LECTURE

Ashton lecture. Ophthalmic pathology from its beginning to the high technology of this millennium

GORDON K. KLINTWORTH

It is a distinct honour and privilege to deliver this third Ashton Lecture, especially since Professor Ashton was a friend who provided a professional standard to which all Ophthalmic Pathologists could strive.

Before beginning I was asked by the members of the most prestigious Ophthalmic Pathology Society in the USA to read the following statement on its behalf:

'The members of the Verhoeff-Zimmerman Society wish to express their profound sorrow on learning of the recent death of our esteemed colleague Professor Norman Ashton. A central figure in the development of Ophthalmic Pathology, he contributed immeasurably to Ophthalmology through his remarkably clear scientific contributions and lectures. We shall also remember Professor Ashton as a warm friend whose personal charm helped to cement interactions between Ophthalmic Pathologists throughout the world'.

The opportunity to speak to you on this occasion is particularly pleasurable because this is the last meeting of the Royal College of Ophthalmologists of this millennium.* This historic occasion is also the first Ashton lecture after Ashton's death.[1] After receiving the kind invitation to give this lecture I was at first nervous at the thought of delivering it before the members of this eminent society. It would have been a particularly joyous occasion if I had been able to make the presentation in the presence of Ashton, but the sadness in giving it only a few months after learning about his death makes the task difficult because of my mixed feelings.

After accepting the invitation to deliver this lecture. Professor Ashton wrote to me stating:

'I was delighted to learn today (July 5th 1999) that you have accepted the invitation from the Royal College of Ophthalmologists to give the "Ashton Lecture" next year. It is good indeed to open the Eye Congress of the Millennium with an address from such a good scientist and experienced speaker.

I set up the lectureship with the purpose of keeping the subject of ocular pathology regularly before the assembled company of the College members at an annual meeting – biannually if possible – especially to keep them well informed of advances made and being made in this basic discipline of clinical ophthalmology. It was a rule that the lecture should be published in a leading eye journal.'

Ashton also provided me with his critique of the first two lectures. His comment on the first lecture was: 'Unfortunately John Marshall, who gave a splendid inaugural lecture, failed to submit it for publication despite our entreaties'. Professor Rennie[2] gave the second Ashton lecture and Ashton's comment was 'Professor Rennie, although very good, appeared at the end of a journal, out of modesty, since he was the editor! I have always despaired to find our important specialty dumped at the end of Journals!'

Although Ashton is only able to attend this lecture in spirit, he stated in his letter 'I now look forward to the third lecture fulfilling all the criteria I envisaged! If I can help in any way please let me know.'

Shortly after accepting the invitation, I realised that I would need to decide on a topic and title for the lecture. My initial inclination was to discuss some aspect of my research in detail, but I was not entirely convinced that subjects so close to my heart would be of interest and appropriate for the anticipated audience. The issue soon became resolved when Ashton died soon after the beginning of year 2000. Initially, I did not intend to spend too much time commenting on Ashton and his achievements. I thought that he might wish to hear about my research rather than be placed in an uncomfortable position of hearing laudatory remarks about his own contributions to Ophthalmology.

With the passing of Ashton I realised that a major milestone in Ophthalmic Pathology had come to an end and his death inspired the title of my lecture.

Gordon K. Klintworth ✉
Duke University Medical Centre
Durham
NC 27100, USA
Tel: +1 (919) 684 3550
Fax: +1 (919) 684 9225
e-mail: klint001@mc.duke.edu

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*Despite the wide misbelief that the new millennium began at midnight on 31 December 1999, the second millennium only ended at midnight on 31 December 2000.

Because Ashton played an important role in establishing Ophthalmic Pathology as a discipline, I would like to remind everyone of his tremendous contributions to Ophthalmic Pathology. Ashton was a superstar who inspired many individuals, including me, to a career in Ophthalmic Pathology. Almost immediately after my humble serendipitous beginnings in Ophthalmic Pathology it became apparent to me that Ashton was an academic Ophthalmic Pathologist, superb scientist and scholar.

