

Common Questions About Burkholderia cepacia

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This article attempts to answer some of the commonly asked questions about Burkholderia cepacia. It is based on a previous article written by Dr Burns for HomeLine, the magazine produced by Cystic Fibrosis Services, Inc. in association with the United States Cystic Fibrosis Foundation. This enlarged multiauthored revision takes account of further advances in B. cepacia research and includes additional questions raised by CF individuals in Canada and the United Kingdom.

Q What is *Burkholderia cepacia* and where is it found?

A *B. cepacia* is a bacterium whose natural habitats are river sediments and the moist areas of soil around the roots of plants. Prior to its emergence in the CF community, *B. cepacia* was best known as the cause of a type of soft rot in alliums, plants which include garlic and onions. *B. cepacia* is one of the most adaptable of all bacteria and has an uncanny ability to survive in hostile environments, including disinfectants. Soil contains many natural antibiotics to which *B. cepacia* has become resistant to the extent that it can even use penicillin as a nutrient. *B. cepacia* rarely causes infection in healthy people but infections can occur in immunocompromised patients who do not have CF. Contaminated antiseptics may lead to “pseudo-epidemics” in which the cleansed skin is contaminated with *B. cepacia* which then contaminates the blood culture. The patient is not actually infected, but appears to be since the blood culture is positive with a worrisome type of bacterial pathogen.

Q Why is *B. cepacia* a problem in CF?

A *B. cepacia* was first described in patients with CF in the late 1970s; infection was more common in older patients and appeared to be linked to hospitalisation. During the 1980s, it was noted that the incidence of *B. cepacia* varied from centre to centre suggesting a number of possibilities: first, the organism was not being identified accurately, second, epidemic spread was occurring between patients, third, patients were acquiring the organism from contaminated environmental sources. It also became clear that some individuals with CF have more severe lung disease after they have become infected with *B. cepacia* than they would otherwise. An additional problem is that the organism’s natural resistance to most of the antibiotics used for CF infections makes it difficult to treat *B. cepacia* infections and slow down the lung deterioration. At the present time, in most CF centres in Europe and North America, only a relatively small proportion of individuals with CF are colonised by *B. cepacia*. For example, in the United States data collected by the Cystic Fibrosis Foundation's National Patient Registry shows that in 1995, an overall total of 3.5 percent of all CF patients were infected. However, this percentage shows considerable regional variation and in some regions may reach much higher levels. Individuals can check with their local CF physician to find out how common *B. cepacia* is in their CF care centre.

Q Why does the incidence of *B. cepacia* differ from region to region?

A By the early 1990s, laboratory culture of *B. cepacia* had improved and research had provided bacterial ‘fingerprinting’ techniques to identify individual strains of *B. cepacia*. Detailed epidemiological studies then confirmed that *B. cepacia* could spread from patient-to-patient, or to a lesser extent be acquired from contaminated equipment. Furthermore, it appeared that some strains of *B. cepacia* are more easily transmitted than others. Spread of these highly transmissible epidemic strains explains the high incidence of *B. cepacia* acquisition in some centres. However, it also seems likely that the changing social structure of the CF community during the 1980s, in particular an increase in social contacts between CF adults contributed to the spread of epidemic strains at both a national and intercontinental level.

Q If I become colonised with *B. cepacia*, what impact will it have on me? Why is it more dangerous than *Pseudomonas aeruginosa*?

A Three different clinical outcomes can occur once someone with CF is infected with *B. cepacia*. In about one-third of individuals, there is no impact upon the disease or its progression. In another third, the rate of deterioration of pulmonary function appears to accelerate slightly. In a third group, there is a very abrupt deterioration with severe disease and even death occurring within several months of acquisition; this type of unexpected deterioration which sometimes involves spread of *B. cepacia* into the patient’s bloodstream has been called ‘cepacia syndrome’. At present, we cannot predict which colonised patients are more susceptible to ‘cepacia syndrome’. For example in epidemic outbreaks in which several people are colonised by the same strain, the clinical outcome in individual patients can vary from asymptomatic colonisation for many years to rapid fatal deterioration within a few months. Recent research, however, suggests that it may be possible to identify the most virulent and transmissible types of *B. cepacia* and specifically protect patients against these organisms. The exact mechanisms to explain why *B. cepacia* is more dangerous than *P. aeruginosa* are unclear. It seems, however, that *B. cepacia* not only resists CF lung defences but can ‘prime’ the lung to a damaging form of inflammatory response towards other bacterial or viral infections, or even possibly to invasive diagnostic techniques, including bronchoscopy. In conclusion, the variable clinical outcome of *B. cepacia* colonisation is very different and much more of a dice game than what we see with *P. aeruginosa*.

