Dr Ashirwad Merve

Diagnostic neuropathology – old wine in new bottles

Diagnostic neuropathology is now recognised by the GMC as a discrete specialty. This article provides a wonderful insight into this 'new' specialty, from an author whose enthusiasm for the subject is never in doubt.

First of all, I would like to thank Royal College of Pathologists (RCPath) for providing this platform to write about diagnostic neuropathology – a specialty which has transformed in recent years. In this article I have focussed on recent changes and developments in the specialty, and I have also included an overview of training and recruitment, ending with few points about the specialty from a personal perspective.

What's in a (new) name?

In the UK, since 2012, 'diagnostic neuropathology', previously known just as 'neuropathology' has evolved as a separate specialty. It has uncoupled from histopathology and is now recognised by the General Medical Council (GMC) as a specialty in its own right. Diagnostic neuropathology is concerned with diagnosis of diseases of the central nervous system (CNS), peripheral nervous system and skeletal muscle. It involves reporting on the pathology of neurosurgical tissue resections/biopsies, intra-operative smears/frozen sections, skeletal muscle and peripheral nerve biopsies, neurocytology (mainly cerebrospinal fluid) specimens. It also involves performing full autopsies and examination of post-mortem brain/spinal cord as a part of coronial, hospital, forensic or brain bank work.

Informal subspecialties include CNS tumours, neurodegeneration, skeletal muscle, epilepsy, paediatric and forensic neuropathology. Neuropathologists work with multidisciplinary teams to ensure appropriate clinical management of CNS-related diseases. Neuropathologists are actively involved in research, bridging the gap between clinicians and basic scientists. Most neuropathologists undertake undergraduate and postgraduate teaching.

New developments

Progress in molecular biology and genetics has revolutionised the laboratory diagnosis of many groups of neurological diseases. Neuropathology stands at the forefront of implementation of these developments. Although by no means exhaustive, a few major developments are summarised below:

Tumours: The 2016 update to 4th edition of WHO Classification of the Central Nervous System[1] is probably the most conspicuous development in the field of neuropathology in recent years. For nearly a century, the classification of brain tumours has been based on histological parameters. The 2000 and 2007 WHO classifications considered underlying genetic changes along with histological features. The genetic status, however, had served as supplementary information until now. By contrast, the 2016 classification incorporates well-established molecular parameters into the classification of brain tumours. Combined phenotypic-genotypic diagnosis, popularly known as 'integrated diagnosis', is now implemented. This represents a major restructuring of the diffuse gliomas, medulloblastomas and other embryonal tumours. For example, the commonest brain tumour glioblastoma is now classified as glioblastoma IDH-wildtype; glioblastoma IDH-mutant; and diffuse midline glioma, H3 K27M-mutant.

Neurodegeneration/dementia

The process of classification of neurodegenerative diseases, dementia in particular, has substantially improved over decades of meticulous clinicopathological correlation and by discovery of biomarkers. The neuropathological (post-mortem brain examination) diagnosis of dementias has gained importance, partly because a definitive diagnosis can only be achieved by histopathological and biochemical studies. There is increasing awareness of hereditary diseases, which makes a definitive diagnosis important to families for prognostication and counselling, and increasing prevalence has resulted in the recognition of dementia as a priority for healthcare and social support systems. As an example of a significant development in this field, neuropathological reporting of Alzheimer's disease is now based on updated criteria known as the National Institute on Aging/Reagan Institute of the Alzheimer Association Consensus Recommendations.[2]

Diseases of skeletal muscles

Recent years have seen dramatic developments in the diagnosis of neuromuscular disorders. The main reasons for this are: improvements in protein-

based assays; enhanced clinical and electrophysiological studies; wider application of magnetic resonance imaging; and, importantly, the molecular genetic revolution brought about by techniques such as next-generation sequencing. This started with the identification of the gene responsible for Duchenne muscular dystrophy, following which the genetic basis of numerous neuromuscular disorders is now known.[3] The list is growing almost on a weekly basis, and includes genetic diagnosis for spinal muscular atrophy, myotonic muscular dystrophies, limb-girdle muscular dystrophy and facioscapulohumeral muscular dystrophy.

Delivery of diagnostic neuropathology services: workforce considerations.

