

MOLECULAR EPIDEMIOLOGY – NEW WINE IN NEED OF AN OLD BOTTLE?

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The term “molecular epidemiology” was first used in 1973 in the context of a discussion of the antigenic variability of the human influenza virus⁽³⁾. By the mid 1970s it was being applied more specifically to studies examining strain variability through the use of gel electrophoresis on structural proteins⁽⁷⁾. Initially the phrase was by no means standard, and similar work being undertaken at the time referred to “molecular aspects” and “molecular approaches”. However, it gradually gained acceptance and since the 1980s the trickle of medical and veterinary papers using the term has turned into a literal flood.

There is little controversy over the definition of “molecular epidemiology”, being generally accepted as the use of molecular biology techniques in epidemiological studies⁽⁴⁾. Accordingly, this promises to be an exciting hybrid discipline combining the benefits of reductionism of molecular biology with the more holistic approaches of traditional epidemiology. Nevertheless, as epidemiologists embarking upon studies using spoligotyping to investigate paths of transmission of bovine tuberculosis⁽¹⁾, the hypothesis emerged that very few of the publications defining themselves as molecular epidemiology were fulfilling this promise.

Materials and Methods

In order to explore our hypothesis, we sampled the bibliographic database “VETCD”. The sampling frame were papers from 1973 to 1999 which contained the term molecular epidemiology either in the title, the abstract or as one of the key words. A manual edit was then done to sift out papers not of direct veterinary relevance and to remove redundancies and duplications. All papers were then classified according to the disease agent being investigated (i.e. viruses, bacteria, rickettsias, protozoa and toxins. Papers discussing or investigating both protozoa and helminths were classified under “parasites”.

From the sampling frame of peer-reviewed journal articles, 15 were randomly selected and a more detailed investigation undertaken. All papers were read, and an assessment made on the “epidemiological content” of each based upon three criteria: clear definition of the epidemiological problem, sampling strategy detailed, and use of biostatistical data analysis apart from cluster analysis.

Results

The total number of filtered citations was 159, of which 134 were peer reviewed journal articles, and 18 were conference summaries. The first cited paper was in 1983, being an investigation of types of antibiotic-resistant *Salmonella* spp. isolated from dairy cattle⁽²⁾. The number of papers remained generally low until the early-1990s, when a phase of exponential growth became apparent (Figure 1a). The use of the phrase was dominated by microbiologists, who accounted for over 95% of usage (Figure 1b). There was a wide range of journals used (76) for publication, the four most frequent being *Journal of Clinical Microbiology* (n=10 articles), *Journal of General Virology* (n=8), *Magyar Allatorvosok Lapja* (n=6), and *Veterinary Microbiology* (n=5). Only one specifically epidemiological journal was cited, the *European Journal of Epidemiology*, which published two articles.

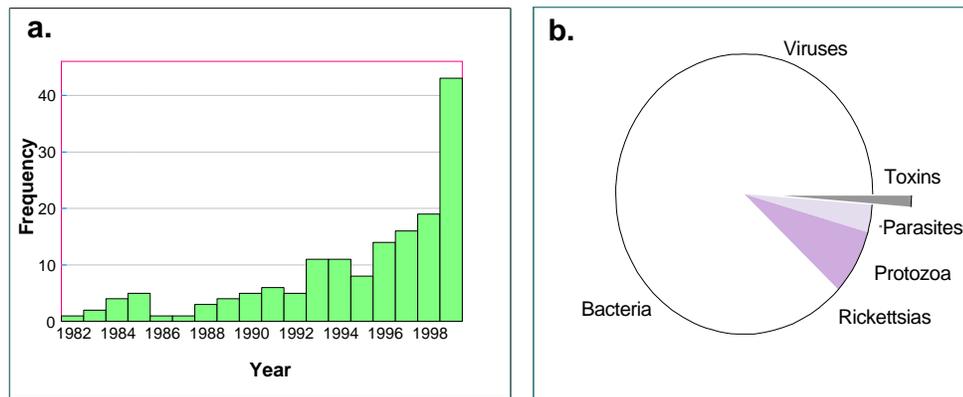


Figure 1. (a) Number of scientific papers per year cited in VETCD including the term “molecular epidemiology” in the title, abstract or key words; (b) classification of the subject according to the disease agent being investigated

The analysis of the 15 papers showed that not one fulfilled all the three specified criteria for epidemiological content. Seven provided a clear definition of the epidemiological problem, 4 outlined their sampling strategy, but none used any biostatistics apart from cluster analysis. Five fulfilled none of the criteria.

