HEALTH SIGNIFICANCE OF *KLEBSIELLA* IN THE ENVIRONMENT

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Ontario Ministry of the Environment

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CONTENTS

This position paper is based on a literature search, on the personal experience of the author, and on discussions with other experts in the field. It was written under contract with the Ministry of the Environment of Ontario, at the suggestion of the Ministry's Klebsiella Committee, to provide an assessment of the potential of *Klebsiella* present in the non-hospital environment to cause infections in human beings exposed to them.

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The views and ideas expressed in this paper are those of the author and do not necessarily reflect the views and policies of Environment Ontario, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

SOMMAIRE

Les deux espèces les plus courantes de *Klebsiella*, à savoir *K. pneumoniae* et *K. oxytoca*, se trouvent dans les matières végétales et dans les eaux de surface, y compris les eaux de surface servant aux loisirs. Les souches de *Klebsiella* sont peu dangereuses pour l'homme; en effet, elles ne causent des infections graves qu'en cas d'affaiblissement *de* la victime. Les types de souches de ce bacille sont nombreux, mais aucun ne semble plus susceptible qu'un autre de provoquer ces infections opportunistes.

De nos jours, la pneumonie primitive imputable à *Klebsiella* est rare et les personnes atteintes sont généralement des hommes affaiblis par l'alcoolisme. La plupart des infections attribuables à *Klebsiella* observées de nos jours chez les gens qui ne présentent pas d'autres problèmes de santé sont des infections urinaires et parfois intra-abdominales (p. ex., la cholécystite). Rien ne permet de croire que ces infections font suite à une contamination par des souches de *Klebsiella* en milieu naturel. Elles résulteraient plutôt de la présence de *Klebsiella* dans la flore intestinale de certaines personnes.

La présence de *Klebsiella* dans les eaux de surface utilisées à des fins de loisirs n'est pas considérée comme une cause de maladies. Bien que les travailleurs des usines de pâtes et papiers soient particulièrement exposés à *Klebsiella*, la formation de colonies de *Klebsiella* n'est pas très rapide et n'entraîne pas de maladies graves.

La collectivité en général et le milieu hospitalier sont deux milieux entièrement différents en ce qui a trait aux infections par *Klebsiella*, et les données cliniques et épidémiologiques se rapportant à l'un de ces milieux ne peuvent pas s'appliquer à l'autre. Il n'est pas rare que *Klebsiella* cause des infections graves chez des patients hospitalisés, mais ces infections sont imputables à l'état déjà affaibli de ces patients

et à l'utilisation intensive d'antibiotiques dans les hôpitaux. S'il était possible de protéger les malades hospitalisés contre toutes les souches de *Klebsiella*, il est certain que ces patients seraient alors infectés par d'autres espèces de bacilles Gram-négatifs comme *Serratia marcescens* ou *Pseudomonas aeruginosa* et souffriraient des mémos types d'infections cliniques nosocomiales que celles causées par *Klebsiella*.

Il semble donc que certains auteurs se soient inquiétés à tort du risque que posent pour la santé les souches de *Klebsiella* présentes dans l'environnement parce qu'ils n'ont pas distingué le milieu hospitalier de la collectivité en général à cet égard.

EXECUTIVE SUMMARY

The most widely occurring species of *Klebsiella* are *K. pneumoniae* and *K. oxytoca*. They are found in nature in association with vegetable matter and surface waters, including surface waters used for recreational purposes. *Klebsiella* strains have low pathogenicity for man and cause serious human infections only when the resistance of the human host is impaired. *Klebsiella* strains may be subdivided into many different types and there is no evidence that some types are any more able to cause these opportunistic infections than others.

Primary pneumonia in the community due to *Klebsiella* is now a rare disease and when it does occur the patients are generally males debilitated by chronic alcoholism. The *Klebsiella* infections seen today in previously healthy people in the community are mainly urinary infections. There are also some intra-abdominal infections such as cholecystitis. There is no evidence to suggest that any of these community infections occur following exposure to *Klebsiella* strains in the natural environment. They result from the carriage of *Klebsiella* by some people as part of their normal bowel flora.