Q Why was the name changed from *Pseudomonas cepacia* to *Burkholderia cepacia*?

A The names of bacteria are not changed without good reason. When necessary, changes are enforced by specialists, called taxonomists, who attempt to classify bacteria into families according to shared properties or "relatedness". Bacterial names are usually derived from Latin or Greek and their meaning may not be obvious. The family name or genus is used first and is followed by a species name; both names may indicate some special property or identifying feature of the organism. Within a species, further differentiation can be achieved by ‘bacterial fingerprinting’ to identify individual strains within the species. Strains share the major properties that identify a species but differ in secondary properties such as antibiotic sensitivity, transmissibility and virulence. The human equivalent would be individual members of the same family belonging to the same sex but having different eye colour. The genus name

Pseudomonas means false unit or germ and can be traced back more than 100 years to the early days of microbiology. The species name *aeruginosa* describes the blue-green bacterial pigment seen in laboratory cultures of *P. aeruginosa*.

Until recently, in addition to *P. aeruginosa*, the genus *Pseudomonas* contained over 200 other species. Many of these 'pseudomonads' were plant pathogens including *P. cepacia*, *P. tomato* and *P. gladioli*. Later it became obvious that this group of bacteria had become a microbiological rubbish tip containing a range of very diverse bacteria.

By the 1990s, taxonomists had shown that *B. cepacia* is sufficiently different from *P. aeruginosa* to merit renaming as the type species of the new genus *Burkholderia*. *Burkholderia* derives from the American microbiologist, William Burkholder, who described the organism in 1950 as the cause of onion rot (the Latin name for onion is *cepa*). Recently, Dr Peter Vandamme in Belgium has used state-of-the-art techniques to show that organisms presently identified as *B. cepacia* can be divided into further groups or subpopulations. The scientific term for these subpopulations is genomovars and we shall return to the importance of genomovars in CF infections in the final question of the article. Strains within *B. cepacia* genomovars are related but may be more or less resistant to antibiotics or have other traits that might effect how well they spread from patient to patient or whether they cause severe infections.

Q Since it is found in the soil, can I get infected with *B. cepacia* from the environment?

A Until recently, techniques to compare strains of *B. cepacia* cultured from the environment with human isolates were not very sophisticated. However, we are gaining expertise in identifying the bacterial properties that seem to be associated with epidemic spread and the risk of severe pulmonary infection. It now appears that the strains found in individuals with CF often have characteristics that are absent in environmental strains. However, the fact that CF individuals can become sporadically colonised by unique strains of *B. cepacia* even in clinics where the organism has previously been absent, or where strict infection control measures are exercised, suggests that acquisition of *B. cepacia* from the environment is possible. It should be emphasised, however, that although *B. cepacia* can be found in some natural environments it does not usually inhabit home environments such as sinks and drains; it is also far less common in the environment than *P. aeruginosa*.

Q How long does *B. cepacia* survive in water or on food?

A *B. cepacia* is a very hardy organism and can live for a very long time if kept in moist environments; for example, it can survive for several weeks on sputum-contaminated surfaces and for years in water. Heating and drying are two of the best ways to eradicate this organism. Despite the fact that researchers currently think that the possibility of any *B. cepacia* residue on fresh vegetables and fruit is minuscule, it is always a good idea to wash and dry any fresh fruits or vegetables that you are not going to peel or cook before you eat. 'Healthy' onions carry little risk of *B. cepacia*. The type of onion rot caused by *B. cepacia* requires growth of large numbers of bacteria on a previously damaged, 'severely compromised' onion. If you came into contact with a *B. cepacia*-infected onion you would not want to handle it never mind eat it!