I found the blend of his high scientific standards and his elegant writings that reflected a masterly command of the English language most appealing. Because I was attracted to the calibre of his research I spent a sabbatical leave in London at the Institute for Ophthalmology in 1970 to learn more from the master. During a most enjoyable time in London I performed some of my initial experiments on coerneal vascularisation using the hamster cheek pouch chamber.[3,4]

Despite an aversion to travel Ashton crossed the Atlantic Ocean several times and was fond of Americans even though he had difficulty accepting the American informality. He told me about his dislike of the American tendency to call someone by his or her first name after an initial meeting. He thought that relationships on a first name basis should take place only between friends. I was delighted when he eventually requested that I call him Norman. When Alec Garner and I edited a major text on the *Pathobiology of Ocular Disease*[5] Ashton kindly wrote the preface.

Ophthalmic Pathology and Ophthalmic Pathologists

Ophthalmic Pathology, the subspecialty of Pathology and Ophthalmology, focuses on diseases of the eye and its neighbouring tissues. Ophthalmic Pathologists are a vital component of Academic Medical Centres because of their comprehensive knowledge about diseases of the eye. Ophthalmic Pathologists examine diseased tissue from the eye and its adnexa macroscopically and by light microscopy. This may involve a variety of special stains.[6–8] Transmission and scanning electron microscopy,[6–11] histochemistry and immunohistochemistry,[6,12–19] energy dispersive X-ray microanalysis,[20] cell and organ cultures, as well as molecular biological and other techniques[17,18,21,22] are also sometimes employed. In addition information about certain diseases can be derived from analyses of serum and DNA in the peripheral blood even in disorders thought to be restricted to ocular tissues.[23–27]

Patient care

Studies on surgically excised tissue enable the Ophthalmic Pathologist to provide the practising Ophthalmologist with a precise diagnosis of the disease and with information about its cause, pathogenesis and prognosis. Aside from this essential role in patient care Ophthalmic Pathologists contribute to quality control in hospitals by providing important information regarding complications of therapeutic interventions and in assessing the appropriateness of procedures.

Education

By teaching Ophthalmologists and trainees in Ophthalmology, partly through lectures, conferences and courses, Ophthalmic Pathologists contribute to the maintenance of high-quality eye care. The importance of Ophthalmic Pathology in Ophthalmology training programmes has been appreciated for a long time. In the USA the American Board of Ophthalmology and the Accreditation Council for Graduate Medical Education, which accredits Residency Training Programs, sets stringent requirements in Ophthalmic Pathology. In the USA all Ophthalmology Residents (Registrars) are currently required to have training experience in ocular pathology. It 'should be comprised of continuing intramural lectures, clinicopathological conferences and a minimum of 50 hours of laboratory experience in gross and microscopic examination of pathological specimens. This latter experience with a qualified pathologist may take place intramurally or extramurally at a laboratory considered by the Residency Review Committee to be capable of providing such training. If utilised, this extramural effort should occur during the 36 months of residency training, preferably early in the program, and would not be construed to be a substitute for the continuing intramural program. A short exposure to Ophthalmic Pathology at a remote course may supplement this training but will be not considered as a substitute for the pathology requirement.' It is my understanding that no specific time requirement exists in Ophthalmic Pathology for the training of Ophthalmologists in the United Kingdom, but that the examination for Membership of the Royal College of Ophthalmologists (MRCOphth) includes Pathology and, specifically, a 20 minute oral examination.

Research

Apart from the diagnostic and teaching aspects of Ophthalmic Pathology, Ophthalmic Pathologists increase knowledge about diseases of the eye through research. Ophthalmic Pathologists, other physician scientists (academic pathologists and academic ophthalmologists) as well as basic scientists and other researchers continue to struggle with the eye diseases that have plagued man since antiquity – glaucoma, uveitis, retinal diseases, cataracts and corneal diseases, in addition to cancer of the eye and its adjacent tissues. Remarkable advances in knowledge about different diseases come not necessarily when more individuals tackle the problem or when more resources become available, but rather when relevant technological advances occur[28–33] or when new concepts stimulate new approaches as to how to tackle old problems. With diseases that are genetically determined amazing advances are taking place at an unbelievable rate.