The presence of *Klebsiella* in recreational surface waters has not been documented as a cause of human disease. Although pulp and paper mill workers are exposed to particularly large numbers of *Klebsiella* in the course of their work, their rate of colonization is not particularly high and when colonization occurs *it is not* followed by serious disease.

The community environment and the hospital environment are entirely different as settings for infections by *Klebsiella* and clinical and epidemiological data from the one cannot be transposed to the other. Serious infections in hospitalized patients are not uncommonly caused by *Klebsiella*, but this is a consequence of the already debilitated state of these patients and the widespread use of *antibiotics* in hospitals. If it were possible to prevent sick hospitalized patients from encountering any strains of *Klebsiella* there is no doubt that they would instead acquire other species of gram-negative bacilli such as *Serratia marcescens* or *Pseudomonas aeruginosa* and would suffer the same sorts of hospital-acquired clinical infections from these species as they would have from

Klebsiella.

The concerns that have been expressed in some of the scientific literature that environmental strains of *Klebsiella* are likely to pose a hazard to human health, seem largely to be based on the failure of the authors of these papers to appreciate that hospital findings do not apply to the community setting.

GENERAL INTRODUCTION

This position paper presents the state of current medical knowledge on the circumstances in which *Klebsiella* infects man and whether these circumstances would be affected by the presence of large numbers of *Klebsiella* in the natural environment. It will emphasize in particular the fundamental differences between infections occurring in the community and in hospitalized patients.

Bacteria of the genus *Klebsiella* represent somewhat of a problem in environmental science because they are very common in natural waters and at the same time there has been considerable disagreement about the degree to which they are pathogenic for man. In particular, it is now well known that. *Klebsiella* may give a positive fecal coliform test even when present alone and in the absence of *Escherichia coli* (1,2). There has therefore been considerably more interest on the part of environmental microbiologists in *Klebsiella* than in other bacteria such as *Serratia* and *Providencia* which are also present in the natural environment and also, like *Klebsiella*, may infect debilitated patients in hospitals.

The fecal coliform test was devised as a means of screening water for fecal contamination and is used for that purpose in Ontario (3) but it is now realized (1,2) that the presence of *Klebsiella* in water in the absence of contamination with sewage or fecal matter may give rise to a positive fecal coliform test. There has been some reluctance to give it up in favour of a test for *E. coli* alone because of a fear amongst some workers that *Klebsiella* also was a "pathogen" for man which ought to be absent from water with which human beings come into contact (1).

The probable reason for these worries about the pathogenicity of *Klebsiella* is a major change that has taken place, particularly over the last twenty years, in infectious disease medicine on the concept of what constitutes a "pathogen". Some organisms are clearly pathogenic, such as *Salmonella typhi*. Their presence in water supplies or in the excretions of a human carrier would always present a danger to the community. Some bacteria, such as the plant pathogen *Erwinia amylovora*. do not infect man and can be clearly thought of as "non-pathogens" for man. However, some agents that forty years ago were considered non-pathogens under any circumstances are now known to be capable of acting as pathogens in the limited circumstances of the infections that they produce in sick debilitated patients in hospital. A good example of this is *Serratia marcescens. Klebsiella* is now considered to fall into this latter category as an organism of the environment which is an opportunist that infects mainly debilitated patients in hospital. However there remains repeated comments in the environmental bacteriology literature that *Klebsiella* is a "pathogen" and could well be a "health hazard" (1,4,5).

BACTERIOLOGY OF KLEBSIELLA

Friedlander in 1882 described the organism that was later to be known as *Klebsiella pneumoniae* as an organism that he had found at autopsy of several cases of pneumonia and which he wrongly thought to be the principal cause of lobar pneumonia (6). A common name of the organism used in some of the older literature was therefore Friedlander's bacillus. Although it was very soon shown that the pneumococcus, now known as *Streptococcus pneumoniae*, was the true cause of lobar pneumonia the strict rules of bacterial taxonomy made it proper to call the major species of the genus *Klebsiella, K. pneumoniae* (7). In the past some *Klebsiella* were wrongly referred to as non-motile strains of *Aerobacter aerogenes* (8,9).

