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PATHOLOGY – ITS ORIGINS, PROGRESSION AND FUTURE

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Summary

The science of laboratory medicine was founded by Morgagni in the 18th century and developed on a predominantly morphological basis to the early 1900's. Its further progress suffered a temporary setback when it became trivial and increasingly distant and irrelevant to the needs of clinical medicine whose proponents sought independent means of laboratory based investigation. The incorporation of new techniques both morphological but, more importantly also functional, stimulated a new philosophy and rekindled an era of rapid further progression which restored pathological disciplines to their former prominent positions in investigative medicine. The ways in which this progress has been maintained and can extend into a bright, important future are discussed.

Key words: Pathology, history, future of

INTRODUCTION

Since the science of pathology was founded as a result of the work of Morgagni (1682 – 1771) (Fig. 1) its growth as a basic and practical science within medicine has been extremely rapid. Perhaps the pace of change has been most intensive in the 20th century, though this has been unevenly distributed, containing as it has a significant period of stagnation and decline in credibility, particularly during the second to fifth decades.

Fortunately, largely as the result of a basic change in attitude of pathologists, but aided considerably by introduction of new technology to the science, pathology has regained much of its previously unrivalled position as the leader of laboratory-based medical science.

The introduction of a more functional attitude in the various specialties within pathology has largely superceded the previous purely morphological static approach to advancing the subject. The explosion of knowledge has inevitably led to the need for specialisation in individual branches of laboratory science and the result is an exciting and bright future.

There were times in the 35 years of my professional career as a pathologist when I was depressed for the future as it became irrelevant and trivial to a significant degree and those of other trainings and disciplines took the lead in development of laboratory-based investigation. However, I now look back over my career with gratitude at having been privileged to have had a very full and stimulating professional life with periods of considerable excitement and satisfaction. This historical review and glimpse into the future is inevitably a personal view magnified by my good fortune at also having been able to visit pathology in many parts of the world, recognising local differences and difficulties and learning much from the endeavours of others.

This was largely made possible by my association with the International Academy of Pathology, particularly during my term as President. During this time I had the honour to be invited to participate in the celebrations of the 300th anniversary of the birth of Ciovanni Battista Morgagni[1] in the town where he was born, Forli, Italy, in 1982. It is with Morgagni that I shall begin.

THE EARLY DAYS

Before Morgagni, the doctrine propounded by Galen was widely accepted, namely that all diseases are dyscrasias, i.e. alterations of mixtures of the four cardinal humours – *humores:*

Blood
Phlegm
Yellow bile
Black bile

This doctrine was swept aside by the writings and practice of Morgagni who was the first to relate changes in organs and tissues after death to the clinical features of disease during life.[2] Morgagni was a remarkable man in many respects. He became a student of medicine and philosophy at the University of Bologna at

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the age of 15 and there became a demonstrator for Valsalva. He subsequently became an assistant to him at the age of 19 years when he also received the degree of Doctor of Medicine. In 1711, aged 29, he was installed in the Chair of Theoretical Medicine in Padua and taught there for nearly 60 years. He was 79 years of age when he published *"De Sedibus et Causis Morborum per Anatomen Indigatis."*[1] This remarkable text demonstrated the very great qualities which Morgagni, though purely a morphologist, possessed (Table 1).

TABLE 1
MORGAGNI'S CONTRIBUTIONS TO SCIENCE

(i) The discarding of fantasy.
(ii) Accuracy of observation.
(iii) Obsessiveness of record-keeping.
(iv) Care in correlation.
(v) Width of discussion.
(vi) Critical analysis.

FIG. 1 : Giovanni Battista Morgagni (1682 – 1771): The founder of pathology.

It has to be realised that in bringing about a change of attitude to accept scientific observation, Morgagni had to overcome considerable opposition from the church who previously had supported Galen's doctrine.

Though simple microscopes were available during Morgagni's lifetime he chose to restrict his observations to exceptionally accurate detailed descriptions of gross appearances of organs whilst correlating individual organ changes to a concept of a single disease process. Microscopical observations were subsequently added by others, notably by Laennec.[3] Many other distinguished scientists in a number of European countries recorded and accumulated data about the natural history of disease culminating perhaps in the work of Karl von Rokitansky in Vienna where the pathology institute which he built (it is believed with his own money) remains as a very active department of education, service and research to this day. Rokitansky is credited with having personally conducted detailed autopsies on 50,000 cases and the manuscripts of his reports (in Latin) are still available.

