In search of an elusive key –
Unlocking the secrets of gonorrhea

Until recently, the condition was referred to as a "social disease", a euphemism that cushioned the sensitivities against the reality of the infection's origin. Gonorrhea, a sexually communicated disease, is caused by a delicate, kidney-shaped bacteria, *Neisseria gonorrhoeae,* more commonly known as the gonococcus. It is a surface invader in its primary stages, infecting the mucous membranes of the urethra in men and the vagina and cervix in women. From these initial sites it spreads into other organs of the body.

The disease has now reached epidemic proportions in spite of the effectiveness of such antibiotics as penicillin and the problem appears to be growing worse every year. In Canada, as in many other countries, it has exceeded the high levels of the war years of the 1940's and now ranks as one of the most common communicable diseases in the world. During 1973, the reported number of cases in Canada totalled 45,266, up from 41,467 cases in 1972, and a median value of 31,552 cases over the years 1968-1972. These figures can be compared with a total of 823,380 cases reported in the United States in 1973 alone.

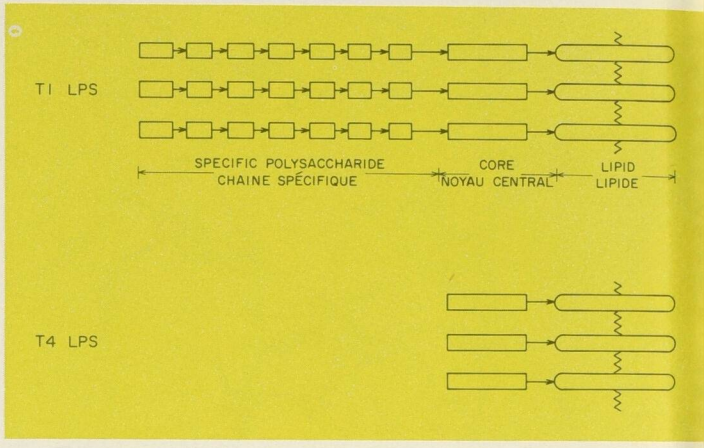
What is peculiar about gonorrhea is that it should be totally eradicable, at least theoretically. Only humans can carry the disease, there being no intermediary vector, such as the mosquito in malaria, and it can be quite effectively cured by treatment with various antibiotics. The persistence of gonorrhea would appear to be more of a social problem then, but certain advances in medical science could be of great assistance in the battle against the disease.

One problem involved in the control of the disease is the lack of a reliable diagnostic procedure. The presence of gonorrhea is usually determined by examining, under the microscope, smears taken from patients, or by culturing the bacteria for further examination and identification. These methods not only give false positives at times but often fail to detect the disease when it is present. In so-called "asymptomatic" people, recognizable symptoms of the disease fail to appear, and anywhere from 20 to 30 percent of the infected population may fall into this category. Because these diagnostic techniques usually involve a waiting period of two or three days, many patients do not reappear at the clinic, either through embarrassment or a mistaken idea that the disease, which can cause sterility, is no more serious than the common cold.

Another problem lies in the inability of the body's natural defences to cope with the gonococcus. The human immune system responds rather poorly to challenge by the organism, and treatment with antibiotics is normally a necessity. Very few people establish a long-term immunological resistance to the disease.

Some fifty years ago it was recognized that freshly isolated gonococcus grow in healthy or "typical" colonies at first, with the bug retaining its infectivity and virulence for humans. But as time elapsed the appearance of the colonies changed with a concomitant loss of infective power. In 1964, Douglas Kellogg of the Centre for Disease Control in Atlanta, Georgia, showed that four types of gonococcus colonies could be defined morphologically, type I (TI), or healthy bugs, and moving in a direction of increasing degeneration through types 2, 3 and 4 (T2,T3,T4). Only cells in the T1 and T2 condition were virulent, while T3 and T4 cells had lost their virulence.

As a subject of basic research, *N. gonorrhoeae* has not received much attention in the past, with only two or three laboratories in Canada concerned with fundamental investigations of the disease (the outlay of money and facilities has been much greater in the United States).



An illustration of the molecular structures of the T1 and T4 lipopolysaccharides. The polysaccharide portion, an important antigenic determinant, is missing entirely in the T4 molecule. As healthy laboratory cultures of gonococcus degenerate with time, the T1 molecule found on the organism's outer membrane loses its polysaccharide moiety, resulting in the T4 or incomplete form. • Illustration des structures moléculaires des lipopolysaccharides T1 et T4. La molécule T4 est totalement dépourvue de l'important facteur antigénique qu'est le lipopolysaccharide. Étant donné qu'il y a dégénération dans le temps des cultures saines de gonocoques obtenues en laboratoire, la molécule T1 se trouvant sur la paroi extérieure de la membrane du micro-organisme perd sa partie constituée de polysaccharide ce qui aboutit au type T4, c'est-à-dire à la forme incomplète.

One of the main obstacles to gonorrhea research has been the difficulty in culturing the organism outside the human body while maintaining full potency and virulence. The gonococcus appears to be a somewhat fastidious bug, with fairly stringent growth requirements. Another problem has been the lack of a suitable animal model, or host, that is infected by the disease organism in a manner that simulates human infection. These models are vital from the experimental point of view in disease research, and to date researchers have had to rely on human volunteers. There remains, however, a pressing need for a rapid, reliable diagnostic method and an effective vaccine to check the disease at the challenge stage. Recent research in the Division of Biological Sciences of the National Research Council of Canada aims at providing the background chemistry to meet both of these requirements.

Dr. Malcolm Perry, of the Division's Immunochemistry Section, has been investigating the substances that make up the outer surface of the gonococcal cell wall and has discovered an important difference between the virulent and the non-virulent or inactive forms of the organisms. Working in collaboration with Drs. B.B. Diena and Fraser Ashton of Health and Welfare Canada's Laboratory Centre for Disease Control, Dr. Perry is exploiting this knowledge in the development of specific diagnostic methods and the possible production of an effective vaccine against the disease.

"We decided on the following approach to the problem," says Dr. Perry. "We would take the infective form of gonococcus (T1) and the non-infective form (T4) and examine them with a view to determining their differences. If these differences