Q Why are people with CF more susceptible?

A It is not totally clear why people with CF get colonised and sick with *B. cepacia*, while healthy people have little problem with this organism. As we mentioned earlier, *B. cepacia* is very resistant to antibiotics which are used to treat people with CF, enabling it to survive while other bacteria are killed by the same antibiotics. However, antibiotic resistance including resistance to the widely-used colistin, does not explain the emergence of *B. cepacia*. Potentially important bacterial traits that may make this organism more dangerous to individuals with CF, including the interaction of *B. cepacia* with CF lung defences, are currently under investigation

Q Will having cepacia affect my chance to have a transplant?

A At present, the answer to this important question is dependent upon which transplant centre is involved. Attitudes towards transplanting *B. cepacia*-positive individuals vary from centre to centre both in Europe and North America. On the positive side, transplantation may remove an important reservoir of *B. cepacia*, namely the infected lung. However, for a period of time, transplantation also carries with it increased susceptibility to infection whether the individual concerned has CF or not. Some transplant teams are reluctant to expose patients to the increased risk of a multiresistant organism like *B. cepacia* spreading to other sites, in particular the bloodstream. The International *B. cepacia* Working Group, which includes transplant specialists, is very aware of this problem and is attempting to coordinate discussions and scientific data to see if advances in cepacia research might help to clarify the situation and achieve some form of consensus.

Q How is *B. cepacia* transmitted?

A There is now definite evidence that *B. cepacia* can spread from one CF person to another. However, the exact ways by which *B. cepacia* is transmitted from person-to-person, or is acquired from a contaminated environment, are unclear. *B. cepacia* can be difficult to grow and identify in the laboratory. In addition, human experiments to determine risk factors for the spread of these bacteria raise serious ethical questions. Epidemiological investigations of patient contacts within and outside hospital in association with progress in bacterial fingerprinting to identify the relationship between isolates has provided compelling evidence that *B. cepacia* can be transmitted from one CF individual to another. To date, there is no evidence that CF-carers (including home health visitors), or non-CF companions of CF patients, become colonised and act as carriers or indirect sources of infection; cross-infection of a highly transmissible strain of *B. cepacia* from CF siblings to their non-CF mother has been reported but this type of transmission is very rare. Occasionally, nebulisers can be contaminated if not thoroughly cleaned and dried but the available evidence suggest that these and other types of health care equipment are not major factors in transmission. *B. cepacia* does not colonise the intestinal tract thus it cannot be caught by sharing toilet facilities with someone with cepacia. While, we still do not know exactly how *B. cepacia* spreads from one patient to another, we do know that certain types of contact increase the chance of cross-infection. The degrees of risk associated with certain situations are outlined in the guidelines published by some national CF organisations. It is unlikely, however, that we will ever be able to provide foolproof answers to a list of “Can I do this, Can I do that” situations. What is certain is that the

respiratory secretions of colonised individuals contain very large numbers of *B. cepacia* and that exchange of these secretions carries the greatest risk of transmission.

Q How can people with CF reduce their risk of transmission?

A Close contact between CF individuals one of whom is colonised with *B. cepacia* always involves a risk of *B. cepacia* transmission. As stated previously, it is most likely that *B. cepacia* is spread during direct contact with the respiratory secretions of a colonised individual. Individuals with CF should be told if they have acquired *B. cepacia* and be advised about how these bacteria are thought to be transmitted. Although cross-infection does not seem to occur so readily with *P. aeruginosa* and other CF pathogens, all individuals with CF should exercise good personal hygiene. General guidelines which apply particularly to reducing the risk of *B. cepacia* transmission include:

