Thos Pullar and the philosophers stone

Michael Legge

First I would like to acknowledge the honour of being asked by the NZIMLS to give this very important address which is part of the ongoing tradition of the profession and one I believe should not be lost.

TH Pullar

Every year we acknowledge the significance of Thomas Henry Pullar to both Pathology and Medical Laboratory Scientists education and career structure. I doubt now if anyone has had personal contact with Thos Pullar as he was known. I certainly have not but I have heard a lot of TH Pullar addresses. So a small reflection. Thos Pullar qualified as pathologist in the UK and initially worked as a Biochemist before moving to London where he became an authority on tumour pathology, before moving to a new position in New Plymouth where he would work for 26 years. He was probably the first New Zealand pathologist with a strong clinical biochemistry background at that time. During this time he was largely responsible for the introduction of the BCG vaccination in New Zealand and the establishment of a blood group reference laboratory in Auckland. In his day he was one of New Zealand's leading clinical pathologists with a passion for training and establishing education structures for the then, Technologists and travelled New Zealand as an advisor and examiner. He was a central figure in establishing the New Zealand Medical Technologists Training Board to produce unified training standards. Regrettably Thos died at the age of 59 in 1965 after a long illness. In 1966 in Thos Pullar's Obituary it is stated that his staff worked with him rather than working for him and he frequently worked on the bench with his staff.

The first TH Pullar address was given at the NZIMLS Annual Meeting in 1967 by one of his colleagues and acknowledged Thos Pullar's contribution to pathology, science and education. The topic was cytogenetics and the cell cycle, which at the time were rapidly emerging fields and the presentation probably lasted well over a good hour, which brings me to the main body of this presentation. What I found interesting in the TH Pullar address was the speculation that genes are presumed to consist of largely DNA, which was 14 years after the first publication of the structure of DNA by James Watson, Francis Crick and Maurice Williamson in 1953. Maurice Williamson was a New Zealand scientist working in the UK, often forgotten that he was a New Zealand Nobel Prize winner, and all three received the Nobel Prize for their work. Until this discovery, inheritance was presumed to be by proteins. So 14 years after the discovery of DNA structure, there was still speculation on the roles of genes and DNA in the first TH Pullar address. In a press release by Watson and Crick on the structure of DNA they announced that they had found the "Philosophers Stone of Life". This pre-dates Harry Potter.

So what did Watson and Crick mean by the "Philosophers Stone of Life"?

A second century Egyptian Alchemist, Maria Hebrea described a method to 'fabricate' the "Philosophers Stone", which at the time was translated and corrupted into making gold from base metals. This quest consumed alchemists up to and including the 17th century. However, it is believed that Maria's original meaning of the Philosophers Stone related to transforming knowledge. However in their quest for the impossible alchemists, including Isaac Newton, started laying the basis for modern science by systematic observations and documenting experimental techniques. By commenting on the discovery of the "Philosophers Stone of Life" Watson and Crick considered that they had unlocked the essential key to the knowledge of life. By making this statement they were starting to merge centuries of magic and alchemy into a foundation for modern science and ultimately genomics.

Fast forward now to 1967, where we had the knowledge of chromosomes but there was incomplete knowledge of DNA, hence the comment in the first TH Pullar address that DNA may be involved with genes. "Units of inheritance" were understood from Mendel's work and his subsequent contemporaries and William Bateson in 1905 provide the term genetics from the Greek "genos" (to give birth), and the gene became units of inheritance, but what they were was unknown. At that time science and knowledge progressed by the decade and was frequently not accepted by all. Take for example a German physician who cut off the tails of mice, bred them, and 'proved' that no tails was not inherited as a physical characteristic.

Thos Pullar have would been fascinated by our science, knowledge and training today and just as he had published in the New Zealand Medical Journal in 1965 in an article on training laboratory technologists being at a crossroads, we as a profession are at a significant modern crossroad. Thos considered that the profession had to evolve and that education and training were paramount to establishing a skill base for pathology. He was however, torn between "on the bench" training and creating and using university graduates. Of course the universities in those days considered anything of a 'technical nature' well below their image of an academic institution, how things have changed.