Discussion

Two distinct usages of “molecular epidemiology” have developed in the biomedical literature. The first places the emphasis on using molecular biology to detect *biomarkers* of cellular and sub-cellular damage and alteration⁽⁸⁾. This is grounded in cancer epidemiology and, on account of the many limitations of traditional epidemiology in untangling the path from exposure to disease, has aroused considerable interest and debate⁽⁶⁾. This strand of molecular epidemiology is poorly represented in the veterinary literature due, no doubt, to oncology being a minor sub-discipline in comparison to human medicine.

The second usage is the application of molecular techniques to the *subtyping* (or genotyping) of micro-organisms⁽⁵⁾. This is a more conventional application, as in essence it is not substantially different in intent from subtyping based upon phenotypic characteristics such as surface antigens or the expression of metabolic

proteins. However, genotyping has a particular relevance for those organisms such as *Mycobacterium bovis*, for which no successful phenotyping system exists, or the Rickettsias, that pose considerable problems in culture and identification.

Based on the evidence of our analysis, “molecular epidemiology” as currently practised in veterinary science is overwhelmingly “molecular” and rarely “epidemiology”. As this so substantiates our original hypothesis, an argument can be presented that journal editors must be discriminatory when faced with the “misuse” of the term. Instead of molecular epidemiology, “genotyping”, “molecular characterisation” or “phylogenetic analysis” needs to be substituted where these are the essence of the studies.

In no respects do we conclude that molecular epidemiology is a failure as a sub-discipline. Rather, we suspect that the lack of true “classical” epidemiology in the planning and execution of molecular based studies represents unawareness on the part of microbiologists of the extent to which epidemiology can “add value” through enhanced rigour and structure. Accordingly, we argue, as both an opportunity and a necessity, for closer collaboration between microbiologists and epidemiologists. This way, molecular epidemiology will become a truly hybrid discipline, and should fulfil its considerable potential.

References

1. Clifton-Hadley RS and others. 1998 DNA fingerprinting of *Mycobacterium bovis* isolates using spoligotyping - epidemiological issues. In: Thrusfield MV & Goodall EA (eds). Proc Soc Vet Epidem Prev Med, pp.15-27.
2. Jørgensen, S T 1983. Prevalence and molecular epidemiology of antibiotic resistant *Salmonella typhimurium* and *Salmonella dublin* in Danish cattle. Acta Path Microbiol Immunol Scand 91: 163-8.
3. Kilbourne ED. 1973. The molecular epidemiology of influenza. J Infect Dis 127: 478-487.
4. Last, J.M. 1995. A dictionary of epidemiology, 3rd edn. New York: Oxford University Press, p.107.
5. Maslow JN, Mulligan ME, Arbeit RD. 1993. Molecular epidemiology: application of contemporary techniques to the typing of microorganisms. Clin Infect Dis 17: 153-164.
6. McMichael AJ. 1994. "Molecular epidemiology": new pathway or new travelling companion? Am J Epidemiol 140: 1-11.
7. Pereira L, Cassai E, Honess RW, Roizman B, Terni M, Nahmias A. 1976. Variability in the structural polypeptides of herpes simplex virus 1 strains: potential application in molecular epidemiology. Infect Immun 13: 211-220.
8. Schulte, P.A. 1993. A conceptual and historical framework for molecular epidemiology. In: Schulte PA & Perera FP (eds). Molecular epidemiology: principles and practices. Orlando: Academic Press, pp. 3-44.