The named species within the genus *Klebsiella* are *Klebsiella pneumoniae, Klebsiella oxytoca, Klebsiella planticola, Klebsiella terrigena, Klebsiella rhinoscleromatis*, and *Klebsiella Ozaenae* (10,11). Several decades ago, British bacteriologists suggested additional species including *Klebsiella aerogenes* and *Klebsiella edwardsii* but these names were never widely used outside the United Kingdom.

At present by far the commonest species to be isolated from environmental sources and from hospital patients is *K. pneumoniae*. The next most frequent is *K. oxytoca* which is biochemically similar to *K. pneumoniae* except that it is indole positive. My own findings in the hospital setting are that approximately 15% of strains are *K. oxytoca* (12).

K. planticola and *K. terrigena* are very recently named species which can really be differentiated from *K. pneumoniae* only by sophisticated D.N.A. hybridization studies so that in the ordinary diagnostic laboratory they would be classified by routine biochemical tests as *K. pneumoniae* (10,13). *K. rhinoscleromatis* and *K. ozaenae* are rarely isolated. They are now considered to be biochemically inactive strains of *K. pneumoniae* which do not really deserve the species status accorded to them in the past (7).

In both the environmental and clinical microbiology literature *Klebsiella* can be taken to mean mainly strains of *K. pneumoniae* together with a smaller proportion of *K. oxytoca*. *K. pneumoniae* and *K. oxytoca* can be subdivided into between 70 and 80 serologically different types on the basis of the immunological specificity of the polysaccharide forming the capsule of each *Klebsiella* type. Capsular typing used alone or along with biotyping (12) provides a valuable tool for the epidemiological study of *Klebsiella*.

HABITAT OF KLEBSIELLA

Klebsiella strains have been found widely in nature in association with vegetable matter and in surface waters (4,14). Studies have shown that they may be isolated widely from surface waters in many areas of North America (15). They are found in particularly large numbers in association with the bark of trees and consequently are present in large numbers in the effluents from pulp and paper mills (14,16). It has been shown that there is a very wide range of different capsular types in surface waters in the environment (15).

In the human being, the principal location is the bowel (17).

Approximately one in three human beings carry *the* organism as part of their normal bowel bacterial flora (18). Colonization of the upper respiratory tract occurs but only at a low level of 1-2 % of healthy people in the community (19). There is no evidence to suggest that carriers are affected in any detrimental way by the fact they carry this organism.

Klebsiella are also associated with a variety of animals as normal flora and in some cases as opportunistic pathogens. Animals from which *Klebsiella* have been isolated include monkeys, cows, pigs, horses, dogs, rats and snakes (11).

STATUS AS A PATHOGEN IN THE COMMUNITY

There are many papers in the environmental literature (1,4,5,21,22) that state that *Klebsiella* is a serious pathogen in the general community. It has been suggested that this organism causes a significant number of cases of community pneumonia which have a high mortality rate (5) and that it is an important cause of urinary tract infections and various other infections in the community (1,21). Some literature also suggests that significant health problems may follow heavy exposure to *Klebsiella* in circumstances where there are large numbers of organisms in the environment (23).

In fact, *Klebsiella* is not a highly pathogenic bacterium. Compared with the pneumococcus it is of little significance as a cause of pneumonias developing in the community (24). In urinary tract infections and in the intra-abdominal infections that result from the escape of bacteria from the lumen of the intestine, *E. coli* is a much more successful pathogen than *K. pneumoniae*.

The remainder of this section will deal in detail with the true current status of *Klebsiella* as a community pathogen today. For convenience it is divided into three parts: (A) Pneumonia; (B) Diseases Arising from Bowel Carriage; and, (C) Consequences of Heavy Exposure to *Klebsiella*. In each of these parts, an attempt is made to present the true factors on pathogenicity of *Klebsiella* in contrast to some of the misapprehensions evident in the environmental literature.

(A) PNEUMONIA

A number of papers concerning environmental *Klebsiella* give the impression that *K. pneumoniae* is an important cause of pneumonia in the community. One paper states (5):

"*K. pneumoniae* is an opportunistic pathogen that is extremely virulent and has quickly developed immunity to almost all antibiotics. *K. pneumoniae* cause 2% of all cases of bacterial pneumonia, and as a result of the antibiotic resistance of this organism, it caused 60 to 70% of the deaths from this disease".