Today we take for granted diagnostic pathology and the massive amount of data being produced every day. But, genetic technologies progressed slowly. In 1977, Fredrick Sanger introduced a method for sequencing the genome which is still used today, and in 1983 Kary Mullis invented PCR by transforming knowledge into application. The billion dollar Human Genome Project was launched in 1990 and finally completed in 2022. Now it is possible to get a genome sequence in a few days and costs less than $US1000. Genetic technologies now form an important diagnostic component for understanding inheritance, cancer and genetic diseases – and the list goes on.

We accumulate knowledge and skills faster now than any other time in the history of pathology and life sciences. This has led to the evolution of a highly skilled and competent workforce. We transform knowledge into significant practical applications, which ultimately benefit wider public health and wellbeing. Reflecting back on the original concept of the "Philosophers Stone" and the comments by Watson and Crick, a question I would pose here is whether we are 'touching' the mythical "Philosophers Stone of Life" with our unprecedented transformational knowledge and technologies that did not even exist in the realms of science fiction 50 years ago. Take for example cancer diagnostics where molecular biology, genetics and metabolomics has revolutionised the understanding of these insidious diseases. We can classify cancer, track its inheritance patterns and we are beginning to understand the metabolism of tumours and the potential of targeting cancer metabolism therapy with novel drugs inhibiting cancer metabolism as an alternative to chemotherapy.

This scientific knowledge is progressively leading to cures of previously incurable cancers, longer survival times and the development of new medications. The concept of tailoring cancer medication is beginning to be based on pharmacogenomics, where by clinical treatment can be tailored for both the cancer molecular profile and the individuals own genome. We have a significantly better understanding of inherited diseases which is leading to successful treatment or alleviating the worst complications. For example, the life expectancy of a cystic fibrosis child in the 1950s was no longer than 5 years, a child born with cystic fibrosis in 2022 can expect to live to at least 65 years and the oldest cystic fibrosis person is Maria Pryson in the USA aged 86 years. When the disease was explained to her as a child she through it was citrus fibrosis and that she had an allergy

to orange juice.

So not only is the technology and diagnosis important, so are clear communications. Since the discovery of the cystic fibrosis gene over 1700 mutations have been identified leading to a significant understanding of the disease and treatment protocols. We tend to think that genetic diseases are rare but a recent publication from Europe indicates that 1 in 20 of the population carry a mutation for a rare disease. As carriers it should not manifest itself but may account for an unusual diagnostic pathology result. I think it is safe to say that irrespective of a disease, diagnostic pathology services are the key to modern medicine.

So, how can we as a profession move forward, both in the quest for knowledge and the practical applications?

We are fortunate in New Zealand to have two excellent BMLSc degrees, which are in tune with the increasingly sophisticated requirements of the profession. These are linked to a range of post-graduate qualifications thereby providing a basis for a highly skilled workforce. The NZIMLS has for over 40 years provided the QMLT qualification, which has largely kept pace with new knowledge and developments for technician training. Both qualifications are tailored to the professions requirements and cannot be replaced by a science related BSc or a simple examination to transit technicians to 'registered scientists'. Whilst the HPCA Act protects the public with the regulation process, registration alone does not provide either the knowledge or professional progression required by the appropriately qualified workforce.

In the 1970s we entered the age of automation, especially in chemical pathology, which was being signalled as the end of a skilled workforce. All that was needed were people to load the analysers and send the printed results to the wards. Of course, this proved to be incorrect as new skill sets emerged including knowledge of computerisation. What was starting to happen was the evolution of new knowledge, an understanding of multiple data outputs and the speed that results could be produced. New methods and technologies emerged as well as significant impacts on clinical management. This was the start of the pathology information revolution in diagnostic laboratories. Changes such as these started the long road to the creation of the BMLSc degree. This recognised the necessity for a skilled graduate workforce to meet the changes starting to occur.

