CORRESPONDENCE

Use of the Polymerase Chain Reaction for the Detection of Legionella pneumophila DNA in Serum Samples

Sir—We read with interest the article by Murdoch et al. [1], which described the use of PCR to detect Legionella DNA in urine and serum samples from patients with pneumonia.

We have previously used the PCR method to detect Legionella DNA in respiratory samples [2]. In the present study a PCR technique with primers that specifically amplify a 700-bp segment of Legionella pneumophila [3] was used to detect the DNA of this bacterium in serum samples from patients with pneumonia. We studied serum samples from 41 patients with proven legionellosis: nine patients had cultures positive for L. pneumophila, and 32 patients had serological evidence of L. pneumophila infection, as shown by indirect immunofluorescence assay with use of L. pneumophila serogroup 1 as antigen. The sera of 10 patients with pneumonia due to other organisms were used as controls.

Total DNA from the serum samples was extracted with use of a DNA extraction reagent containing Chelex anion-exchange resin (Perkin Elmer, Roissy, France). The PCR products were visualized after agarose gel electrophoresis and ethidium bromide staining were performed. L. pneumophila DNA was detected in 12 serum samples (30%) from the 41 patients with legionellosis, and it was not detected in serum samples from the 10 controls. We did not find that the presence of L. pneumophila DNA in the serum samples correlated with positivity in bronchoalveolar aspirate cultures or with serum antibody titers. In addition, L. pneumophila DNA was found both in serum samples obtained early (2–4 days) and later (10–15 days) after the onset of pneumonia.

Our results suggest that PCR assay of serum samples can contribute to the rapid diagnosis of legionella infection. Whether positive results are due to legionella bacteriemia or to breakdown products (nucleic acids) that are present during the infection remains to be elucidated.

Peggy Matsiota-Bernard, Georgia Vrioni, and Charles Nauciel
Laboratoire de Microbiologie, Hôpital Raymond Poincaré, Garches, France

References

Problems with Antibiotic Resistance in Spain and Their Relation to Antibiotic Use in Humans Elsewhere

Sir—We congratulate Baquero et al. [1] and the editors of Clinical Infectious Diseases for their willingness to publish this interesting statement concerning problems with antibiotic resistance in Spain, possible reasons for these problems, and suggestions for future action. The accompanying editorial by Levy [2] reflects some misconceptions regarding the relationship between the use of antibiotics and the development of antibiotic resistance; these misconceptions show that there has until now been a general lack of information about antibiotic use in various settings, i.e., among veterinarians and in veterinary settings.

Scandinavian investigators have in recent years published data on the general consumption of antibiotics by humans, as measured in defined daily doses (DDD) per 1,000 inhabitants per day (figure 1). These data show that in general, consumption of antibiotics in these nations is low in comparison with that in Spain, where there has been a decrease from 31 DDD per 1,000 inhabitants per day to 19 DDD per 1,000 inhabitants per day; these latter figures are in the same range as those reported from Finland and Iceland (figure 1). There have been few reports of antibiotic susceptibility data from the Scandinavian countries in the medical literature, and these data usually have an impact only when they describe unexpected development of antibiotic resistance [3, 4]. The general trend during the past 10–20 years has been to report high frequencies of antibiotic resistance and the mechanisms of this resistance, but seldom the reasons for these high frequencies and how to avoid them; the authors of these reports have had much easier and more rapid access to high-impact journals than have authors reporting low frequencies of antibiotic resistance. A few prospective multicountry surveys of selected human pathogens have been conducted and have unanimously shown that the Scandinavian countries and the United Kingdom have the lowest incidences of antibiotic resistance and that the southern European countries have the highest incidences of antibiotic resistance [5, 6].

Few data on antibiotic use in the southern European countries have been published, but the general impression from congresses, reports, and the literature has been one of high antibiotic consumption and misuse, i.e., too much use and use of too many broad-spectrum drugs. Recent studies have revealed that some of the multiply-resistant pathogens, e.g., Salmonella species, isolated daily in Scandinavian clinics, are imported from abroad, mostly from Mediterranean regions.
countries, the Near East, the Far East, and other developing countries; the isolates are either from patients traveling in these countries or from imported foods [7]. Most Danish hospitals now follow the rule, specified by infection-control authorities, that any patient who has been treated in a foreign hospital within the previous month must be isolated and screened by culturing specimens from various body sites for multiply-resistant bacteria before such a patient can enter the Danish hospital system.

