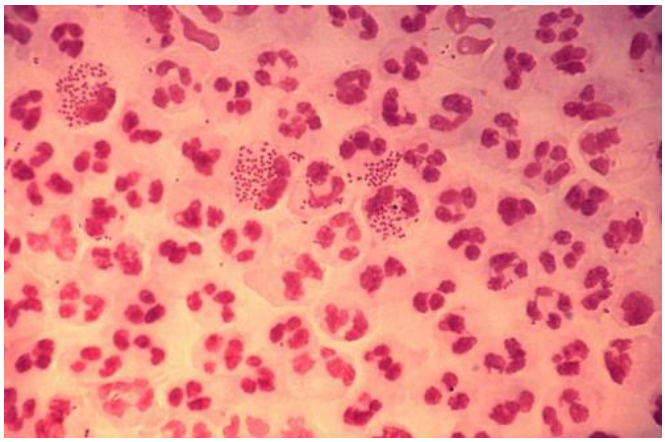
Study identifies existing drugs that could be repurposed to treat gonorrhea

1 July 2021



Credit: CDC

New research being presented at this year's European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) being held online (9-12 July) identifies drugs that could potentially be repurposed for the treatment of gonorrhoea (*Neisseria gonorrhoeae* [Ng]): a sexually transmitted infection which is becoming increasingly resistant to existing antibiotics.

The decreased susceptibility of the Ng bacterium to extended spectrum cephalosporin antibiotics has become an important public health issue as cases of this common infection become more difficult to treat.

The study by Dr. Liliana Rodrigues and colleagues at Global Health and Tropical Medicine (GHTM), Institute of Hygiene and Tropical Medicine (IHMT), Universidade Nova de Lisboa, Lisbon, Portugal, used computer analysis of candidate drugs to predict whether they would interact with proteins in the Ng bacterium involved in energy metabolism and the removal of toxic substances.

One potential method for increasing the effectiveness of antimicrobial drugs is to target certain protein-based structures called efflux pumps which are embedded in the cellular membrane and act to remove toxic compounds which could damage the function or structure of that cell. These pumps play an important role in bacterial survival by removing antimicrobial compounds that have entered the cell, thus making treatments for infection less effective. Drugs which target the specific proteins in efflux pumps could be used to deactivate them, and when used in combination with current antimicrobials could improve or restore the activity of these medications by increasing their concentration within the bacterial cells.

Development of any brand-new drug is a long and expensive process, and a more cost-effective strategy is to study existing compounds which are known to be safe and have been approved for clinical use for other diseases, to find those which act as efflux inhibitors and could potentially be repurposed for this role.

The team's analysis predicted the existence of 100 Ng drug targets which were associated with 680 existing approved drugs. Further detailed examination of these results narrowed this down to 30 potential targets and 57 drug candidates. These included dequalinium (an antiseptic), doxorubicin (a cancer chemotherapy drug), metformin (used for diabetes), and thiabendazole (used to treat worm infections). These already-approved medications target a multidrug efflux protein, and the enzymes NADH-dehydrogenase, flavoprotein-ubiquinone oxidoreductase, and succinate dehydrogenase, respectively.

The authors conclude: "The identified drugs are approved for a variety of indications, such as epilepsy, hypertension, diabetes and cancer and may serve as lead compounds for the development of new drugs against gonorrhoea. This work could help establish a new paradigm for the design of new drugs and therapeutic strategies to be used in

the treatment of gonorrhoea infections."

Provided by European Society of Clinical Microbiology and Infectious Diseases