

## Stomach pain should be seen as a warning sign of meningococcal meningitis

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Patients with meningococcal infections generally develop symptoms including a high temperature, vomiting and a stiff neck. But they might also just have a bad stomach ache. It can be so severe that they are sometimes wrongly diagnosed with appendicitis. Teams from the Institut Pasteur and the Department of Pediatrics at Bicêtre Hospital (AP-HP) decided to investigate the question. And the results speak for themselves: Ten percent of patients infected by the meningococcal strain currently on the rise in Europe suffer from abdominal pain. This atypical form of the disease is becoming increasingly common and needs to be understood by physicians. The findings are published in *Clinical Infectious Diseases*.

Within the first 24 hours of meningococcal infection, which can give rise to meningitis, septicemia, arthritis and peritonitis, patients generally suffer from headaches, vomiting and a stiff neck. Over the past few years, however, abdominal pain has been observed as another early clinical sign—but physicians tend not to think of invasive meningococcal disease. "When doctors see patients suffering from stomach pain, invasive meningococcal disease doesn't immediately spring to mind. They tend to think of gastroenteritis or possibly appendicitis," says Muhamed-Kheir Taha, lead author of the study and head of the National Reference Center for Meningococci (CNRM) at the Institut Pasteur. "But delays in diagnosis and appropriate treatment for those affected can be deadly. Invasive meningococcal disease is fatal in virtually all cases if antibiotics are not administered rapidly."



The team led by Muhamed-Kheir Taha, in collaboration with a team from the Department of Pediatrics at Bicêtre Hospital (AP-HP), decided to take a closer look at these abdominal forms to assess their frequency and raise awareness among physicians of this new face of the disease.

The CNRM has received all the bacterial strains responsible for meningococcal infections in France since the 1980s. So the scientists were able to analyze some 12,000 meningococcal strains kept at the CNRM between 1991 and 2016 and examine the clinical presentations of the patients infected. They isolated 105 cases associated with abdominal pain, gastroenteritis or diarrhea. "That number represents just 1 percent of patients, which is not very many, even if the real figure is probably higher since it is hard to know whether babies are suffering from stomach pains," says Muhamed-Kheir Taha. "But if we focus on the past two or three years and the group W bacterial strain, which arrived in Europe in 2013-2014 and has grown rapidly ever since, the figure rises to 10 percent of cases." In other words, the emergence of these new W isolates changed clinical presentations, and people with meningococcal infection are now more likely to suffer from abdominal pain. So it is urgently necessary to consider this symptom in medical diagnosis. Abdominal pain, together with other signs such as leg pain, headaches and poor blood supply to the nails, should raise alarm bells for meningococcal meningitis.

To investigate their findings further, the team sequenced all the genomes of the bacteria in their collection to identify what sets them apart from other <u>strains</u> and what might explain the resulting abdominal pain. Here again, the scientists' findings were relatively clear. The group W bacterial strain that is currently spreading across Europe and the world has around 100 specific genes, some of which are involved in the inflammatory response. "We should remember that the bacteria infect the vessels which supply blood to the abdomen and the digestive system," says Muhamed-Kheir Taha. "If these bacteria are likely to



induce a stronger inflammatory response in tissues, that could explain the abdominal pain." The scientists will continue their research by looking more closely at these genes to try to understand the mechanism of action of this strain, paving the way for more rapid diagnosis of a disease which still claims some 135,000 lives worldwide every year.

**More information:** Tamazoust Guiddir et al. Unusual initial abdominal presentations of invasive meningococcal disease, *Clinical Infectious Diseases* (2018). DOI: 10.1093/cid/ciy257

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