This statement leaves the reader with a number of misconceptions. Although *K. pneumoniae* is correctly designated as an opportunistic pathogen there is no indication that the opportunistic infections occur in the hospital setting and the reader is left to assume that the statements apply to *K. pneumoniae* infections generally. Community strains of *Klebsiella* are resistant only to ampicillin among the antibiotics generally employed to treat infections due to gram-negative bacilli. It is only strains endemic in hospitals that have been shown to be resistant to multiple antibiotics. It is true that pneumonia due to *K. pneumoniae* has a considerably higher mortality rate than pneumococcal pneumonia but few cases occur in the community so that they make no significant pneumonia. When they do occur, the patients are usually men over forty years of age and frequently men who are chronic alcoholics. Aspiration of oropharyngeal secretions containing *Klebsiella* is thought to be the pathogenic mechanism for the disease (25).

The incidence in the community today appears to be considerably less than 2 per cent. There has either been a true decrease in the community incidence in recent years or there has been an increasing realization in medical circles that the true incidence is lower than the older literature had reported. In the past, the medical literature ended to give the impression that *Klebsiella* pneumonia was not a particularly rare disease and that its severity suggested that *K. pneumoniae* was an organism of considerable natural pathogenicity. One widely quoted paper in the medical literature as recently as the 1950s suggested that community pneumonias

due to *Klebsiella* were much more common than was generally thought and an incidence of over 8% was quoted (26). However, even by 1974 standard medical textbooks were stating the incidence as less than 1% (25). In a 1980-81 survey of 127 community-acquired pneumonia cases in the United Kingdom there were no pneumonias due to *K. pneumoniae* (24).

My own experience in almost 30 years of medical practice in the fields of medical microbiology and infectious disease in Ontario has been that community-acquired cases of pneumonia due to *K. pneumoniae* are very rare. To confirm this impression I have carried out a fairly widespread survey of colleagues specializing in infectious diseases in various parts of Canada from Newfoundland to British Columbia (27). All agreed with this view. Some said that they had not seen a case and others had seen rare cases, all in chronic alcoholics. It must again be emphasized that this applies to community-acquired disease. The epidemiological situation is quite different among compromised patients in the hospital setting as is fully discussed in Section 7.

I also solicited the opinions of three physicians who are international experts on the pathogenicity and epidemiology of *Klebsiella*, two from the U.S. and one from the U.K. Dr. Ted Eickhoff (28), who was a recent President of the Infectious Disease Society of America and who in 1972 compiled a definitive review (29) of the epidemiological significance of *Klebsiella* in the natural environment, wrote to me saying, "I would agree that primary *Klebsiella* pneumonia, the old classical Friedlander pneumonia, is quite a rare entity indeed. We see what we believe to be such a case perhaps every two or three years."

Dr. John Matsen (30), whose published research has provided basic information (15, 18) on the epidemiology of *Klebsiella* in both the outside community and the hospital setting, wrote to me saying: "First, I would agree that the primary *Klebsiella* pneumonia described in the early decades of this century in patients in the community is today a very rare entity. The *Klebsiella* pneumonia that occurs in hospitalized patients, whereas pathogenically similar, is epidemiologically a

different entity". Dr. Mark Casewell (31), who has studied the epidemiology of *Klebsiella* in London, England (32, 33) wrote to me as follows, "The incidence of primary Friendlander's pneumonia is indeed rare in this country.

I saw three or four cases at St. Thomas's (Hospital) in the ten years I *was* there for a 1000 bedded hospital. Since arriving at King's, I have not seen a case in two years". It seems clear that in Canada and in other countries very few cases of primary pneumonia in the community are caused by *K. pneumoniae*.

The reason for the discrepancy between the older medical literature (26, 34, 35) and present day observation can only be the subject of speculation. Aerobic gram-negative bacilli are widely present in the community. Nowadays it is well known that they act as opportunistic pathogens to infect debilitated hospital patients. It is by no means unlikely that individuals in the community with lowered resistance mechanisms would always have been similarly susceptible to opportunistic attack by these organisms.

