Comparative Medicine: An Overview

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Introduction

Comparative medicine brings together the various disciplines to study a particular disease or group of diseases in both human beings and animals. Thus, by its very nature, comparative medicine requires a team effort. This may include field studies among the human and animal populations within a geographic region, as well as definitive laboratory studies in man or animal models. Also, the comparison may involve the whole disease process or it may only include one aspect such as comparative pathology.(Leader, 1967a, b)

Comparative medicine as it relates to agricultural health and safety is concerned with the conditions or diseases that affect the health and safety of individuals engaged in agriculture as a profession e.g. farmer, dairyman, as well as those individuals in allied fields who directly or indirectly support agriculture. In general, the individual engaged in agriculture or an allied profession must be exposed to or come in contact with the agricultural environment. Thus, an individual residing and working in a large, urban area who works as a commodity broker would not be considered from a comparative medical standpoint as it relates to agricultural health and safety.

It is the purpose of this paper, therefore, to present an overview of comparative medicine primarily as it relates to agriculture, proceeding from the general to the specific. The items presented will include the philosophical bases, problems and possible solutions as well as the future aspects of comparative medicine.

Philosophy

Neither man nor animals live in a vacuum. They are exposed to multiple environmental factors, individuals of the same or different species (Parrish, 1973),

disease agents (Top, 1964), as well as their own genetic mosaic (Childs, 1973), and the interactions between these variables (Freeman, 1973). All these variables both directly or indirectly influence their state of health. We have discovered that the physical environment is only one facet of the disease-health continuum. The social and psychological aspects are also important aspects of health. This is as true with domesticated animals as it is with man. These latter areas are important and need to be developed in the future in comparative medicine. The role of the companion animal as it relates to the mental health of man requires further study and evaluation (Fox, 1972; McCulloch, 1973).

Sometimes our reasoning in comparative medicine is by analogy (Beveridge, 1972). For example, if the clinical disease and pathological manifestations of a disease are similar e.g. congenital malformations, then the more we learn about congenital malformations in animals, results in more information that can be applied to human congenital malformations (Marienfeld, 1967; Selby, et al., 1971). Findings in comparative medicine have resulted from studies designed with this objective in mind, as well as, chance observation of medical discoveries where one or more aspects of a disease in a species are applied to the same disease in another species. However, comparative medicine requires more than just extrapolation from one species to another. It must also be supported by other scientific data (Brodie, 1962; Oehme, 1970).

Animals may also help clarify our understanding of the disease process in man by indicating areas which need investigation and methods which might be used (Beveridge, WIB, 1972). For example, it was Jenner's observations that milkmaids, when immunized with exudate from cow pox lesions, were immune to smallpox. His studies instituted the present day immunization practices for smallpox. Today, with more sophisticated smallpox vaccine, with man as the only natural host and an extensive active eradication program by the World Health Organization, smallpox is no longer a major worldwide infectious disease.

Some of the ways in which comparative research on domestic and wildlife diseases aid in improving human health include (Pritchard, W.R., 1962; Beveridge, 1968):

1. Contributions to basic knowledge about the disease. Frequently in man, only the terminal stages of the disease have been studies in detail while in animal studies, it may be possible to observe the complete disease spectrum.
2. Indicates methods of controlling the transmission of the disease.
3. Techniques developed in animal species e.g. surgical techniques that can be applied to man.
4. Provides animal systems as a model for disease research.

Although more research is conducted in the area of human medicine, studies of like conditions or disease agents in animals sometimes have been more productive in a shorter period of time because:

1. The animals' environment could be more clearly defined.
2. Due to the population numbers, more instances of the disease were observed and studied. The shorter life cycle of animals is an enhancing factor and a total generation can be observed in a shorter period of time. In genetic studies, this phenomena is an extremely important variable in the research design.
3. Variations and changes can be made in the animals' ecology, e.g. changes in environment or husbandry and management practices.
4. Animal models may be housed and utilized more economically from an ethical and time-cost standpoint.

