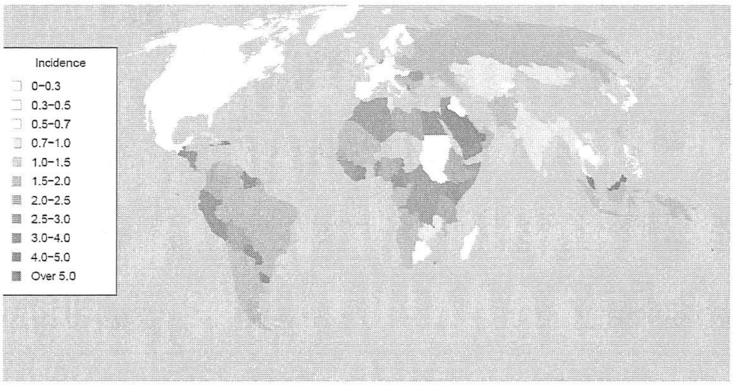

Figure 1 *(coulours see web version). Map of the world-wide incidence, per 1000 births, of congenital Toxoplasmosis in children*

are potentially fatal (e.g. Echinococcosis, caused by the fox tape worm). In particular, we are undertaking research into the global burden of foodborne diseases to answer this question for diseases commonly transmitted through food. This clearly involves many zoonoses as we eat numerous products of animal origin. As an example, Fig. 1 shows the global burden of congenital toxoplasmosis which we have estimated with our research collaborators. Toxoplasma is a small parasite which can be acquired directly form contact with cats or from eating undercooked meat products. It is dangerous to pregnant women as exposure during pregnancy can lead to transmission and damage to the fetus. Children born with congenital toxoplasmosis can have a variety of clinical syndromes ranging from asymptomatic to severe brain damage. The results were published in the Bulletin of the World Health Organization.

An important aspect of any study of diseases in populations is diagnosis and good diagnostic tools are essential if we want to investigate the societal burden of a disease. Diagnostic tools help us to confirm the presence of diseases in individual animals and in groups of animals within populations. However, very few diagnostic tools are 100% accurate. Occasionally,

Figure 2. *Swabs are collected for disease surveillance in a poultry farm. Regular surveillance of animal health can contribute to the protection of humans from zoonotic diseases.*

there may be false positive reactions in healthy animals or false negative reactions in diseased animals. The probability of a diagnostic test giving the wrong result must be incorporated into our analyses. This probability can be affected by such things as the disease prevalence or the prevalence in the population of other related microbes which may not be pathogenic but cause cross reactions with the test. In addition, the test itself may not perform in the same way in different populations of animals. Thus we have to use probability theory to help us interpret the results that diagnostic tests give us, and to evaluate the performance of diagnostic tests. This then answers questions such as «What is the probability of an animal having a disease given a positive diagnosis?», or «What is the probability of the presence or absence of a disease given that all the animals in a group were tested negative?»

2. Veterinary Public Health (VPH)

The World Health Organization defines Veterinary Public Health as «the sum of all contributions to the physical, mental and social well-being of humans through an understanding and application of veterinary science». Human health and well-being are closely linked to animals. Animals provide an important contribution to the physical well-being of people because they provide nutrition, clothing, fertilizer and draught power. In addition, the importance of companion animals for the mental and social well-being of humans is increasing, especially in industrialized countries. Therefore, VPH does not only relate to zoonotic diseases and to highly contagious diseases with devastating effects on economics and nutrition, but also to animal welfare and the human-animal relationship.

Our research on zoonotic diseases at the Vetsuisse-Faculty Bern focuses on the assessment of risks of introduction of new diseases into Switzerland, and on surveillance with the objectives to control endemic zoonoses, and to detect a possible introduction of new zoonoses.