Human antibiotic consumption in Denmark, which is probably among the lowest in the world, corresponds to very low frequencies of antibiotic resistance in most of the usual human pathogens; however, the Danish data show some surprising trends in comparison with the Spanish data [1]. Figure 2 shows the distribution of antibiotic use in general practice and in hospitals in Denmark in 1995. As in Spain, in Denmark 9% of the total amount of antibiotic use is in hospitals, while the majority, 91%, occurs in general practice. Antibiotic use by humans in the years 1990–1993 totaled ~40 tons per year, while therapeutic use in pigs totaled ~70 tons per year, and antibiotics used as growth promoters for animals totaled 120 tons per year. In all, veterinary use of antibiotics totaled ~220 tons per year, a figure at least five times higher than that for human use and almost the same as that for Spain, which has a population five to six times the size of the Danish population. Nevertheless, the frequency of antibiotic resistance has remained low, and we have not been able to prove, apart from a few important examples (e.g., use of avoparcin and the emergence of vancomycin resistance in enterococci), that the veterinary use of antibiotics has had much impact on the frequency of antibiotic resistance among human pathogens.

We agree with Levy that there probably exists a certain level of antibiotic consumption in the community, above which problems with resistance will occur. This assumption is consistent with levels of antibiotic resistance in Streptococcus pyogenes and pneumococci in Finland and Iceland [3, 4]; levels of resistance in these bacteria are lower in the other Scandinavian countries. Another factor of great importance that was not discussed by Baquero et al. or by Levy is the type of antibiotics used. In Spain [1], oral cephalosporins constitute 13% and fluoroquinolones constitute 6% of all antibiotics used. In Denmark in 1995, the same groups of antibiotics constituted 1% and 3% of all antibiotics used. In this context it is interesting that Spain has one pharmacy per 2,000 inhabitants [1], while Denmark has 300 pharmacies for its 5,200,000 inhabitants, i.e., one pharmacy per 17,000 inhabitants. Furthermore, government subsidy has remained an important tool to limit the use of broad-spectrum antibiotics. As an example, tetracycline and oral cephaplorins are not subsidized in Denmark.

For the future we totally agree that monitoring the frequency of resistance in a range of important human and animal bacteria, as well as antibiotic use in all settings, is of utmost importance; data are needed to regulate antibiotic use and to decide what actions to take regarding development of resistance. Since the beginning of 1996, a unique cooperative effort between the human and veterinary health authorities has been implemented in Denmark, with the purpose of monitoring antibiotic resistance in human and animal pathogens as well as antibiotic use in human medicine, animal therapy, and animal growth promotion. The Ministry of Agriculture and Fisheries and the Ministry of Health have jointly funded the project, which is maintained by the Statens Serum Institut, the National Food Agency, and the Danish Veterinary Laboratory. Annual reports will contain data from antibiotic susceptibility studies of selected bacteria recovered from healthy humans as well as from patients, production animals, pets, and various types of domestic and imported food. Furthermore, data on antibiotic consumption by humans via general practice and in hospitals, as well as therapeutic and prophylactic use in production animals, including fish, will be collected and published.

We hope that similar initiatives will take place in many other countries in order to provide data for comparison and research.

Niels Frimodt-Møller, Frank Espersen, Bodil Jacobsen, Jørgen Schlundt, Anders Meyling, and Henrik Wegener

DANMAP, The Danish Antibiotic Resistance and Consumption Monitoring Programme, the Division of Microbiology, Statens Serum Institut, the National Food Agency of Denmark, and the Danish Veterinary Laboratory, Copenhagen, Denmark
Lancefield Serogrouping Alone Is Insufficient for Species Assignment of Streptococci

Sir—The interesting article by Wagner et al. [1] describes the first case of acute diffuse group G streptococcal myositis in association with streptococcal toxic shock syndrome. Since this life-threatening disease has been observed thus far only in association with *Streptococcus pyogenes*, this finding has great impact for clinicians and microbiologists.

Unfortunately, apart from Lancefield serogroup G, no further phenotypic characteristics of the isolated streptococci were given. Therefore, precise taxonomic placement of the involved *Streptococcus* species is impossible, since all of the following large or minute colony-forming streptococcal species can express Lancefield group A antigen and have been isolated in cases of human infection [2-4]: *S. anginosus, S. intermedius, S. canis*, and *S. dysgalactiae* subspecies *equisimilis*. The latter species was recently established by Haase and Schnitzler and in reviews of Lancefield streptococcal groups C, G, and L ([1], 2), the taxonomy of GGS has been controversial. However, the majority of GGS show β-hemolysis [1, 2], and Lancefield serotyping is the principal means by which β-hemolytic streptococci are clinically classified.

Although we agree with Haase and Schnitzler about the need for further study of this interesting strain of GGS, the novelty of this organism producing a previously undescribed toxin and a clinical syndrome consistent with streptococcal toxic shock syndrome remains the same.

John G. Wagner, Patrick M. Schlievert, and Paul Carson
Division of Pulmonary and Critical Care Medicine, University of Michigan Hospitals and Clinics, Ann Arbor, Michigan; Department of Microbiology, University of Minnesota Hospital and Clinics, Minneapolis, Minnesota; and Department of Internal Medicine, University of North Dakota and Veterans Affairs Medical Center—Fargo, Grand Forks, North Dakota

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Reprints or correspondence: Dr. John G. Wagner, Division of Pulmonary Medicine, University of Michigan Hospitals, 3916 Taubman Center, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109-0360.