Problem Areas of Comparative Medicine

In agriculture family members are usually part of the work force. As a result, health problems of the individual as well as their family must be considered. Age is an important variable in considering which diseases have the greatest impact. In the very young, prenatal and postnatal, infectious diseases are important. In the teenager and young adult, accidents are a problem while in the older age groups, chronic and degenerative diseases are a problem. Overall, however, occupational diseases are a major health concern and the primary focus of this conference. Therefore, in this session we will concentrate a major portion of our efforts on the occupational diseases significant to agriculture workers and allied professionals in the same environment.

A number of the infectious diseases are common problems of man and his domestic animals. Many are zoonotic diseases, that is, a disease transmitted from animals to man or one that has a common source of exposure for both animals and man (Schwabe, 1964; Steele, 1973a, 1973b). Zoonotic diseases are considered an occupational hazard for individuals in the agricultural field (Anom, 1964; Diesch, 1974; Donham, 1974). A discussion of this aspect of health and disease was included, a decade ago, in a joint International Labor Organization/World Health Organization Committee report in 1962 (Joint ILO/WHO Committee Report, 1962). Because the zoonoses will be discussed in detail later in this session, (Diesch, 1974; Donham, 1974; Martin, 1974) I will mention the zoonotic diseases only from a comparative medicine standpoint. Specific studies of those zoonoses associated with existing agricultural practices may lead to a more complete understanding of the disease process, more practical and economical methods of control and/or eradication in both man and his domesticated animals.

For example, with leptospirosis, it has been stated that complete control in man depends upon the elimination of the carrier (Menges, 1959). Both domestic and wild animals may have inapparent infections and the organism tends to localize in the kidneys and may be chronically shed in the urine. It is essential that when human leptospirosis cases are

diagnosed, carriers, usually animals, must be identified before preventive medicine measures can be taken. Domestic pets, food producing animals and various wildlife species, especially the rat, may act as reservoirs of leptospirosis. Thus, each instance of human leptospirosis may differ because of the disease's complex transmission cycle which includes an environmental phase. Frequently water is contaminated with leptospirosis and has an important role as a source of infection (Diesch and McCulloch, 1966). The readily visible domestic animal is ecologically a common source of infections, but is probably not the primary reservoir. Therefore, control measures must not be confined strictly to the domestic animal population.

However, the zoonoses are not the only important diseases of individuals or their families in the agricultural field. Diseases with one or more environmental components are, in fact, some of the common, as well as some of the most important health problems in the agricultural population. One may not initially consider environmental factors as having an important role in accidental injury and death, but environmental factors, including location, time of day and general weather factors, are important. Traumatic accidents, discussed later in this conference, are one of the acute non-infectious conditions that cause increased morbidity and mortality in agricultural workers (Cooper, 1971). Comparable problems occur among veterinarians where the farm or ranch was the location for most injuries to practicing veterinarians (Thigpen and Dorn, 1973). In addition to traumatic injuries, other occupational problems may affect veterinarians and they will be presented shortly in this session (Martin, 1974).

Another area of occupational hazards which has been discussed earlier in this conference is the accidental exposure to toxic trace substances e.g. pesticides (Long, K., et al., 1969; Hourrigan, 1970). Recently we investigated a number of acute outbreaks of arsenic poisoning in cattle where residues of the pesticide had been improperly dumped on the ground in pastures where animals were allowed to graze. The potential public health problem from intoxicated cattle entering man's food chain was

evaluated (Selby, et al., 1974). In this particular instance, the animals were not a model of human disease in the strict sense, but rather a model to help evaluate the potential food source, i.e. meat, as a potential public health problem. Thus by understanding the dynamics of arsenic in the ruminant, we were able to assess the potential public health problem to man.

In addition to the zoonoses, traumatic injuries and intoxications, the chronic or degenerative diseases are important in health problems in predominantly rural agricultural populations (Whipple, 1965). Again, age is an important factor for these populations have a tendency to be skewed toward the older age groups.