The Royal College of Pathologists' Neuropathology Specialist Advisory Committee,[4] along with the British Neuropathological Society (BNS),[5] have recently developed a proposed NHS England service specification involving a network of neuropathology services across England, to ensure the sustainable and equitable delivery of diagnostic neuropathology. A diagnostic neuropathology quality assurance programme is used across the world to confirm diagnostic ability of pathologists examining CNS tumours. These organisations have also supported telepathology for remote intra-operative diagnostics in centres where appointment of a full-time diagnostic neuropathologist is not viable. This ensures equitable access to specialist services to areas of lower population density.

As per the compendium collated in 2015–2016, there are 31 NHS Neuroscience centres in the UK, including four in Scotland and one in Wales. Six of these centres do not have their own neuropathology departments and rely on geographically proximate neuropathology departments to service their requirements. One centre maintains a neuropathology laboratory with reporting networked with another centre.

In the UK, currently there are approximately 65 consultants (including full-time and part-time consultants). In addition to being fully employed NHS consultants, many hold formal academic positions such as senior clinical lecturers with university contracts. Several consultants are at the forefront of research fields including those that were set as national priorities by the government, such as neurodegeneration. Owing to to the expected imminent retirement of many consultants in diagnostic neuropathology, there has been a drive to increase trainee intake, which is currently at around four per year.

New recruitment and training process

Prior to 2012, recruitment to training in neuropathology was solely from the histopathology stream. The position of diagnostic neuropathology as a specialty is distinguished by the fact that in addition to histopathology, it recruits from clinical neurosciences specialties such as neurology and neurosurgery.

Training in diagnostic neuropathology is regarded as higher specialty training. Post- graduate trainees discover diagnostic neuropathology as a career option when they are in histopathology training or training in neurology/neurosurgery rather than in core medical/surgical training. They may encounter neuropathologists in practice within the context of a multidisciplinary clinical neuroscience service.

Currently duration of training in diagnostic neuropathology is four years full-time equivalent.[6] Basic criteria for entry is at either ST2+ level from histopathology having completed FRCPath part 1 or ST3+ level if moving from neurology/neurosurgery (clinical neurosciences) having passed MRCP or MRCS or equivalent. Those entering from clinical neurosciences stream will have to do a basic histopathology rotation for one year equivalent before they sit FRCPath part 1. Those entering from the histopathology stream are required to do basic clinical neuroscience attachments for one year equivalent. The current scheme does not stipulate a single required 'core' training; it rather stipulates the competences required of a neuropathologist. Following achievement of required competencies for both streams of intake, a two year common 'consolidation' phase is recommended (figure 1).

Currently there are 11 trainees across the UK, based in Southampton, Oxford, London, Newcastle, Cambridge, Bristol, Glasgow and Edinburgh.

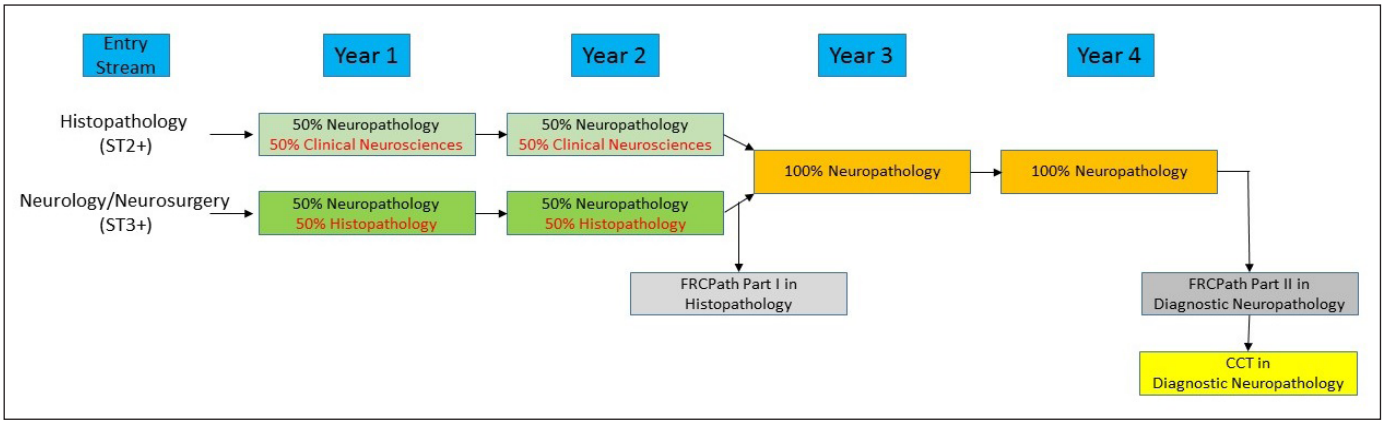

Figure 1: Entry and training pathway in diagnostic neuropathology. Adapted from RCPath curriculum and assessment system for specialty training in diagnostic neuropathology.[6]