Pre-Ashton Ophthalmic Pathology

The beginning of any specialty cannot be defined with precision. Ophthalmic Pathology is no exception. The introduction of dissections and macroscopical studies of ocular tissue eventually became the specialty of Ophthalmic Pathology. Descriptions and illustrations of some ocular diseases are present in many early books, but texts on the Pathology of the eye did not exist before 1808. In that year James Wardrop (1782–1869)[34] published the first edition of *Essays on the Morbid Anatomy of the Human Eye*, when he was only 26 years old. Several years later the second edition appeared. In 1809 Wardrop documented his observations on Fungus Haematodes (Soft Cancer) in the eye and various tissues, including a description of the tumour that became known as retinoblastoma.[35]

A major figure in establishing Ophthalmic Pathology as a discipline was the famous Viennese Ophthalmologist Ernest Fuchs (1851–1930), who devoted his life to understanding the morphological basis of ocular disease. Progress in light microscopy during the late nineteenth century and early twentieth century had a major impact on Pathology. Its use in laboratories led to an enormous expansion in knowledge about disease and the development of histopathology. This progress also provided information about diseases of the eye. From its early development Ophthalmic Pathology has mainly been a part-time interest of busy clinical ophthalmologists and the discipline initially focused principally on the recording of macroscopical and microscopical features of diseased tissues in the eye and its adjacent structures and in clinicopathological correlations. These observations led to numerous textbooks dealing entirely or predominantly with these aspects of ocular disease. Some of the books are marvellously illustrated with magnificent paintings and drawings. Later texts had photographs, but although they captured reality, they lacked the aesthetic appeal of the creative artist. These masterpieces on ocular disease will remain treasures of our heritage for future generations to cherish. Without doubt one of the classics is the four-volume textbook, *The Pathology of the Eye*, by Sir John Herbert Parsons (1868–1957).[36]

I was fortunate to be an invited participant at a Symposium on Ocular Pathology at the Centenary meeting of the Ophthalmological Society of the United Kingdom in April 1980.[21] In his Presidential address to the parent Society of The Royal College of Ophthalmologists in April 1980 Ashton pointed out that eight individuals attended the first meeting of the Ophthalmological Society of the United Kingdom on 23 June 1880.[37] Among them were three pathologists, including two Professors of Pathology. I do not yet know their names, but the original members of the Ophthalmological Society of the United Kingdom included four individuals with appointments in Pathology. They were: Sidney Coupland, MD (Physician to, and Lecturer on Pathological Anatomy at The Middlesex Hospital), W.S. Greenfield, MD (Professor of Pathology in the University of Edinburgh), the Vice-President of the Society Jonathan Hutchinson (Senior Surgeon to the London Hospital and Professor of Pathology and Surgery at the Royal College of Surgeons, England) and W. Allen Sturge, MD (Assistant Physician and Pathologist to the Royal Free Hospital).[38] The attendance by pathologists at the early meetings, and the election of some as original members of the society clearly indicated an interest by at least some pathologists in Ophthalmic Pathology at that time. However, none of them devoted a career entirely to Ophthalmic Pathology. The many reasons for this probably include the fact that they were more concerned with major fatal diseases and disorders that provided copious tissue for study with the limited tools of the day. In 1947 the first professional organization devoted specifically to Ophthalmic Pathology (currently called the Verhoeff-Zimmerman Society in honour of the two greatest American Ophthalmic Pathologists) started meeting annually to study histological sections from ocular specimens that had been obtained in different laboratories throughout the USA. Most participants were board-certified Ophthalmologists; one was a certified Pathologist (Edith M. Parkhill of the Mayo Clinic).