Cardiovascular diseases (Clarkson, et al., 1970; Lufinbuhl and Detweiler, 1970), cancer (Willham, Jr., 1971; Dorn, 1972a, 1972b), and arthritis (Van Pelt, 1965; Sokoloff, 1973) are some of the more important chronic diseases that have been studied from a comparative medicine standpoint, the first two having received the most attention. There is also a group of diseases that we do not mention frequently and when we do, it is often with the attitude that it is someone else's problem. This group of diseases are mental disorders, including illness, retardation, alcoholism and addiction disorders (Hilleboe, H.E., 1968).

But what about possible solutions, in the comparative medicine sense, for the major health problems of those individuals living and working in agriculture? Defining the problems involved is only one aspect of comparative medicine. Providing a solution is a more complex issue.

Possible Solutions

Solutions to the agricultural health problems just reviewed require the combined efforts of many individuals and disciplines. No one profession or discipline can solve the complete problem.

Therefore, team effort is the only practical method that can be used in studying those diseases that are important in comparative medicine (Busse, 1965; Hamilton, 1967; Argyris, C., 1968). For example, Table 1 presents the disciplines which were involved in a comparative study of congential malformations in man and swine (Marienfeld, et al., 1967; Selby, et al., 1971).

Table 2 shows the link between the medical research team and those individuals in agriculturally related fields who are involved in various ways with the production of pork. Interdisciplinary research in comparative medicine was discussed at the First Institute on Veterinary Public Health Practice (1960) as well as the congressional hearings on Human and Animal Health that were held in 1961 (Veterinary Medical Science, 1961). More recently, a bill was before Congress, primarily for animal disease research (Animal Health Research, 1973). The direct intent of this latter bill was not to emphasize the public health aspects of medicine. Yet, there is no doubt that research on animal diseases, many of them zoonotic diseases, will lead to a better understanding of the disease process in both animals and man, including newer methods of prevention, treatment and control.

To illustrate how possible solutions to disease problems can be solved by comparative studies, two situations will be presented: one on histoplasmosis and the other on an instance of pesticide intoxication.

Histoplasmosis was once thought to be a rare and highly fatal disease. During World War II numerous inductees into the Armed Forces of the United States had calcified pulmonary lesions suggestive of tuberculosis. However, their tuberculin skin test reactions were negative. A number of investigators hypothesized that the high incidence of pulmonary calcification associated with negative tuberculin skin tests might be due to another fungus disease (Rogers, 1966).

However, the reservoir for the causative organism Histoplasma Capsulatum, was unknown. At one point, it was suggested that animals, probably the rat,

was the reservoir of infection for man (Emmons, 1950). Subsequent studies by Emmons and others indicated environmental factors are important, that soil is the reservoir (Furcolow, 1965), and that old bird roosts and abandoned chicken houses are a foci of infection with aged guano acting as a growth stimulant for the fungus. Further studies with domestic animals including epidemiologic skin tests and culture studies, indicates histoplasmosis occurs among most species of domestic animals and many species of wildlife (Selby, 1974). As field studies indicate, it is suggested that even within the endemic area foci of infection for histoplasmosis may tend to be localized (Menges, et al., 1967). Coincidental studies of wildlife, primarily rodents, support this hypothesis. However, H. Capsulatum was isolated from some farms with negative histoplasmin skin test reactors and not isolated from some farms with positive histoplasmin skin test reactors in the domestic animals. In addition, soil isolation studies sometimes appear to be contrary to domestic animal or human sensitivity studies, yet the wildlife animal isolations studies correlate fairly well with domestic animal sensitivity studies. This suggests that although H. Capsulatum may tend to have a local foci, the fungus may be more widespread than presently realized and that not all these foci are related to infection in man or animals (Menges, et al., 1967).