Current trainees along with tutor Prof. Johannes Attems at a recent SpR training day held in Newcastle. Standing (left to right): Ashirwad Merve, Aled Daniels, Prof. Johannes Attems, Mark Fabian, histopathology trainee name not known, Colin Saysell, Abel Devadass. Sitting (left to right): Annelies Quagebeur, Miren Aizpurua, Olimpia Curran. SpRs not in the picture: Atul Kumar, Kevin Kinch, Javier Alegre.

Several other centres are looking to have trainees in the near future.

Perks of neuropathology – a personal note

Coming from the histopathology stream with no prior neuroscience experience, it was a steep learning curve in the initial two years. Of course, one needs to have a quest for knowledge and eagerness to learn new subjects. Many diagnostic challenges and constant intellectual stimulation were part of the process which I have thoroughly enjoyed. Participation in multidisciplinary team meetings involving neurosurgeons, neurologists, neuroradiologists and allied neuroscience specialty staff has been very interesting. Importantly, it has given me fantastic opportunities to become involved in research and academia. I am glad to say this has enabled me to achieve accolades such as the RCPath research medal award in 2015 and Pathological Society plenary presentation prize in 2017.

Diagnostic neuropathology offers opportunities to subspecialise and have academic interests in numerous areas such as neuro-oncology, the musculoskeletal system, neuro-inflammation, neurodegeneration, epilepsy, prion diseases, paediatric, perinatal and forensic neuropathology. We are fortunate to have world-class experts and mentors available in the UK for each of these subspecialties. The (BNS) is the key membership organisation for national and international neuropathologists, neuroscientists and clinicians.[5] The Annual BNS meeting and alternate year BNS summer school meetings are both educational for trainees and a platform to network and collaborate with people from other departments nationally and internationally. The training programme is highly organised and we even have BNS-sponsored teaching days held three times a year held at various centres (picture 2).

Naturally, in choosing a specialty, one must consider personal choices and interests, including geographical location and family circumstances. Nevertheless, if you are even remotely captivated by the complexity of the brain, then diagnostic neuropathology will surely be a very promising specialty for you. Although 'small', it is certainly 'beautiful'. With its new face as a specialty, recent scientific and technological developments, a fantastic support network across the UK and dedicated teaching centres, I doubt anyone would regret making this career choice. Visiting your nearest neuropathology department, reading other available articles[7] and speaking with trainees or consultant neuropathologists is advised. I would like to end with one of my favourite quotes, by Abraham Lincoln – "whatever you are, be a good one" .

Dr Ashirwad Merve
NIHR Clinical Lecturer and Senior SpR in Neuropathology
Former Member of Neuropathology SACText

References

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (eds). *WHO Classification of Tumours of the Central Nervous System (4th edition).* Lyon, France: International Agency for Research on Cancer, 2016.
2. Hyman BT, Phelps CH, Beach TG, Bigio EH, Cairns NJ, Carrillo MC *et al.* National Institute on Aging – Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimers Dement* 2012;8:1–13.
3. Kaplan JC, Hamroun D. *GeneTable of Neuromuscular Disorders.* Available at: www.musclegenetable.fr
4. The Royal College of Pathologists. *Neuropathology Specialist Advisory Committee.* Available at: https://www.rcpath.org/profession/committees/neuropathology.html
5. British Neuropathological Society. Available at: www.bns.org.uk
6. The Royal College of Pathologists. *Diagnostic Neuropathology training curriculum.* 2012. Available at: https://www.rcpath.org/resourceLibrary/diagnostic-neuropathology-curriculum-.html
7. Cohen N. *A career in neuropathology.* BMJ Careers, 2012. Available at: http://careers.bmj.com/careers/advice/A_career_in_neuropathology