Impact of Norman Ashton on Ophthalmic Pathology

Despite an early curiosity by pathologists in eye diseases, it is noteworthy that no professional pathologist in the world devoted a career to Ophthalmic Pathology until Sir Stewart Duke-Elder invited Norman Ashton in 1948 to become the Pathologist at the Institute of Ophthalmology that he founded in London. Sir Stewart, who was indisputably one of the greatest Ophthalmologists the world has known, picked a remarkable 35-year-old man for the job. Ashton provided a clinical service to Moorfields Eye Hospital and established an internationally renowned Department of Ophthalmic Pathology at the Institution of Ophthalmology on Judd Street, where he trained a generation of Ophthalmic Pathologists and facilitated the careers of many outstanding Ophthalmologists by providing them with a fundamental background in research and clinically relevant Pathology. Impressed by the success of the American Ophthalmic Pathology Club (now called the Verhoeff-Zimmerman Society) Ashton founded the European Ophthalmic Pathology Society with Willem Manschot of the Netherlands and Ry Andersen of Denmark, and was made life president of that organisation.

Ashton made numerous important scientific contributions during his career, sometimes in collaboration with colleagues, and it is through his writings that he will be forever remembered and judged by future generations. Ashton's research covered a broad base of topics. He focused primarily on the vasculature of the eye in health and disease. His investigations on the retinopathy of prematurity (originally called retrolental fibroplasia),[39–45] diabetic retinopathy,[46–50] hypertensive retinopathy,[51–54] retinal ischaemia,[55] cotton wool

spots[56,58] and retinal vein occlusion[59,60] and Coats disease[61] are models of how important clinical conditions can be approached in the laboratory. He also studied the effect of oxygen on the growth and development of retinal blood vessels, the blood–retinal barrier and other aspects of the normal retinal vasculature.[62–76] He made additional contributions on corneal disease,[77–79] ocular infections (due to *Toxoplasma gondii*,[80] nosema,[81,82] *Amoeba*,[83] cytomegalovirus,[84] nematodes[85] and the trematode *Diplostomum spathaceum*,[86,87] ocular cancer (rhabdomyosarcoma,[88] lacrimal gland tumours,[89] lacrimal sac tumours,[90] iris tumours,[91] metastatic carcinoma[92]) and inborn errors of metabolism.[93–95] He was not just concerned with human ocular disease, but was interested in eye diseases regardless of species, and his publications contributed to our knowledge about toxoplasmosis in wallabies,[80] trematode infection in fresh water fish[86,87] and retinal dysplasia in the Sealyham terrier.[96]

In this era of computerised databases it is easy to find references to subjects. It is also possible to identify important papers by specific individuals, by using the citation index. I thought it would be interesting to determine how many times various articles by Norman Ashton had been cited. I discovered that between 1988 and the present nine of his articles had been cited more than 100 times, and one article[44] has 225 citations. This is a remarkable feat for a paper written more than three or four decades ago, when one considers the short half-life of most manuscripts. The second most cited paper of Ashton reported studies of the diabetic capillaries in relation to diabetic and other retinopathies.[47]

In this era in which information and technological advances accumulate exponentially, no one can become familiar with all the developments in Pathology and Biomedical Research. The task is even more difficult for someone who tries to do it as a part-time venture. While acknowledging the important contributions of practising clinical Ophthalmologists to the knowledge base in Ophthalmic Pathology, Ashton became convinced many years ago that future progress in Ophthalmic Pathology would come not from Ophthalmologists who undertook the discipline as a part-time pursuit. I am convinced that this is even truer today. The reason is simple, as Ashton stated: 'perhaps it would be as reasonable to expect them to have had the time to become conversant with the many developments in pathology as it would be to expect a general pathologist to be skilled, for instance, in the latest methods of cataract extraction or the management of glaucoma.'[97]

In his acceptance of the Proctor Medical in 1957, Ashton[98] wrote:

'If in the future, eye pathology is to be taught and practised in the traditional way, as an elaborate recording of histologic minutiae, then the subject is not too demanding and may well be undertaken as a part-time pursuit, and probably best by the ophthalmologist who is most able to extract the greatest clinical value from the findings. But if the study of ocular pathology is to have its full meaning, the eye must be regarded as a unit of an entire organism, and its behaviour in disease must as far as possible be related to that of the whole. Research in this field, in common with the general tendency, should concern itself with disease mechanisms rather than with disease patterns, and for this purpose the widest possible knowledge of pathologic processes is desirable and the whole armamentarium of modern scientific method should be available. To establish ocular pathology on this broad basis will demand the full and concentrated attention of workers trained and experienced in the appropriate disciplines.'