The second situation that illustrates the documentation of human health problems by comparative medical studies, in the environment and domestic animals, is the epidemiologic investigation related to an instance of an apparent pesticide intoxication. During the early phase of the Community Study of Pesticides (Louisiana), (Selby, et al., 1969), a request was received to investigate an instance where a spray plane operator had "accidentally" released pesticide while flying over the yard, cistern, chicken house and house of a family living adjacent to a sugar cane field. Further history indicated that occupant's wife was hospitalized with neurological symptoms. She had been admitted to the hospital unable to stand ot walk without aid. Initially, organic pesticide intoxication was not considered because she had a history of being treated for neurological problems, possibly psychological, the previous year. When

interviewed, she stated, however, that she remembered that a similar spraying accident had also occurred the year before at the same time as her original hospitalization. In both instances, approximately 300 laying hens began to molt and laid "Hard-boiled eggs" and died.

We were unable to detect pesticide residues in the patient's blood. We were, however, able to detect levels of Carbaryl (1-naphthyl-N-methylcarbamate) residues in vegetation from her front yard. By adapting the existing analytical methods, we also were able to detect similar residues in the blood from a surviving chicken. Thus, comparative medical studies in the environment and in the animals aided in the documentation of an instance of human intoxication. At this point our investigation ceased at the request of the patient and her husband. Their request, in turn, had been initiated by the spray plane operator who objected strenuously to our studies.

The two situations, the first on the general problem of histoplasmosis and the second, on the specific problem of an instance of apparent pesticide intoxication, are presented to illustrate how comparative medicine studies can further our understanding of diseases related to agriculture health and safety. In an overview of comparative medicine, it is impossible to completely review all the various aspects of comparative medicine. There is, however, I feel, a responsibility, although not clearly stated, to explore from philosophical viewpoints, the future of comparative medicine.

Future Considerations

Because of the diverse nature and urgency of some of society's problems, comparative medicine is beginning to expand into "new frontiers" (Beveridge, 1972). True, many animal models in biomedical research have been discovered (Cornelius, 1969; Doyle, et al., 1969; Valtin, 1974) but there is a need for additional models (Prichard, 1970). Comparative medicine is also expanding into the area of environmental quality (Carson, 1974). Man in his rapidly changing world has become more concerned about his environment and himself

as an individual as well as a member of society as it relates to man's survival (Knutson, 1965; McCulloch, 1970). With this increased interest and concern of society, a number of issues have come to the forefront which are important considerations in comparative medicine. Newer dimensions of the legal and ethical concepts associated with human research are being explored (Ladimer, 1970). Research only on animals as an alternative is one option, but the same legal and ethical concepts need to be considered. Another option is to use data collected on animal populations, sharing the same environment with man or exposed to the same environmental factors. Although this type of study may have limitations (Parrish, et al., 1968; Hugh-Jones, 1973), newer, more sophisticated methods can be developed to minimize these limitations and be used in comparative studies of diseases common to animals and man. The feasibility of these studies is enhanced by the team-approach to disease research. For well-organized, planned team research is the key to our understanding those environmental quality variables that are related to agricultural health and safety. This conference depicts this philosophy. We must, however, be selective in using the appropriate biological model in studying the environment of man and his domestic animals (Leader, 1967a, b; LeMunyan, 1969). Many of the direct effects of environmental variables have been studied in man or animals, but we can learn even more from comparative studies (Hyslop, 1971). This is especially true in the study of environmental trace substances where biological variations between species and within species (Al-Shahristani and Shihab, 1974) can create difficulties in interpretation. But society with its newer technology and use of modern drugs has created new problems e.g. the problems of drug-resistant pathogenic bacteria and its transfer from one species to another (Dulanegand and Laskin, 1971; Smith, 1974; Burton and Blenden, 1974). This drug transfer mechanism, because of the close environmental relationship between agricultural workers and their domestic food producing problem is one of the more important areas of comparative medicine research today and it will be even more so in the future.

Another area of concern related to societal pressures is that of alcoholism. Comparative medicine studies hold the key to developing more sophisticated methods of prevention and eventual control of the problem accentuated by the ecosystem in which we live (Mello, 1973; Lester and Freed, 1973). Because man and his domestic animals are living longer, the chronic and degenerative diseases associated with aging will continue to be studied extensively (Breslow and Catcott, 1960; Steels, 1960). These studies by their very nature are complex studies with multiple variables.