The aristocratic German scientist and politician Virchow added a new diameter to the morphological approach to disease processes by his exposition of the cellular concept indicating the basic premise that they were caused by disordered cellular function – "Every cell from a cell".[3]

His pupil Cohnheim explored the dynamic approach of watching the development of diseases through the experimental method: a philosophy which was to prosper for many years.

So far the development into the second half of the 19th century had concerned itself with what was called "morbid anatomy and experimental pathology". The identification of infective agents through the work of Pasteur and Koch in particular. added a new parameter to the understanding of disease and created the discipline of microbiology. This science initially concerned solely with bacteria has subsequently expanded to incorporate other micro-organisms including viruses and the products of microbial activity as they could be recognised in blood and body fluids which started with the name of serology and subsequently and in more recent years has rapidly expanded into the field of immunology.

The two traditional "classical" disciplines were joined in 1916 hy the concept of "biochemical lesions" largely through the availability of methods of increasingly accurate chemical analysis and the distinction of the English chemist Rudolph Peters. The expansion and refinement of analytical techniques was of enormous importance conveying a further functional component to the study of diseases.

Special attention was also being paid to the importance of the study of blood, its cells and its diseases, a specialty which we now recognise as haematology.

By the end of the second decade of the 20th century, though predominantly morphological in concept, the disciplines of pathology were firmly established as the leaders in the scientific aspects of medicine.

THE FIRST 60 YEAKS OF THE 20TH CENTURY

Concentration on structural change, overemphasis of minutiae, triviality of attitude, physical and to some extent intellectual isolation from other parts of medical science, particularly the clinical sciences, led to a loss of purpose, enthusiasm and credibility in spite of a major increased requirement brought about as a result of clinical and analytical developments.[4] Both medically trained and non-medical scientists. not getting the right support and relationships with pathologists. set up their own laboratory investigative bases diminishing the role of pathology but offering much to progress in medical science generally. Amongst non-medical scientists one can include in this context chemists, particularly biochemists: biologists, physicists, immunologists, statisticians. geneticists and more recently computer scientists.

Persons in such disciplines were largely excluded from pathology departments, though it should have been very apparent that they had special skills and had much to offer.

'The decline of pathology during this period had a very severe effect on recruitment at a rime when rapid expansion of services became necessary.[4] This was particularly evident in the specialty which we now identify as histopathology, where the static. largely or entirely morphological. approach was coupled with an unjustified arrogance and isolation.

Some of the revealed defects relate to a failure to identify a proper role in functional terms for qualified pathologists. Because they are laboratory and department based they have four major areas of responsibility.[4,5] Inevitably they have to assume an amount of administration. They need to be significantly involved in teaching, often both at undergraduate and postgraduate level; they need remaining contact with a patient-relevant service in diagnostic terms and they should retain an enquiring mind for investigative work at either basic science or clinically-orientated levels.

There are those who misguidedly felt that they were able to carry out all these functions with equal distinction, but in my view such paragons of virtue are exceptionally rare and what is necessary is to identify that individuals have differing orders of priorities within their responsibilities. It should be recognised that different mixtures of enthusiasms are desirable and that one mixture is not necessarily superior to any other. Skills in the whole range of functions must be encouraged and harnessed appropriately.[5,6]

INCORPORATION OF NEW TECHNOLOGIES

In more recent times there has been a marked resurgence of enthusiasm, quality of output, status and relevance of pathologists, much of which is probably due to the perceived needs of some to incorporate new techniques originally developed in other sciences and disciplines.[1,5,6] At the structural level the advances have been less spectacular but the ability to study the fine structure of cells by electron microscopy, to look at their surfaces by scanning electron microscopy, to accurately measure cell parameters by the techniques of morphometry, and to study individual cells aspirated from tissues or exfoliated from cell surfaces have all made valuable contributions to progress. The study of sequential biopsies of internal organs has enabled a more dynamic picture of diseases to be evaluated and the introduction of resin-embedded semithin sections has enabled greater cell detail to be identified at light microscopy level.