Aside from his scientific contributions Ashton was a gifted man with many other talents. Ashton's sense of humour and aptitude as a humorist reached a peak in his dedication address at the opening of the Alan C. Woods Research Building and the Jonas S. Friedenwald Library of the Wilmer Ophthalmological Institute of the Johns Hopkins University School of Medicine on 25 May 1964. He appeared on the same program as the internationally famous comedian Bob Hope and was able to steal the show with his wit. The Baltimore Sun reported the event and informed the world about the funny eye doctor. Happily a videotape of the event was recorded. For those not fortunate enough to see the performance the text of the dedication was published.[99]

Ashton's talent as an artist was also recognised by his peers. He designed the Badge of the President of the Association of Clinical Pathologists.[100] The design contains coloured portions with thoughtful symbolism: orange (bilirubin) for chemical pathology, red (blood) for haematology, blue (haematoxylin) for morbid anatomy and purple (methyl violet) for medical microbiology.

Contemporary Ophthalmic Pathology

Information

A vast body of information on Ophthalmic Pathology has accumulated and continues to do so. To keep abreast of the subject individuals have access to traditional methods such as books and journals that are housed in libraries. Access to some of this information that is so important for Continuing Medical Education is available via databases such as MEDLINE and OVID that are accessible on the Internet.

Computers

As this millennium draws to a close we have not only word processors but also software that enables dictations to be typed using voice recognition. Under several circumstances digital cameras have replaced the much slower photography of the past and are getting better by the day. Computers have become an essential part of everyone's life and keep getting smaller and less expensive. Computerised databases contain information on publications, disease, the amino acid sequence of proteins, the nucleotide sequence of genes and much more.

Digital images

The conversion of photographs to digitised images enables photographs to be improved by eliminating scratches and by cropping away undesirable portions. The pictures can rapidly be sent across the world without recourse to the traditional methods of sending mail. Digitised images have also enabled individuals to give lectures without needing to insert slides in a carousel, with the attendant worry of whether they are in order or in the correct orientation. Presentations can be made from laptop computers.

Internet

Using the navigational system of the World Wide Web the Internet has provided individuals throughout the world with access to more information at a faster rate than was possible before. At present it is growing at more than 1 billion pages every 6 months. The Internet has allowed groups of individuals with a common interest to communicate with each other rapidly and readily. In this regard a discussion forum for academicians interested in various aspects of Ophthalmic Pathology (such as diagnostic work, research, higher education, scientific meetings) is available (http://www.mailbase.ac.uk/lists/eyepathology). A site also stores archived images, records and other information (http://www.mailbase.ac.uk/cgi-bin/files?eyepathology). The Internet provides access to a wide variety of other pages relevant to Ophthalmic Pathology (including http://pathology.mc.duke.edu/sectionpages/fulleyepath.htm).

Molecular biology

Numerous extremely powerful research techniques are currently available for the study of human and experimental eye diseases. These methods include molecular genetic techniques to map and identify the genes responsible not only for conditions with a simple autosomal or X-linked Mendelian mode of inheritance as has been demonstrated in recent years for retinitis pigmentosa and other inherited retinal diseases,[101] several corneal dystrophies[102] and many other ocular diseases including some types of glaucoma. After the identification of the responsible gene the mechanism whereby the mutated gene causes the disease can be studied in cultured cells transfected with plasmids containing the mutant gene. Normal and abnormal genes can also be introduced into the ova of animals to produce transgenic animals,[31,103–108] and animals that lack a specific gene ('gene knockout animals') can be created. Transgenic models of human disease can open new vistas for the investigation of the basic mechanisms of understanding disease at a molecular level. In this regard Petters and colleagues[108] have developed an important transgenic pig model of retinitis pigmentosa.