Another particular area of health that relates directly to individuals in agriculture and their families as well as the aging phenomena is that of mental health. Laboratory animals have been used extensively in the study of behavior, but what of animal behavior as it relates directly to man's physical and mental well being? Dog bites are a problem (Graham-Jones, 1972), as well as traumatic injuries from the large food producing animals e.g. the dairy bull. This physical interaction of man and domestic animal can, besides physical injury, also cause mental injury to the individual and his family. These problems require further study, especially general population studies. For example when, because of disease problems, a producer, i.e., farmer or dairyman is forced to sell animals or his complete herd, this not only has an economic impact, but also a mental impact, e.g. mental depression (Leinbach, 1958). Another aspect of the mental health will be the study of the companion animal as related to mental health in man (Antyeles, 1967; Fox, 1972; McCulloch, 1973). A recent study of interest in this area was the evaluation of "affection for people as a function of affection for dogs" (Brown, et al., 1972). Yet, comparative ethology and psychology in general populations is in its infancy (Tobach et al., 1973). It will continue to grow and develop in the years ahead, through multidiscipline research. These efforts in comparative medicine can best be summarized by a statement made by Sir William Osler when he stated, "There is but one medicine."

Table 1. Professional Disciplines Involved in the Multi-species Study of Congenital Malformations in Man and Animals Primarily Swine (Marienfeld et al., 1967; Selby et al., 1971)

Professional Discipline	Activities
Program Staff	
Physician Pediatrician	Design and evaluation of overall program; classification of human malformations from hospital and vital statistics records.
Veterinarian Epidemiologist	Design and evaluation of field studies in domestic animal population; classification of animal malformations from pathology reports and data collected from field surveys.
Pathologist	Autopsy of malformed domestic animals and preparation of pathology reports.
Demographer	Evaluation of vital statistic records for natality, morbidity, and mortality related to malformations.
Statistician	Design and evaluation of field studies and data collected from existing reporting systems or special surveys.
Systems Analysis	Design and direction of computer staff and programs to support data collected from vital statistics and field studies.

Table 1. (Continued)

Professional Discipline	Activities
Computer Programmer	Develop computer programs for analysis and evaluation of data collected during the study.
Cartographer	Design methods to be used to evaluate spatial relationships between malformed offsprings and environmental variables.
Field Staff	
Veterinarian Epidemiologist	Collect and evaluate data on malformed offsprings in domestic animal populations primarily swine.
Practitioner	Examine and report occurrences of malformations in domestic animal populations.
Toxicologist	Collaborate and consult on outbreaks of fetal wastage and malformations related to environmental toxicants.
Extension Specialist Livestock Agent	Act as liaison between livestock producers and program staff in reproting information on animal population numbers and occurrences of malformations.

Table 1. (Continued)

Professional Discipline	Activities
Livestock Producer	Report animal population numbers and numbers of malformed offspring.
Consultants and Support Disciplines	
Mammologist	Collection and evaluation of natality and mortality data on wildlife populations as related to fetal wastage.
Embryologist	Consultant on the embryogenesis in domestic animals.
Geneticist	Consultant on genetics as related to outbreaks of malformations in animals.
Geologist	Collaborator and consultant on environmental trace elements patterns in the geochemical environment.

Table 2. Sectors of the Swine Industry and their Main Concern with Swine Diseases

Sector	Diseases
Producers	Abortions, stillbirths, neonatal deaths, anemia.
Feeder	Pneumonia, arthritis parasites.
Buyer	Shipping loss, excessive shrinkage.
Packer	Loss of meat or body organs due to parasitism and disease.
Veterinarian	Disease outbreaks; sporadic instances of swine disease, primarily in sub-adult or adult animals.
Farm Advisor (e.g., Extension Specialist)	Reproductive performance, nutritional deficiencies.
Researcher	Genetic infectious or noninfectious diseases, e.g., anomalies

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