It is significant that many of the older described cases of "*Klebsiella* pneumonia" were elderly and many were chronic alcoholics. Possibly there were more such people in the community in the earlier years of this century because of less adequate social services. Pneumonia due to *Klebsiella* may therefore have been genuinely more frequent in these earlier years although even then the literature suggests that it was not a common disease. One paper in 1915 (36) could only find records of 33 cases in the literature to that point.

In addition I believe that it is probable that many of the cases described as *Klebsiella* pneumonia may have been wrongly diagnosed. *K. pneumoniae* is a bacterium which is very easy to grow and recognize as it produces a large obvious colony on common culture media. If *K. pneumoniae* happened to be present in the respiratory secretions because it was being carried in the throat of someone who incidentally developed pneumonia caused by some other organism, the *K. pneumoniae* might have been recognized while the true etiological agent might

have been missed. I have reviewed some of the older papers (26) and some more recent papers (37) on pneumonia alleged to be due to *Klebsiella* and many of these cases do not today satisfy the scientific criteria which must be fulfilled before an etiological diagnosis is assigned.

In summary, current data suggests that *K. pneumoniae* does not cause a significant number of cases of primary pneumonia occurring in the community.

(B) DISEASES ARISING FROM BOWEL CARRIAGE

While there is no doubt that some *Klebsiella* infections in patients in the community and many infections in the hospital setting are associated with carriage of *Klebsiella* strains in the bowel, some papers from the environmental literature have suggested that there has been increased human infection associated with the environmental frequency of *Klebsiella*. One such paper (1) states:

"The ubiquitous distribution of FC-positive *Klebsiella* found in finished drinking water, foods, wood products and industrial environments may already be manifested in the changing patterns seen in documented reports. Included are the increase in both cell densities and colonization rate of the human intestinal tract and the increase in human infection rates caused by *Klebsiella* during the last two decades".

This statement leaves the reader with a definite suggestion that there has been a cause and effect chain with increased, environmental contamination with *Klebsiella* leading to increased human colonization with *Klebsiella* leading in turn, to increased human infections with *Klebsiella*. The reader who is not familiar with the fundamental epidemiological differences between *Klebsiella* infections in the community and in hospitals could take from this statement that increased numbers of *Klebsiella* in the environment have led to a general increase in human infections with this organism. There is no evidence of recent increases in non-hospitalized patients of the *Klebsiella* infections that are associated with carriage of the

organism in the bowel.

It is an accepted medical fact (18) that approximately one third of healthy members of the community carry *Klebsiella* as part of their normal bowel flora. When for any reasons, organisms found inside the large bowel leave that normal habitat and come into contact with body tissues that are normally sterile they may infect these tissues. This happens with *Klebsiella* as it does with other members of the bowel flora. The remainder of this portion of the paper discusses these infections in patients in the general community, dealing with the question of the relative importance of *Klebsiella* and other members of the bowel flora in causing these infections, and the existence of any evidence for an increase of such *Klebsiella* infections in recent years.

In peritonitis resulting from some type of direct leakage of large bowel bacteria into the peritoneal space, *Klebsiella* is a relatively insignificant pathogen. The major organisms cultured in peritonitis are the bowel anaerobes and the main aerobes are *E. coli* and *Streptococcus faecalis*. Presumably roughly one in three of such patients would be expected to have strains of *Klebsiella* amongst their bowel flora (18) and it must be assumed that the other organisms overgrow it during the process of infecting the peritoneum because it is seldom isolated from cultures taken from peritonitis at surgical operation.

The main type of intra-abdominal infection from which *Klebsiella* is regularly isolated is sepsis of the biliary tract. Inflammation of the bile ducts is frequently associated with gall stones and the bacteria that cause the sepsis are bowel bacteria that enter the liver with the portal blood or up the common bile duct. *E. coli* is the commonest organism associated with biliary sepsis which is caused by a variety of different bacteria. In four reported series of patients with biliary sepsis (38, 39, 40, 41) *E. coli* was the commonest organism in all cases and the number of *Klebsiella* in each series expressed as a percentage of the number of *E. coli* was 12.5, 20, 22 and 48.

