Science commentary

Science commentary: HLA typing

Human leucocyte antigens (HLAs) are cell surface molecules found on all nucleated cells. Each individual has a unique set of these antigens, half inherited from each parent, and their typing becomes important before organ transplantation. Typing is also used to identify markers for specific diseases, such as HLA B27, which is known to be closely associated with conditions such as ankylosing spondylitis.

Two main classes of HLA antigens are recognised: HLA class I and HLA class II. HLA class I antigens (A, B, and C in humans) render each cell recognisable as "self," whereas HLA class II antigens (DR, DP, and DQ in humans) stimulate the immune system.[1] Both have been implicated in the rejection of transplanted organs.

Three main processes are used to perform HLA typing. The first is the more conventional serological cytotoxicity method where tiny samples of lymphocytes (taken from from blood or spleen) are added to Terasaki plates. These plates hold individual wells that contain different specific antibodies (from either maternal sera or manufactured monoclonal antibodies). The best cells for class II typing are B lymphocytes, and class I typing can be performed with the remaining leucocytes. Magnetic beads are used to purify the required cells from blood or spleen.

If the HLA antigen and specific antibody bind, and complement is added, the cells in that well will be killed. The pattern of wells showing this cell death allows the deduction of which combination of HLA antigens were present on the original tissue cells.

Another potential method used for HLA typing is flow cytometry, particularly when looking for specific alleles. Here fresh nucleated leucocytes are added to monoclonal antibodies that are labelled with a molecule that fluoresces. Cells with surface antigens that bind to the antibody become fluorescent. The flow cytometer detects the fluorescent cells by detecting the light emitted from them as they pass through a laser beam. Flow cytometry takes about 30 minutes to complete—the time taken to prepare the cells and then run the machine.

A third process is gaining favour where very detailed typing is required—for example, for precise matching in bone marrow transplantation. This process involves extracting the DNA from cells and amplifying the genes that encode for the HLA peptides using polymerase chain reaction techniques. The genes may be matched with known HLA nucleotide sequences found stored in several gene bank databases, including the IMGT/HLA database.

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1 Immune mechanisms in health and disease. In: *Oxford textbook of medicine*, 3rd edn. Oxford: Oxford University press, 1996:139-89.

Progress

After many years at sea as a cruise ship doctor, I am often asked: "How do you keep up to date?" Practising medicine in isolation from other doctors, we may be regarded by our peers as out of touch.

Not at all. We see a frequently changing population of well over 1000 passengers, mainly elderly and most taking at least one prescription medication. So we are in a unique position to observe the medicine currently practised ashore, and this gives us a good insight into "progress." Our therapeutic armamentarium is limited to the more tried and tested generic drugs of proven efficacy.

I doubt that any two people on board are taking exactly the same medication, although I am sure that many medical conditions are similar. It is not uncommon to find patients, especially from the United States, taking a dozen or more different drugs prescribed by different specialists, often without reference to what others have already prescribed. Despite this the patients thrive.

Generic prescribing is sadly becoming increasingly rare and I am sure that, for instance, a lot of normotension is expensively treated with state of the art branded products as a result of peer or patient pressure. Zithromax "Z-Pak" (azithromycin) has replaced Biaxin (clarithromycin), and before that Cipro (ciprofloxacin) as the fashionable antibiotic that American travellers carry to self-medicate for various conditions. And still we see just about every antiemetic apart from our preferred drug of choice (promethazine) prescribed to prevent motion sickness. When scopolamine patches were popular (indeed, for a time, de rigueur) we treated far more passengers for the many and varied side effects of this drug—which is ineffective for seasickness anyway—than we ever saw suffering from motion sickness, which is rare nowadays given the size and stability of modern passenger ships.

What progress have I observed? In nearly a quarter of a century at sea there are only four great therapeutic advances that spring to my mind. Firstly, the advent of cimetidine has greatly reduced the frequency of gastrointestinal haemorrhage, that worst of maritime medical disasters on account of the difficulties involved in blood transfusion at sea. Then, aciclovir, in its various forms, makes treatment of genital herpes, chickenpox, and shingles possible. Streptokinase is of proven value and in our unique situation we are able to administer it within minutes. Lastly, and in my view most importantly, is the use of intramuscular non-steroidal anti-inflammatory drugs to rapidly alleviate the fever and associated symptoms of acute viral illnesses.

With the global increase of seasonal pyrexial flu-like viral illnesses and viral gastroenteritis, we occasionally have outbreaks on board and we see a lot of acutely ill, febrile, elderly people. I learned of the use of non-steroidals anecdotally from a colleague several years ago and I never cease to wonder at their efficacy. As far as I am aware this usage is not documented and no trials have been performed. I am convinced that a lot of seasonal suffering and morbidity could be alleviated if this treatment were trialled and promulgated. When I describe this apparently miraculous treatment to colleagues ashore they look at me as if I have come from the moon, not the ocean deep. Progress?

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