- ❑ It is very important for people colonised with *B. cepacia* to handle their respiratory secretions, especially their sputum, very carefully. Tissues should be disposed of immediately after use.
- ❑ Wash and dry hands frequently, especially after coughing and before having contact with other CF individuals.
- ❑ Individuals who are colonised with *B. cepacia* should not share eating or drinking utensils or personal items like toothbrushes with other CF individuals. Kissing and other intimate contacts with other CF persons should also be avoided.
- ❑ Use the appropriate care programme for PEP masks and aerosol equipment. Wash and dry nebulisers to minimise bacterial contamination.
- ❑ Patients colonised with *B. cepacia* should not share hospital rooms, physiotherapy and exercise programmes, showers or nebulisation equipment with patients who are not colonised.
- ❑ Individuals with CF should not attend summer camps with other CF persons. *B. cepacia* cross-infection at camps is well documented and the cepacia-free status of other CF individuals cannot be guaranteed.
- ❑ Lengthy meetings in small or poorly ventilated rooms, weekend visits and lengthy shared car rides may entail an elevated risk of cross-infection. Activities involving casual contact, especially in large rooms at national meetings or outdoors, are thought to carry a much lower risk subject to the considerations outlined previously. Some individuals may have *B. cepacia* without knowing it. Persons with CF who plan to attend meetings should be advised that individuals with *B. cepacia* may be present and should arrive at their own decision as to whether or not to attend.
- ❑ It is not certain that *B. cepacia* can be spread by coughing. Nevertheless, it is advisable in a group setting to try and stay one arm's length (approximately three feet) from other people. Bacteria that can be spread by coughing can usually only travel about three feet.
- ❑ CF care centres have taken steps to prevent transmission of *B. cepacia* from one person to another by grouping patients in the hospital and in the clinic, and by special precautions with clinic rooms and respiratory therapy equipment. Very young children who may play with toys by chewing on them may be at some risk, if those toys have been contaminated by contact with secretions from other CF patients. If you have a small child with CF, you should discourage them from playing with any toys in the hospital waiting rooms or clinic rooms because you do not know who might have had previous

contact with them or when they were last decontaminated. Instead you should get in the habit of bringing some special toys from home that are just for clinic visits.

Q Why shouldn't a person with CF and *B. cepacia* participate in CF social group activities?

A With the exception of contact with the respiratory secretions of a colonised individual, the mechanisms of how *B. cepacia* is acquired are not clearly understood. This is particularly the case in situations where only a few individuals attending a CF centre are colonised by different strains and environmental bacteria seem to be involved. However, the evidence for transmission from one patient to another both in medical and social situations is overwhelming. Thus, until we know more about the transmission of the organism, it is strongly recommended that *B. cepacia*-colonised patients and those who are not colonised do not socialise with each other.

Q Should individuals with CF and *B. cepacia* be isolated in the hospital?

A Transmission of *B. cepacia* from one CF individual to another can occur in hospital. Transmission of *B. cepacia* to seriously ill non-CF individuals in hospital has also been documented. Airborne spread presents a small risk of *B. cepacia* cross-infection during close short-term contacts in the outpatient clinic or waiting room and further information on this situation is needed. In CF clinics where strict isolation policies have been put into place to prevent epidemic spread, the incidence of new infections with epidemic strains has diminished. Lapses in infection control have also been linked to new cases of colonisation, particularly with epidemic strains. For these reasons, although there are regional differences in isolation practice, isolation of *B. cepacia*-positive individuals is standard policy in many CF centres.

Q What should I do if my brother has cepacia and I haven't and we both have CF?

A This is a difficult situation. The best advice must be to avoid high risk situations as much possible; for example, sharing toothbrushes and drinks and avoiding activities that involve the exchange of respiratory secretions or contact with sputum. On a positive note, research shows that some strains of *B. cepacia* are more likely to be transmitted than others. Epidemic markers in strains can be identified in specialised laboratories; the problem, however, is that it is not possible to guarantee that other strains will not spread. Despite the close contacts that occur between CF siblings, transmission is not inevitable; the risk is highest when epidemic strains are involved. A very informative Italian study showed that although transmission can occur between CF schoolmates, it occurred in only three of eight pairs of CF siblings.

Q Can't conferences be arranged for cepacia-only patients.