Today, I think we are at another major crossroads for our profession. For me, it is evident that just as Thos Pullar had a vision of a graduate profession we now have to consider how diagnostic pathology services may evolve and the nature of the workforce needed to progress these changes. I consider that there are three emerging issues, stabilisation of the workforce, continuing education and career pathways. The first would rely on a single pathology provider who is not linked to returning profit to investors. My vision is a national pathology service using common data bases and the freedom to exchange information. The second, is with rapidly changing scientific information that continuing education for scientists and technicians is recognised as being essential for both good practice as well as career progression. Unless someone wishes to be a 'manager' the career progression in diagnostic pathology basically does not exist. Again, this is hampered in part, by private providers with their eyes on profit. Inter-linking these are the issues with the Medical Sciences Council. Their publication of the "Scopes of Practice" document in December 2022 indicated that they lacked both the knowledge of the disciplines in diagnostic pathology and the profession itself.

So where to from here?

It is hopeful that Te Whata Ora will heal the fractured pathology services and bring together a national pathology service under a single authority. This is essential to try and resolve the ongoing issues in New Zealand Pathology. Pathways for continuing education exist but the workforce is restricted on access. There needs to be clear pathways that can be followed to allow new knowledge and skills to flow and we need to explore how these can be best achieved. I think it is safe to say that career progression is virtually non-existent and we need to work on how this can be implemented for the profession as a whole. As an adjunct to this is perhaps the Medical Sciences Council could employ medical laboratory scientists to advise on the profession.

In this ideal world, what could the future of pathology look like? The key is an equitable system across the country and the profession that it is not considered as an 'add-on'. Like Thos Pullar I have tried to renew his vision. For me the key is the security of the BMLSc programmes at the two universities with an appropriate funding model to sustain a four year programme. Graduates need to be employed as scientists and not technicians and both groups need to see a way ahead. Career progression is key to the security of New Zealand's diagnostic pathology services. We need to recognise special skill sets working within pathology and based on experience and post-graduate qualifications. These would be specialist scientists.

And then there are Clinical Scientists. This high level qualification has been available in the United Kingdom for over 40 years and in Australia for over 12 years. We need a clear route for the training programme similar to that of pathology registrars and the recognition of the knowledge, skills and seniority these scientists bring to pathology.

Finally, where do we place research?

The new buzz-word is "Precision Medicine". If the Ministry of Health, Te Whata Ora and other health agencies are to be believed this will be a significant step forward for pathology. Translational research links with Precision Medicine, providing the new knowledge by linking research to routine pathology. We will see new emerging disciplines, which will deliver unprecedented diagnostic power and patient treatment with the identification of disease signatures. We have already entered the 'genomics era' as well as the progressive development of metabolomics and proteomics. These technologies will evolve into stem cell therapies, therapeutic gene editing, pharmacogenomics, novel cellular therapies and the use of Artificial Intelligence (AI) in data management and decision making as well as new, as yet unthought of laboratory technologies emerge. When such powerful technologies are linked with image analysis, computational biology, informatics systems etc, we will have more powerful diagnostic tools than ever before in the laboratory.

In ancient magic the "Philosophers Stone" was linked to the "Elixir of Life". If we accept that the "Philosophers Stone" was transforming knowledge then we are at a significant cross-roads. Knowledge is ethereal, it cannot be touched but it can transform; a similar concept to the "Philosophers Stone". While we do not possess the mythical "Elixir of Life" consider how many results from pathology laboratories in New Zealand have changed or transformed people's lives, often for the better and longer, a new concept of the "Elixir of Life". We are entering a new age of medicine and diagnostic pathology is central to many of the new innovations. Just as Thos Pullar many years ago had faith in the profession, now is the time for the profession to have faith in itself.

Thank you.

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