How has pathology changed in the last sixty years?

By Saumya Singh

Introduction

From diagnosis, to monitoring of treatment effect and screening for unsuspected disease - Pathology is an integral part of healthcare. As the Royal College of Pathologists celebrates its sixtieth anniversary this year, we will consider some of the ways in which pathology has changed over the last sixty years.

Increase in demand, automation, and digitalisation

Nearly 800 million pathology tests are performed annually in the UK, which equates to fourteen tests per person in England and Wales.[1] Demand on pathology services has risen and is predicted to continue rising due to an ageing population, higher rates of chronic disease, and, as our understanding of disease advances, an increase in predictive and preventative investigations.[1] Laboratory medicine has become increasingly automated and digitalised to cope with this demand and to improve efficiency.

Faster diagnostic technology and growing threats

Faster and more efficient diagnostic methods have also developed. This is especially true in Medical Microbiology. Some bacteria are technically challenging to culture and take a long time to isolate. Commensals and contaminating bacteria can be difficult to distinguish from pathogens with culture and microscopy alone. However, newer techniques like mass spectrometry enable faster and more specific identification of microbes.[2] Advances in genetic sequencing and the development of ucleic acid amplification tests (NAATs) such as the polymerase chain reaction mean that microbial identification is possible from small fragments of microbial genetic material, enabling faster and earlier detection of some infections. NAATs are routinely used in diagnosing chlamydia, gonorrhoea[3] and SARS-CoV-2.[4] In the case of Mycobacterium tuberculosis, NAATs can not only detect the bacteria but can also determine drug susceptibility.[5] With the WHO declaring antimicrobial resistance as one of the top ten global public health threats facing humanity, drug susceptibility testing and antimicrobial stewardship has become progressively more important and topical.[6]

Safer and easier blood transfusion

Microbes we did not understand sixty years ago such as hepatitis B and HIV are now better understood and consequently screening methods, antiviral treatments and in the case of hepatitis B, vaccination are now available. An understanding of the routes of Hepatitis and HIV transmission revolutionised blood transfusion medicine with the introduction of routine donor blood screening for Hepatitis B in 1972, HIV in 1985 and Hepatitis C virus in 1992 to prevent transfusion related infections.[7]

Blood transfusion medicine was also revolutionised by the humble plastic bag. Until 1975, blood was collected and stored in bulky, fragile glass bottles. The introduction of disposable plastic bags facilitated easier storage and transport of blood and reduced bacterial contamination.[8]

Expansion of screening and development of Personalised Medicine

Pathology is increasingly involved in the diagnosis of disease before it is even suspected through screening programs. More conditions have become amenable to screening due to advances in our understanding of disease pathophysiology and in laboratory methods of detection.[9] For example, the

newborn blood spot test today screens for nine serious but treatable conditions including phenylketonuria.[10] When the blood spot was first invented by Robert Guthrie in 1962, it served only as a phenylketonuria screen to replace the messy and less reliable Phenistix nappy test which involved pressing a ferric chloride containing paper strip onto a wet nappy and observing a colour change.[11] The number of conditions screened for in the blood spot may increase further as the NHS is currently considering screening for severe combined immunodeficiency.[10] Cystic fibrosis is one of the conditions screened for in the blood spot test. It is a genetic disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. The CFTR gene was discovered in 1989 and was the first disease-causing gene identified.[12] In 1990, the Human Genome Project was initiated. One of its aims was to sequence the entire human genome to facilitate the identification of the genetic roots of disease and development of treatments. The project was declared complete in April 2003.[13] Since then, multiple CFTR mutations have been identified and people can be screened to determine if they are carriers. Modulator therapies targeting the most common F508del mutation are now available to eligible patients on the NHS.[14] There are hopes of other personalised, mutation specific treatments developing in the future. Personalised medicine is based on the premise of using peoples' phenotypes and genotypes to tailor therapeutic strategy or to determine predisposition to disease and deliver timely, targeted prevention.[15] Personalised medicine is likely to grow over the next few decades.

Molecular characterisation of Cancers

The genetic and molecular mechanisms driving cancers have also been increasingly understood and targeted therapeutically. For example, human epidermal growth factor receptor 2 (HER2) is a membrane tyrosine kinase overexpressed in approximately 15% of early invasive breast cancers, creating a powerful proliferative drive. Using immunohistochemistry, pathologists can identify if breast tumours are HER2 positive and thus amenable to targeted HER2 inhibitor treatment.[16] The molecular features of cancers are included in many classification systems and clinical cancer guidelines. Thus, the role of histopathologists has expanded from diagnosing cancers by morphology to also guiding treatment decisions through the application of molecular techniques to identify biomarkers of prognostic or therapeutic significance.

Conclusion

To conclude, pathology has changed tremendously in the sixty years since the founding of the Royal College of Pathologists. The diagnostic, preventative and therapeutic applications of pathology have grown, increasing demand on pathology services, and driving laboratory digitisation and automation. The College oversees the training of pathologists working in seventeen different subspecialities. This is testament to how the scope and complexity of Pathology has increased alongside our growing understanding of the body and disease. Better knowledge has translated to safer practice in blood transfusion. Pathologists are more involved in complex treatment decisions such as in infectious diseases where antimicrobial resistance is on the rise, and in Oncology where the detection of certain biomarkers identify treatment options or determine a prognosis. Molecular pathology and advances in genetic sequencing are ushering in an era of personalised medicine. These trends are sure to continue, making pathology an exciting field to work in. Pathology is now more than ever, the science behind the cure.

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