

Breathless - understanding asthma

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An asthma inhaler in use. Credit: Wellcome Library, London.

More than 5 million people in the UK suffer from asthma, and we still don't know what causes it. Researchers have drawn up a long list of possible risk factors but findings are frequently contradictory. There is also as yet no clear and uniform definition of what asthma is or consensus how to diagnose it. Dr Bruna Galobardes is searching for some of the answers by looking at how patterns of the disease differ between social classes.

By all accounts, an [asthma](#) attack is a petrifying experience. You're drowning, choking, gasping for breath, blackness at the edge of vision. You're terrified of dying (understandably so - people do die of asthma). Thanks to your inhaler or other medicines, you survive, but often with the sense that you'll never be able to really trust yourself. Because you don't always know what triggers these attacks or how to avoid them. They can come out of nowhere.

What causes asthma in the first place - and precipitates those frightening attacks - is one of biology's many unanswered questions. The enigma persists despite considerable advances in understanding the biology of asthma and treating it.

Experience and research point at some likely culprits: tobacco smoke, pollution, stress, diet, alcohol, pets, cleaning products, and damp and mould in the house all seem to play a part. But we don't know how significant that part is for each factor, or which of these (or which other factors) actually originate the disease.

At the University of Bristol, Dr Bruna Galobardes has been awarded a Wellcome Trust Intermediate Clinical Fellowship to look at the problem from an epidemiological vantage point. She hopes that doing so will give her a better handle on the many inconsistencies that muddle the picture of the disease.

"There are so many unanswered questions in asthma," she says. "Boys tend to get it more in childhood; girls in adulthood. It can start in infancy and cease by adolescence, or continue into adulthood. Or it can first appear in adults. Why? We don't know yet. This is a very important question that remains unanswered."

Asthma can also materialize in epidemic form in disparate parts of the world then disappear again, often without any obvious explanation. A series of such epidemics struck Barcelona - and Dr Galobardes' imagination - at the end of the 1980s.

At the time, she had just completed medical school and was looking to move into research but had not made up her mind in which direction. "I read the articles that were published then about the asthma epidemic, and it was like an investigation, a detective story. What was causing these very serious attacks and deaths from asthma that were suddenly

occurring in Barcelona?"

Epidemiologists at the Institut Municipal d'Investigacio Medica (IMIM) eventually apprehended the offender: soya beans being unloaded in the harbour. An inland wind blowing particles towards the city was triggering the attacks in susceptible people.

Dr Galobardes was hooked. She joined the IMIM team for two years, working on the epidemiology of asthma, then headed to the USA to complete a Master's in public health at Johns Hopkins University. Now at the University of Bristol, she will be exploring the part social class plays in the origin, severity and duration of asthma.

Confusion

One of the challenges for researchers trying to get a clearer picture of the disease is the lack of a clear definition of what it actually is - other than a wide acceptance that it is a complex, heterogeneous disease. It used to be thought of as an allergic disease (but we now know not all asthma is allergic), and to cloud the picture further, many features of asthma overlap with chronic obstructive pulmonary disease.

The symptoms vary too. There may or may not be wheezing - and a 'wheeze' is extensively interpreted: it can be a whistle, squeak or gasping sound. Coughing, shortness of breath and a feeling of tightness in the chest may all be present too. Or not.

The lack of clarity and consensus is compounded by the different methods used to diagnose it. "We use questionnaires about wheezing and about doctors' diagnoses, and we have some tests on lung function. And they all are correlated, they all have a certain agreement with each other. But not fully," says Dr Galobardes. Assessment also depends on how early the patient (or parent) reports the disease, on the extent to which

they use health services, and on how easily or readily individual doctors apply the diagnosis.

All these different variations make interpreting trends in asthma - and identifying the agents responsible - very difficult.

Dr Galobardes hopes to dispel some of the fog by looking at patterns of asthma within large birth cohorts. These long-term studies of babies followed from birth into adulthood collect vast amounts of data on the health and lifestyle of each participant over the course of his or her lifetime.

She will be following up novel work already carried out at Bristol by Professor John Henderson, using the ALSPAC cohort (a study of around 14 000 British children born in the early 1990s, also known as 'Children of the 90s'). Now nearly 21 years old, the study provides detailed information about when the children in the cohort first wheezed and when they were diagnosed with asthma.

Professor Henderson and his colleagues fed this information into a new statistical method looking for trends and patterns in the disease. His aim was to try and separate the unwieldy agglomeration of symptoms lumped together under the term 'asthma' into several more precisely defined subsets of disease.

They identified six different subsets or 'phenotypes', based on when the disease first appeared and its remission or persistence over a life time. Dr Galobardes now wants to investigate how social class influences the development of these six phenotypes of asthma.

Rich man, poor man

She will be using different indicators to measure social class, such as

occupation, education, income and housing, and mapping these to the patterns (phenotypes) of disease she identifies in the cohorts she'll be studying. Since inequalities in disease occur between countries as well as social classes, she will be using birth cohorts from Spain, Denmark and Brazil in addition to the ALSPAC one.

"Asthma cases increased significantly in quite a few countries in the 1950s and 1960s. In England at one point the disease affected 20 per cent of the population and caused a number of deaths. It seems to have levelled off in England and in some other countries now. But we don't know why. And it still seems to increase in poor countries, and again, we don't know why. These trends in asthma are completely unexplained," she says.

It is, she adds, an approach to asthma that hasn't been taken before.

"There have been reports on inequalities in asthma and how it's not equally distributed in a society. Early reports actually say that it's more common in higher social classes, in more educated people. Whereas now we know it's more common in poor people, people with lower education. So why, what has driven this change?"

She speculates that this may be because people who are more educated and better off are more likely to report the disease to doctors, causing an initial spike in reported disease in the upper classes. Subsequently, because the wealthy have more resources with which to tackle the disease, or because its diagnosis becomes more widespread, the trend is reversed and it becomes more common in the lower social classes.

And this, she says, offers a very important clue. "There may be something that the wealthier classes are doing that helps them manage asthma better. We don't know what. Part of it is going to be the extent to which people use health services; and what those services were. Maybe the doctor did different things depending on the social class of the

person who consulted. But this is something that hasn't been explained yet. By looking at what generated this change, from higher social class to lower [social class](#) nowadays, I might be able to find the factors or exposures that generated inequality and therefore generated the disease."

By comparing the levels and severity of each of these six types of asthma in different social groups, she hopes to pinpoint specific factors explaining the inequalities in disease between these groups. "If we can find the factors that explain the inequalities, we can find the factors that explain the disease. And then we might have an idea of how to prevent it."

She says those factors may well turn out to be the main, traditional risk factors people have always associated with the disease - things like smoking, diet, breastfeeding and low birth weight. But at least we'll know which ones really do cause asthma. She's not trying to reinvent the wheel - just to focus the picture. "We might not need new things. If we know which of those traditional risk factors to target, we should be able to at least decrease the inequalities."

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