Numerically the most common type of infection caused by *Klebsiella* in patients in the community is urinary tract infection in women. The source of the infecting organisms is the large bowel flora and the mechanism is that in a proportion of women, aerobic bacteria from the bowel colonize the skin of he perineal area. Periodically the bladder of a woman with such perineal colonization becomes infected by retrograde spread up the urethra of the bacteria colonizing the perineum (42). The major cause of such urinary infections is *E. coli. Klebsiella* causes a much lower proportion. *E. coli* causes 80-90% of these infections and *Klebsiella* from 2-5% in different series (31, 43, 44, 45).

Neither I nor colleagues that I have consulted (46) have seen any evidence of an increase in the incidence of *Klebsiella* urinary infections in recent years.

Klebsiella is present in the normal bowel flora of one third of people in the community. As a result it causes a number of genuine primary infections in patients in the community. However, it causes fewer of these infections than comparable bowel bacteria which suggests that its pathogenicity is considerably lower than that of other bowel organism such as *E. coli* and the anaerobes in comparable situations. I found no evidence in the literature nor in my personal experience or that of colleagues that I have consulted, that there has been any increase in recent years in any of the infections that originate from the carriage of strains of *Klebsiella* by people in the general community outside hospitals.

(C) CONSEQUENCES OF HEAVY EXPOSURE TO *KLEBSIELLA*

There have been suggestions in some environmental papers that pulp and paper mill workers may develop serious *Klebsiella* infections as a result of colonization following exposure at work. One such comment (23) stated:

"There is a strong suggestion that upper respiratory tract colonization, with potential health hazards, can occur in pulp and paper mill workers occupationally exposed to *Klebsiella* bacteria. *K. pneumoniae* has been identified as the

predominant coliform bacterium from such an industrial waste source and is responsible for 2% of the bacterial pneumonia cases in the susceptible population of the United States and 60-70% of the deaths attributed to this disease".

However, study of the limited literature available on the topic really suggests that the rate of colonization of workers is not particularly high and is not followed by serious disease. The other errors in the quotation above on the importance of *K. pneumoniae* in community-acquired pneumonia today have previously been mentioned in Section 5A of this position paper.

In the U.S. one report (47) showed that only 1 of 24 workers became a nasal carrier of *Klebsiella* and there was no information on any consequent ill effects. In a much more thorough study from Finland (48) it was shown that 10-11% of exposed workers became nasal carriers of *Klebsiella* as compared to 3-6% of individuals in control groups. this suggests that *Klebsiella* has fairly limited abilities even to colonize human beings in conditions of heavy exposure.

The most important information in the Finnish paper was that no evidence of symptoms resulting from even the low levels of colonization could be elicited by careful questioning of the workers. I know of no papers in the literature that present definite evidence that *Klebsiella* infections occur in workers in the pulp and paper industry to any greater extent than in other people. This suggests very strongly that *Klebsiella* does not have the capacity to act as a significant pathogen in previously healthy people in the community.

KLEBSIELLA **IN RECREATIONAL SURFACE WATERS**

I know of no evidence that disease is produced by the presence of small or large numbers of *Klebsiella* in natural waters including recreational surface waters. It is always considerably more difficult to prove that an organism does not cause disease than it is to document the epidemiology of outbreaks and the clinical features of individual cases with an organism, such as *Salmonella*, that definitely does produce disease.

However, it is very likely that if *Klebsiella* in recreational waters did cause disease it would have been documented in the literature. There are many references in textbooks and in scientific papers to surface infections caused by another bacterium commonly found in the aqueous environment, *Pseudomonas aeruginosa* (49). Ear and skin infections have long been recognized to be associated with swimming and bathing. *P. aeruginosa* is known to cause infections both in outdoor swimming pools and lakes and such indoor facilities as whirlpool *baths (50,* 51). *Klebsiella* is as easy to grow and produces as recognizable colonies on culture media as *P. aeruginosa* and it would not be likely to have been missed had it caused similar infections to *P. aeruginosa* in similar circumstances.