A This is a very reasonable question. In fact, such a conference was organised in the UK several years ago. At the time, concern was raised about the prospect of individuals acquiring a second cepacia from someone else attending the conference! Multiple infections with different strains of *B. cepacia* occur naturally in some patients and raise the question of balancing the benefits of such a conference with the risks of further *B. cepacia* transmission during the frequent and close social contacts that occur during such occasions. It has now been confirmed that epidemic strains of *B. cepacia* can co-infect and then replace existing *B. cepacia* in some patients. Since epidemic strains are more likely to spread it would seem unwise to arrange cepacia-only conferences at present.

Q If cepacia has been cultured from my sputum on a single occasion will I always be colonised?

A In some CF individuals, *B. cepacia* is cultured from sputum on one or two occasions then appears to disappear. Microbiologists and clinicians call this ‘transient colonisation’. It occurs in less than 10% of individuals, and is rarely observed when epidemic strains are involved. A difficult issue facing the CF community is whether individuals who have exhibited transient colonisation remain infectious and thus should be subject to the same segregation as individuals exhibiting chronic infection. A similar dilemma exists with patients who are culture-negative but whose sputum shows some evidence of *B. cepacia* using very sensitive diagnostic techniques which can identify minute amounts of the bacterium’s DNA.

Q Are there any good treatments for *B. cepacia*? If not, why not?

A Soil contains many natural antibiotics produced by its fungal and bacterial inhabitants. Thus soil bacteria including *B. cepacia* have developed a natural resistance even to most of the powerful antibiotics that we use to treat infections in CF. This multiresistance makes treatment of *B. cepacia* a problem. However, there are a few antibiotics to which the organism sometimes remains susceptible, especially in combination with other antibiotics. A laboratory at Columbia University in New York City funded by the U.S. CF Foundation is currently serving as a referral laboratory for physicians to send isolates of resistant organisms to look at the activity of combinations of antibiotics in killing the bacteria. This laboratory can sometimes identify novel combinations of antibiotics which are effective. In addition, new antibiotics, including meropenem, that appear to be active against *B. cepacia* in the laboratory are currently being tested in patients to see if they are active in treating infection; meanwhile, other agents are at the laboratory-testing stage.

Q I heard that there are plans to use cepacia in agriculture to control seed rot. Is this true?

A This is true. The U.S. CF Foundation and other national CF organisations are aware of this development and discussions are taking place to investigate the potential risks to humans, and the CF community in particular. As a result of the CF Foundation’s intervention the application for agricultural usage has not been approved.

Q I am a health professional. Where can I get help or advice about cepacia?

A If cepacia has been a problem in your area then try your local CF clinic in the first instance. National CF organisations are also a source of advice and copies of guidelines to reduce the risk of *B. cepacia* cross-infection are available. Regional clinics or national organisations may also provide advice on cepacia issues not covered by guidelines or may direct you to a research laboratory for specialised advice.

Q What research is underway to outsmart *B. cepacia*?

A A great deal of research is underway to fill the gaps that exist in our knowledge about *B. cepacia*; only a brief summary can be provided here. National CF organisations in Europe and North America are funding research projects to help answer the many cepacia questions that remain. Studies of antibiotic resistance and evaluation of new antibiotic agents in the fight against *B. cepacia* are currently underway. In addition, studies of specific bacterial traits are being investigated in many laboratories, with the hope that the identification of factors that make the bacteria more dangerous will result in strategies to prevent or eliminate infection. Since individual diagnostic laboratories typically do not have the capacity to store *B. cepacia* isolates, the Canadian CF Foundation funds a national *B. cepacia* repository at the University of British Columbia, Vancouver. Recently, a cepacia research laboratory and repository for all *B. cepacia* recovered from patients attending U.S. CF centres has been set up by the U.S. Foundation and the Allegheny University of the Health Sciences in Philadelphia. With financial support from the pharmaceutical industry and national CF organisations, the International *B. cepacia* Working Group has been set up to exchange the latest research data, to devise research and clinical care strategies and to select from national collections the most important *B. cepacia* isolates to analyse the properties of virulent and highly transmissible strains. This specialised collection contains representatives of each of the new *B. cepacia* genomovars some of which seem to be closely associated with life-threatening decline. It is hoped that by these international collaborations that we will soon be able to outsmart this challenging organism.

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