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Covid can infect cells in pancreas that make insulin, research shows

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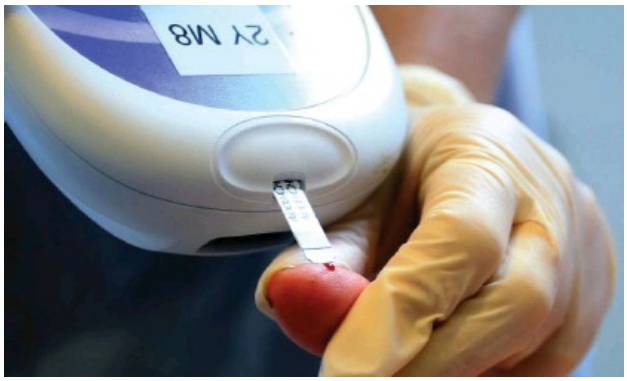
Covid-19 can infect insulin-producing cells in the pancreas and change their function, potentially explaining why some previously healthy people develop diabetes after catching the virus.



Doctors are increasingly concerned about the growing number of patients who have developed diabetes either while infected with coronavirus, or shortly after recovering from it.

Various theories have been put forward to explain this increase. One is that the virus infects pancreatic cells via the same ACE2 receptor found on the surface of lung cells, and interferes with their ability to produce insulin – a hormone that helps the body to regulate levels of glucose in the blood; alternatively, an over exuberant antibody response to the virus could accidentally damage pancreatic cells, or inflammation elsewhere in the body may be making tissues less responsive to insulin.

To investigate, Prof Shuibing Chen at Weill Cornell Medicine in New York screened various cells and organoids – lab-grown clusters of cells that mimic the function of organs – to identify which could be infected by Covid. The results suggested that lung, colon, heart, liver, and pancreatic organoids could all be infected, as could dopamine-producing brain cells.

Further experiments revealed that insulin-producing beta cells within the pancreas were also susceptible, and that once infected, these cells produced less insulin, as well as hormones usually manufactured by different pancreatic cells.

"We call it trans-differentiation," said Chen, who presented the results at the annual meeting of the European Association for the Study of Diabetes on Wednesday. "They are basically changing their cellular fate, so instead of being hardcore beta cells which secrete a lot of insulin, they start to mix different hormones. It could provide further insight into the pathological mechanisms of Covid-19."

Scientists have observed a similar phenomenon in some individuals with type 2 diabetes, although the disease is more strongly associated with the body's tissues becoming less responsive to insulin.

It is not yet clear whether the changes triggered by Covid infection are long lasting. "However, we know that some patients who had very unstable blood glucose levels when they were in the intensive care unit and recovered from Covid-19, some of them also recovered [glucose control], suggesting that not all patients will be permanent," Chen said.

Separate research by Prof Francesco Dotta at the University of Siena in Italy and colleagues confirmed that Covid attacks pancreatic cells by targeting the angiotensin-converting enzyme 2 (ACE2) protein on their surface, and that insulin-producing beta cells express particularly high levels of this protein.

They also demonstrated that ACE2 levels were increased under inflammatory conditions, which is important because people with existing type 2 diabetes may already have some inflammation within their pancreas. "This means that these insulin-producing beta cells could be even more susceptible to viral infection when inflamed," Dotta said.

This could imply that people with existing diabetes or prediabetes are at greater risk of pancreatic dysfunction if they catch Covid-19 – something he now plans to investigate. "Diabetic patients in general are not more susceptible to Covid-19 infection in terms of frequency, but once they are infected they develop more severe complications and severe metabolic derangement," said Dotta.

Prof Francesco Rubino, chair of metabolic surgery at King's College London, said: "These studies seem to be consistent in supporting a biological rationale for the idea that Covid-19 could increase the risk of developing diabetes in people who are either predisposed to it, or even potentially completely from scratch."

He is co-leading an international effort to establish a global database of Covid-19-linked diabetes cases, to better understand whether the infection can cause a new form of diabetes, or trigger a stress response that leads to type 1 or type 2 diabetes.

"Whether such changes are enough to permit this virus to cause diabetes is a question that these studies do not answer, but it gives us another reason to believe this is a possibility," he said.

However, this may not be the only way in which the virus increases diabetes risk. "At least clinically, one of the things we're seeing is that in some cases, patients who already had type 1 diabetes have started to express severe insulin resistance, which is a typical feature of type 2 diabetes," Rubino said. This may imply a problem with how cells elsewhere in the body are responding to insulin after Covid-19 infection.

Dr Lucy Chambers, head of research communications at Diabetes UK, said: "People with diabetes have been disproportionality affected by Covid-19, and many people with the condition have tragically died as a result. Diabetes is a well-established risk factor for serious illness from Covid-19, and there is emerging evidence that Covid-19 may be triggering new cases of diabetes, but how these two conditions are biologically linked is not yet well understood.

"This research deepens our understanding of how diabetes and Covid 19 may interact biologically. This will help in the development of new, effective ways to treat people at risk of – or living with – diabetes who have Covid-19. Taking the Covid-19 vaccination, including a booster when offered, remains the best form of protection from the virus."