The new technology of molecular biology has answered many longstanding questions. It has also provided insight into the definition of certain clinicopathological entities. For example entities that appear different clinically and histopathologically, may be much more similar than previously imagined, as illustrated by the fact that several apparently different corneal dystrophies merely represent different mutations in the BIGH3 gene.[102]

Today we have the ability to assay the differential expression of different genes in pathological states by extracting the mRNA from tissue and hybridising it against numerous species of cDNA representing over 5000 different genes that are spotted by a robot in microarrays onto positively charged nylon membranes.[32,109] The expression of over 30 000 human genes can be evaluated in these DNA microchip arrays and the hybridisation uses ^{33}P and a phosphor imaging system. The data are analysed with a computer using special software (http://www.resgen.com). In addition the technique of SAGE (serial assay of gene expression) allows all types of mRNA to be identified within a tissue (http://www.sagenet.org).

Service/teaching

Telepathology and telemedicine have already become valuable in assisting pathologists to arrive at diagnoses at institutions that lack certain expertise and in providing conferences at remote sites. The ability of pathologists to direct the processing of tissue in remote sites and to make diagnoses on specimens in these locations by dynamic robotic telepathology has been successful.[110,111] With this method tissue can be examined macroscopically at a far-off place by placing it in a dissecting microscope that is connected to a video camera. A pathologist many miles away can observe the diseased tissue and interact with the local personnel, who can process the specimen locally and prepare haematoxylin and eosin stained sections. After the slides are placed on a robotically controlled microscope a pathologist at a distant site can not only move the stage of the microscope at the distant institution, but can see images of the stained tissue sections that are transmitted electronically via Integrated Services Digital Network (ISDN) telephone lines to the host site. The pathologist views the images in real time and makes a diagnosis. Digital images of the specimen can be downloaded for archiving. The pathologist telephones a report, using a dictation system, to a transcriptionist who enters the report on a computer, and the pathologist at the host site retrieves this information to review and verify the report, which is printed locally. An application of telepathology in the United Kingdom using a 'Virtual Double Headed Microscope' is described on the Internet (http:video.cbcu.cam.ac.uk/).

Interactive Eyepathology Tutor

A solid foundation of Ophthalmology and Ophthalmic Pathology reflecting the observations of our predecessors has stood the test of time and forms the basis for future research. Over the ages libraries and archives have stored

this information. Unfortunately, but not unexpectedly, the number of books and journals has expanded exponentially with time and most literature accumulates dust and takes up precious space. New journals compete for precious resources of room and money. Because of this and the fact that very few individuals are specialising in Ophthalmic Pathology I decided to develop a CDROM multimedia Instructional Interactive Ophthalmic Pathology tutor with Anthony N. Benson and Ann Bushyhead. The program contains thousands of images and enables persons with different backgrounds to study Ophthalmic Pathology and relevant anatomy at their convenience (http://eyepathologycd.mc.duke.edu).

The anatomy of a specific structure can be reviewed by clicking on the appropriate title of the structure on a pull-down menu. In the anatomy section some hotwords identify structures within images on the same page. Clicking on an illustration increases the magnification and the user can move to different parts of the illustration. Clicking with the right-hand button of the mouse makes legends appear on the illustrations. By using the Link Button, the user moves from the Anatomy directly to the Pathology.

The major portion of the program dealing with Pathology follows the Anatomy section.

Diseases of different parts of the eye are covered in the Pathology Section. An introduction in each component of this portion of the Program covers the important diseases so that a beginner can obtain an overview without becoming overwhelmed with the vast content. Other units cover Tissue Reactions, Developmental Anomalies, Inflammation, Infections, Tumours, Cysts, Vascular Disorders, Metabolic Disorders, Trauma and other pathological states. Specific diseases are highlighted as hotwords and persons wishing to become conversant with details about any of them can do so via embedded links to detailed documentation and then return from whence they came. As in the Anatomy Section, direct links can be made between Pathology and Anatomy and the user can readily return to the same page after viewing part of the Anatomy. At the end of each unit, the user has the choice of continuing to the next one, going back to the main menu or picking another alternative portion to study.

A section containing clinicopathological cases provides selected clinical information followed by a multiple-choice question, which must be answered correctly before moving on to the next section. If an incorrect answer is selected the user is provided feedback and can continue until the correct answer is obtained. At the end of each case, a discussion is provided together with appropriate references.