It is, however, in the functional aspects of pathology that the greatest advances have been made and which has enabled several of the pathological disciplines to reclaim their former predominant positions in medical. science. This is in part chemical, identifying contents and products of tissues and their accurate estimation in blood and body fluids. More particularly, however, it relates to the development of radioimmunoassay and immunocytochemical techniques. The use of the former to measure with great accuracy minute quantities of substances has revolutionised the study of disorder of the endorcrine glands as well as many other aspects of diseases. Immunocytochemical techniques, particularly utilising the continuously expanding range of highly specific monoclonal antisera, identifies the ability of cells to express particular functions and specific products. Furthermore, by combining ultrastructural techniques with those which are immune-based it is possible to anatomically localise the site of cell function. In this field immunofluorescence has largely been superceded by more precise anatomically localising techniques such as immunoperoxidase or avidin-biotin systems. These techniques are not only semi-quantitative but provide accurate localisation within tissues and cells, can be retrospective, produce a more permanent preparation and, particularly recently, are more specific.

The ability to provide a more useful range of services has provided the opportunity for a change of attitudes which fortunately pathologists have readily and enthusiastically accepted. This philosophical change has moreover been incorporated in the work of both "academic" and "clinical" investigators and service pathologists.[5,6]

Though the image of pathology has markedly improved and its recovery of leadership in some areas recognised, it still lags behind many clinical specialties in recruitment of the better students. Perhaps this has to be accepted, though the situation could probably be improved by an acceleration of recent trends for pathologists to become much more closely associated with patients, particularly by carrying out some of the techniques for obtaining the samples which they require for their analytical and interpretative skills. Chemical pathologists have become "clinical chemists" by having clinics where their knowledge is particularly valuable; microbiologists can become microbial disease physicians; haematologists in many parts of the world have the dual roles of clinician and laboratory scientist; histopathologists now not infrequently carry out biopsy techniques, colposcopic examinations and fine needle cytology aspirations, etc.

LESSONS FOR THE FUTURE

Obviously this section significantly overlaps comments made in the preceding paragraphs, for change is a continuum and not readily packaged into neat campartments. It clearly becomes of fundamental importance to maintain a functional viewpoint to remain relevant and to search for utilisation of new technologies.

Computer Technology

We have been slow in utilising fully the opportunities given to us by computer science development. This not only relates to the banking of data and its retrieval but to statistical analysis to the making of disease models and expansion of morphometric techniques. Both research and service needs are relevant to computer utilisation.

Ultrastructure and Immunocytochemistry

One would hope for more sensible use of ultrastructural studies, at present rather unintelligently selected without prior identification of what is valuable at this morphological level. Similarly one looks to an extension of immunocytochemical techniques but at the same time a rationalisation of the usefulness of such methods in specific cases. Immunocytochemistry remains a rapidly widening field in both research and practice but it needs to be well and selectively performed and the cost of such tests not ignored. There is a tendency to do a whole battery of such investigations at the same time rather than to use the more intellectual approach of the "step-by-step" method.

TABLE **2**

SOME USES OF MOLECULAR BIOLOGY IN THE DIAGNOSTIC LABORATORY

5 Genetics

- Prenatal diagnosis.
- HLA typing.
- Creation of genetic linkage maps.
- Detection of genetic rearrangements.

Microbiology

- Detection and identification of viruses.
- Correlation of infectious agents in neoplastic tissues.
- Determining antibiotic resistance in bacteria.
- Tracing epidemiology of infections.
- Detection and quantification of microbial agents which are hard to culture or are poorly antigenic.

Tumour Diagnosis, Classification and Prognostic Assessment

- Detection of genetic rearrangements.
- Detection of genetic rearrangements in known and infrequent patterns of tumour-associated karyotype abnormalities.
- Study of oncogenes and their expression.
- Gene amplification related to any resistance.
- Diagnosis of cell lines by gene expression.

Molecular Biology

Molecular biological techniques are already becoming incorporated in many aspects of medical science, not least in pathology.[7] Table 2 identifies some of the uses of such techniques in the diagnostic laboratory and there are many more in the research field. We must be quick to utilise the help which they provide in the investigation of disorders which have not proved easy to make progress with by hitherto available techniques.