There is no evidence of bowel symptoms arising from ingestion of *Klebsiella*. It is not reported as a cause of food poisoning (52, 53). It is not known if bowel carriage might *be* increased by the ingestion of *Klebsiella* but it is not particularly likely because it has been shown experimentally that large numbers of *Klebsiella* must be given by mouth to cause even bowel colonization of short duration (54). This is in agreement with what is known about human acquisition and maintenance of the normal flora of all areas of the human body that are colonized. Virtually nothing is known about why particular organisms colonize certain parts of the body and why some strains remain constantly present for very long periods while others do not. It has proved difficult to change the colonization pattern simply by feeding new organisms or exposing healthy individuals to new organisms in other ways.

The three *Klebsiella* experts that I consulted in the U.S. (28, 30) and the U.K. (31) all stated that they knew of no evidence that the presence of *Klebsiella* in natural waters constitutes a significant hazard to human health. Dr. Eickhoff (28) wrote that although he had "not comprehensively reviewed the literature of the past 15 years", from his general knowledge of the field he was "not aware of any substantive information that has been developed in the past 15 years that would significantly alter my opinion as stated in the review paper written from the National Council of the Paper Industry". This is a very valuable opinion from a most knowledgeable infectious disease physician. Dr. Eickhoff's conclusion in that paper (29) written in 1974 was, "There is thus no evidence to be found in the literature that presence in natural waters of *Klebsiella pneumoniae*

represents a human health hazard".

In summary, the presence of *Klebsiella* in recreational surface waters has not been documented as a cause of human disease. Therefore, the fecal coliform test when positive due to the presence only of *Klebsiella*, would erroneously suggest that surface recreational water was a potential health hazard when in fact it was not.

KLEBSIELLA IN THE HOSPITAL ENVIRONMENT

Although this position paper primarily concerns *Klebsiella* in the non-hospital environment a brief overview of hospital-acquired *Klebsiella* infections is essential to a full understanding of the literature on the pathogenicity of this organism. The major cause of hospital-acquired infections in the 1950s was *Staphylococcus aureus*. Staphylococcal infections continued into the 1960s but from then onwards aerobic gram-negative bacilli became increasingly prominent as causes of nosocomial infections. The major three genera involved were *Klebsiella, Pseudomonas*, and *Serratia*. There is now an enormous literature which clearly documents the serious infections caused by all three of these organisms in hospital patients. I will therefore refer to only two review papers dealing specifically with *Klebsiella* nosocomial infections (55, 56).

The increase in *Klebsiella* and other gram-negative nosocomial infections correlates with the increase in numbers of patients with highly compromised host defences in our hospitals today as compared with a generation ago. Patients who simply would not have survived in the past are now maintained by modern medical and nursing techniques in our hospitals for lengthy periods in a very seriously debilitated state. They are readily susceptible to infections by organisms of low pathogenicity such as *Klebsiella*. In addition, some forms of treatment such as anti-cancer drugs and corticosteroids are widely used and greatly lower patients' resistance to disease. Many inanimate objects are now implanted in the tissues of hospital patients to treat disease or to monitor the patient's condition. These include such things as prosthetic joints, prosthetic heart valves, heart pacemakers, and numerous plastic tubes connected with venous or arterial circulation, the peritoneal space or *even* the cerebrospinal space. These both allow the entry of

bacteria and the multiplication of the bacteria in the area of the inanimate object once they have entered.

Finally, treatment with antibiotics eliminates part of the normal human bacterial flora and allows its replacement by gram-negative bacilli which are frequently resistant to the antibiotics commonly used to treat hospital patients. The widespread use of antibiotics in hospitals has been thoroughly documented as the major factor predisposing debilitated patients to infection by gram-negative rods such as *Klebsiella*. An excellent illustration of the phenomenon is described in a paper from the U.K. which shows how the picture could be changed by discontinuing antibiotic use (57). The use of antibiotics described in this paper is typical, but the circumstances which permitted the medical staff to cease using them for a period, were unique to this institution. They are unlikely to be repeated on many other occasions. It is therefore worth quoting in detail.