Each disease is covered in the same format and has seven pages that cover sections on Overview, Introduction (definition, synonyms, history, epidemiology and prevalence, cause), Pathobiology (histopathology, pathogenesis, basic defect, biological behaviour and prognosis), Systemic Manifestations, Ophthalmic Manifestations, Diagnosis (diagnostic tests, differential diagnosis) and Treatment.

Multiple-choice questions are dispersed throughout the program and the user selects an answer by clicking on the statement that is considered correct. Immediate feedback is provided as to whether the answer is correct or incorrect. With wrong answers an explanation is given and the user can try other answers until the precise one is found. In addition a specific examination section provides options of a practice or final examination. Both have questions on Anatomy or Pathology. Questions are derived at random from a large computerised database containing hundreds of multiple-choice questions. The user clicks on the selected answer. The practice mode provides immediate feedback as to the correctness of the response. Feedback is also obtained in the review mode at the end of the test, when the user receives a score for the exercise. In the final examination, the questions are identical to those in the practice mode but there is no immediate feedback as to the correct answer. The answer selected by the user is indicated below the question. The user continues to answer questions until they are all completed. The user can change the answer in the final examination if desired and can also go backwards and review as well as change answers to previous questions. The user can finish the examination by continuing to the last question, or can stop at any time. The user is told how many questions are correctly answered and has the option of reviewing the incorrect answers if interested.

Additional components of the program contain numerous references and an interactive glossary. Representative references for additional reading related to topics covered on that page become available if desired by clicking on a reference button. By clicking on glossary hotwords, the meaning appears on the screen.

Databases on diseases, images, references and questions can be searched directly, as can the glossary. The disease database can be searched under the disease process or alphabetically according to the name of the condition. Free text searches are not allowed because users often misspell words.

A notebook feature allows the user to copy text from any pages of interest directly into an ASCII text file that can be imported into any wordprocessing program or downloaded to a printer. At any stage in the program the user can also print the entire screen.

The comprehensive online Help section illustrates the features of the program and works in the same way as the program.

Currently, the program is approximately 75% complete and we hope to release version 1 of the product in 2002. When complete, this extremely ambitious program will contain information on all diseases that involve the eye and its adnexa.

Future of Ophthalmic Pathology

We have reached the most exciting period in the history in Biomedical Research. There are boundless opportunities in Ophthalmic Pathology and the armamentarium of research techniques and computerised databases applicable to the study of ocular

disease is greater than ever. Diseases of the eye can be studied by methods that are extremely powerful and which were unimaginable when Ashton embarked upon his career. Within a few years all human genes will be known and future research will focus on the elucidation of the metabolic pathways controlled by these genes and on how they are disrupted under pathological conditions. In addition communications throughout the world move at an amazing speed as result of telecommunications, the Internet and e-mail.

Unfortunately we have also entered a period of uncertainty in which the future existence of Ophthalmic Pathologists is being questioned. That at least some academic institutions still recognise a need for Ophthalmic Pathologists is reflected in the fact that several faculty positions exist, including some that are vacant. Many Ophthalmologists and Pathologists have an interest in Ophthalmic Pathology and different degrees of knowledge about the subject. Unfortunately, despite numerous opportunities, the subspecialty is not attracting sufficient potential candidates.

Very few medical graduates are being trained specifically in Ophthalmic Pathology and the vast majority of general pathologists and neuropathologists are not exposed to the enormous body of information on ocular disease. Indeed official accredited training programs in Ophthalmic Pathology do not exist and at present no organisation provides an examination on competence in Ophthalmic Pathology. To issue reports on pathological tissue obtained from the eye and its adnexa in the USA, certification by the American Board of Pathology or by the American Board of Ophthalmology with fellowship training specifically in Ophthalmic Pathology is needed. A variety of reasons for not selecting a career in this discipline have been identified and financial disincentives exist. The low volume of surgically excised specimens in most hospitals generates insufficient income to support an Ophthalmic Pathologist for providing diagnoses on such specimens. Funding can come from Departmental resources, philanthropy, research grants and contracts, but salaries for Ophthalmic Pathologists are generally low relative to the effort and in no way near comparable to what general pathologists or other subspecialists in Ophthalmology, such a vitreoretinal surgeons and corneal specialists, who perform LASIK, can generate.

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