Multidisciplinary Teams

Developments of multidisciplinary teams including the incorporation of non-medical scientists has been a welcome development in some special fields of interest in recent times. There is little doubt that in renal diseases such teamwork is essential with frequent joint meetings before important decisions about patient management are made. Table **3** shows the typical membership of such a team and one is aware that somewhat similar groupings

TABLE **3**

MULTIDISCIPLINARY TEAMS IN RENAL DISEASES

Renal Physician	– With overall clinical responsibility
Physiologist	– Special skills relevant to functional problems
Urological Surgeon	– Exclusion of obstruction and other urinary tract contributory factors
Transplant Surgeon	– As part of a renal transplant programme
Immunologist	– For assessment of serolocal and immunofluorescence studies.
Radiologist	– Investigation of renal parenchyma and urinary tract by contrast, ultrasound, arteriography, scans and nuclear magnetic resonance
Histopathologist	– Light and electron microscopic studies of biopsy tissue with immunocytochemistry and fine needle aspirates as necessary
Computer scientist	– Data programming and retrieval

are currently important in respect of haematological disorders (particularly lymphomas), in liver diseases and those of the gastrointestinal tract, etc. In these multidisciplinary exercises the pathologist must always play a prominent part and must attune his opinions directly to the needs of patients.

Technologist Roles

The skills of technologists have too often in the past been taken for granted but particularly with the very high grade of such techniques now required, better recognition of their contribution needs to be made.

Specialisation and Superspecialisation

Within pathology specialisation into the main disciplines has inevitably happened. Within individual disciplines specialisation is rapidly occurring and is also essential because of the need for knowledge in depth in particular fields. What is more debatable is whether it is desirable that there should be "superspecialisation". By this one means restriction of knowledge and interest to a small field but in very great depth. There are areas where this is relevant but expansion needs to be identified with great caution.

Internationality and Recruitment

Progress has recently been made towards a greater degree of international co-operation and in standardisation of nomenclature. Though national rivalries are inevitable (and probably largely healthy) some pooling of resources of information on a regional or wider geographical basis can often be extremely beneficial and should be encouraged. In stimulating recruitment into the pathological specialties we must make better efforts at firing undergraduates with enthusiasm for pathology by teaching them in a more relevant and interesting way. Training programmes need to be controlled and facilities, particularly for sophisticated technical procedures. need to be centralised so that expertise and experience can be developed. Qualities of leadership need to be identified and encouraged.

Future Changes

Finally, we should all retain an open mind about what is necessary in the future. Specific roles of individuals will and should change with time and should not normally be obstructed. It is always important to listen. learn and adapt as necessary and we should never forget the near disaster of closed minds and arrogant attitudes of the recent past.

CONCLUSION

Those of us in medicine must recognise that they are particularly fortunate for they have interesting. often exciting. work and this contrasts with the lot of many persons who have increasingly repetitive. boring occupations. Pathological science is particularly blessed in this respect as it combines basic and clinical parameters and thus forms an exceptionally important link in the educational process at both undergraduate and postgraduate levels. My fears from the recent past are now dispelled and I can most truthfully say that my professional life has been enjoyable and fulfilling and I trust will continue to be so.

We are already aware of huge challenges around us. partly from incomplete knowledge about existing diseases but equally and perhaps even more importantly relevant to new diseases recently appeared or those that will appear in the near future. One has only to consider the global implications of the 'Acquired Immune Deficiency Syndrome' to identify the scale of problems ahead, though it is quite remarkable how different branches of science have collaborated in elucidating at least a partial understanding of this frightening disease in the last five years – a very short time for such a difficult disorder.

Looking at the past should be an exercise to identify previous errors so that they are subsequently avoided. I have always believed that the "retrospectoscope" is a most valuable instrument when used properly for building experience for the future.

The pace of change sets us all frightening challenges in which pathology has a part to play of particular magnitude. These needs were well identified in an allegorical way by Lewis Carroll in "Alice Through the Looking Glass". much beloved by children of all ages in many countries and from which I quote:-

Alice had just met the Red Queen and they had been running very quickly through a country that was like a great chess board. Alice had become very tired and was short of breath and when the Red Queen at last let her rest. she discovered they were still in the same place by the very same tree. Alice was surprised. and said to the Queen that in her country they would have got somewhere with all that running. "A slow sort of country", replied the Queen. "Now here, you see, it takes all the running you can do to keep in the same place. If you want to get somewhere else you must run at least twice as fast as that".

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