Patients in a neurosurgical unit were routinely given the antibiotics ampicillin and cloxacillin in an attempt to prevent postoperative infections with *S. aureus*. As a result *Klebsiella* became prevalent in the unit, causing chest infections in 1 patient in 4 and urinary infections in 1 patient in 8. There were 8 deaths from *Klebsiella* meningitis. Use of all antibiotics, both for treatment and prevention, was stopped and by good fortune no very serious infections such as meningitis developed at this time, as this would have forced the physicians to reinstitute antibiotic use. *Klebsiella* infections of all kinds then virtually disappeared from the unit.

The *Klebsiella* strains that become prevalent in hospitals are usually resistant to many antibiotics. The epidemic mechanism is usually that a strain of *Klebsiella* acquires multiple resistance by conjugation with a bacterium of another species (58, 59). It acquires plasmids and transposons (60) from the other organism which gives the *Klebsiella* the genetic determinants of resistance to various antibiotics. The *Klebsiella*, now resistant to many antibiotics, has a major survival advantage in colonizing patients on antibiotic treatment. Some of these colonized patients will be sufficiently debilitated to go on to serious infections caused by the *Klebsiella*. Many outbreaks of nosocomial *Klebsiella* infection have been reported due to strains resistant to multiple antibiotics (61, 62).

There is virtually no evidence that some strains of *Klebsiella* are more pathogenic than others. The ability to cause numerous infections is linked instead to their survival advantage when resistant to antibiotics.

Hospital-acquired *Klebsiella* infections are of many kinds. Urinary infections are very common. Pneumonia is common but rather less frequent than urinary infections; it has a high mortality rate. Meningitis, osteomyelitis and numerous soft tissue infections also occur. Many of the more serious of these infections progress to bacteremia and sometimes to endotoxic shock.

There is no evidence that the *Klebsiella* causing infections in hospital patients have higher pathogenicity than other *Klebsiella*. It is the particular hosts of the infections that have low resistance. The various capsular types of *Klebsiella* have very similar capacity to act as opportunistic pathogens in debilitated hospital patients (12, 18).

There is little doubt that if *Klebsiella* organisms did not exist, exactly the same sort of infections would arise in these debilitated hospital patients due to other gram-negative bacteria such as *Pseudomonas, Serratia, Enterobacter, Citrobacter*, and *Staphylococcus epidermidis.*

COMMUNITY *KLEBSIELLA* AND HOSPITAL INFECTIONS

There is no real information on whether the presence of particularly large numbers of *Klebsiella* in natural waters would make it likelier that *Klebsiella* would become more prevalent as a cause of nosocomial infections in hospitals in the same area. I believe that this would be unlikely. The ubiquity of *Klebsiella* in all environments makes its entry into hospitals on vegetables and other food an almost constant occurrence (32, 63). In addition, 1 in 3 healthy people have *Klebsiella* as part of their normal bowel flora (18) and this will always provide a constant entry for the organism into hospitals. I believe that the presence of *Klebsiella* in large numbers in lakes and streams would therefore not greatly influence the entry of *Klebsiella* into the hospital environment. Even if it did, I am sure that it would not influence the number or severity of hospital infections due to aerobic

gram-negative bacilli because patients liable to infection would still be infected by other similar organisms.

SUMMARY AND CONCLUSIONS

1. *Klebsiella* strains possess low pathogenicity and succeed in causing serious human infections when the human host resistance is impaired.

2. Primary *Klebsiella* pneumonia in the community is now a rare disease and when it does occur the patients are men debilitated by chronic alcoholism.

3. The *Klebsiella* infections that are caused in previously healthy people in the community, such as urinary tract infections and cholecystitis, are a result of *Klebsiella* being carried by some people as part of the normal bowel flora; and. *Klebsiella* appears to possess less capacity to cause these infections than other members of the human large bowel flora.

4. The presence of *Klebsiella* in recreational waters does not appear to produce human disease.

5. *Klebsiella* strains do not cause serious infections in hospitalized patients as a consequence of the already debilitated state of these patients and the widespread treatment of hospital patients with antibiotics.

6. The community environment and the hospital environment are quite distinct as settings for infections by *Klebsiella* and clinical and epidemiological data from the one cannot be transposed to the other.

7. Concerns expressed in the scientific literature that environmental strains of *Klebsiella* are likely to pose a hazard to human health, seem largely to be based on the failure of the authors to appreciate that hospital findings do not apply to the community setting.

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