An example for the surveillance of endemic zoonoses and risk assessment is a project on Q fever, a bacterium which causes abortion in sheep, goats and cattle. It is excreted in high numbers by infected animals, especially during abortions and while giving birth. In humans, the bacterium can cause acute disease with fever and flu-like symptoms, but also severe disease with pneumonia or hepatitis. Starting in 2007, The Netherlands experienced the largest outbreak of Q fever among humans ever reported, with a total of more than 3500 cases. The outbreak originated from large goat farms which disposed of manure and birth material in open piles. This allowed spore-like particles to be spread to humans living in cities via the wind. Even though the dimensions of goat and sheep farms in Switzerland differ substantially from the situation in The Netherlands, our research had the objective to identify a potential risk of Q fever for humans in Switzerland. Five percent of the Swiss sheep farms and 11% of the goat farms were infected with the pathogen. The study concluded that while an outbreak of the same magnitude as in The Netherlands was extremely unlikely, a substantial risk of smaller outbreaks due to this disease remains. The proof that this estimation was correct was delivered shortly after, through an outbreak with 14 identified human cases in Lavaux.

By presenting and interpreting data on the incidence, prevalence and geographical distribution of zoonoses and their impact on animals and humans, veterinary epidemiology and VPH provide decision makers with the basis for effective disease control and prevention. This can only be achieved by interdisciplinary collaboration with clinicians, pathologists, microbiologists, virologist, biostatisticians and other specialists. In conclusion, veterinary epidemiology and VPH can bridge the gap between basic research and clinical sciences, as well as the one between human and veterinary medicine. This translational research has a great potential to contribute to a better health for all – animals as well as people. ■

Being prepared against viral zoonoses

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Emerging and re-emerging viral zoonoses pose a particular thread to both animals and man as they cannot be controlled by antibiotics and in most cases no vaccines are available. The frequency at which such viruses have emerged appears to have increased in recent years and is likely to continue to do so. This is caused by many factors favoring transmission amongst animals, between animals and man and between man. Amongst them are increased animal densities in farming, increased areas with high density of the human population, globalization with increased travelling and trading activities and climate changes with associated expansion or change of arthropod vector distribution. In addition to the health burden and losses of lives zoonotic outbreaks have caused, their impact on economies can be disastrous. An example for this is the recent outbreak caused by Ebola virus in West Africa. In addition, reverse zoonosis such as transmission of human influenza virus to pigs cause suffering and economic losses in swine farming.

For these reasons the Institute of Virology and Immunology (IVI) have started several research programs on viral zoonoses with the aim to increase preparedness against such infections and to provide knowledge and tools required to control outbreaks. Here we present our efforts focusing on influenza virus, Japanese encephalitis virus, a mosquito-borne flavivirus, and coronaviruses.

1. The Institute of Virology and Immunology (IVI)

Since January 2014 the IVI has been from a merger to the Institute of Veterinary Virology of the Vetsuisse-Faculty Bern and the former Institute of Virology and Immunology, a research facility of the Federal Administration. The present IVI still represents a Federal Research Institute but is now integrated into the Campus of the Vetsuisse-Faculty with both, the divisions of Immunology and Virology headed by university professors. The IVI is responsible for teaching and research in immunology and virology. The laboratory in Mittelhäusern operates at the Biosafety level 3 and BSL-3-Ag, the latter offering maximum protection of the environment for working with the most dangerous livestock pathogens.

2. Influenza A virus

Influenza A viruses are characterized by a genome consisting of 8 segments of single-stranded, negative-sense RNA. Each RNA segment is tightly associated with the nucleoprotein and the three components of the viral RNA polymerase complex thereby forming a ribonucleoprotein. Because the RNA polymerase is devoid of proof-reading activity viral offspring is genetically highly diverse (so-called quasi-species). As different influenza A viruses can exchange gene segments when infecting the same cell diversity of these viruses may become even more complex. Thus, influenza A viruses are highly mutable viruses which can easily evade the host`s immune response and can adapt to new hosts.

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