My Student Elective

Little people of America

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It had taken over a year of letter writing, grant applications, and visa petitioning, but as the lift doors opened I knew I had finally arrived. . . . Family groups were sitting in the waiting area and among them were several people clearly affected by dwarfism—"the little people of America" as I came to know them. This was the Department of Medical Genetics at the Johns Hopkins Hospital, Baltimore, USA, and I was beginning my student elective as a clinical clerk, seeing patients with genetically determined disorders. "Hupkins," as it is affectionately known, is a 1000-bed hospital, serving both a large residential section of east Baltimore and acting as a referral centre for rare and complex conditions. In its century of existence it has earned world renown as a teaching and research hospital. The original nineteenth-century red-brick hospital with its marble floors and cupola-roofed entrance has been skilfully incorporated into the modern glass, steel, and concrete clinical buildings. The influence of William Osler, the first professor of medicine, is still strongly in evidence, and during my visit I was to encounter just one of the syndromes originally described by him. Subsequent physicians there have lent their names to numerous clinical signs, while surgeons have pioneered procedures from the introduction of surgical gloves to the correction of congenital heart malformations. Even the patients at Hopkins have achieved world fame—for example, the cervical tumour of Henrietta Lacks has become the source of the ubiquitous HeLa cell.

Identification and counselling

After confirmation of my status I was given an identification pass and was ready to join the clinic. Passes were essential for moving around the hospital buildings as every entrance was controlled by uniformed security personnel. I found starting work comparatively easy and, at least as a student, was never troubled by the need to have malpractice insurance. Paradoxically, patient registration is far more complex, sometimes taking more than an hour as Blue Cross, Blue Shield, Medicare, or Medicaid health insurance schemes are checked. At this weekly outpatient clinic people were seen for the identification of familial syndromes and counselling about the likely prognosis and risks of recurrence. On my first day I joined a doctor seeing a 6-year-old girl with achondroplasia, a form of short-limbed dwarfism. She was complaining of back pain and reduced exercise tolerance, because her condition caused lumbar spinal stenosis. She was scheduled to have a myelogram and may need surgical decompression in the future. Her condition would eventually leave her little over four feet (1·22 m) tall. In the ensuing two months I was to see families affected by neurofibromatosis, the Marfan syndrome, osteogenesis imperfecta, and various other genetic and chromosomal conditions. For each family seen, a full medical and family history had to be taken and a thorough physical examination performed on all affected and potentially affected members. New physical signs were shown to me, and although these conditions are rare, they provided excellent opportunities to develop my skills of observation and detailed note taking. How often before had I commented on the shape of the hard palate, the configuration of the chest, or the presence of any blueness in the colour of the sclera? It became routine to measure middle-finger lengths, to pull a patient's skin up while looking for hyperelasticity, and to persuade knee and elbow joints into hyperextension. I learnt to recognise that cauliflower ears and hitchhiker thumbs are common features of the uncommon disorder of diastrophic dwarfism.

At midday the clinic members—doctors, students, case-workers, and social workers—gathered together to review the morning's cases under the watchful eye of Dr Victor McKusick, professor of medicine at Hopkins and doyen of clinical genetics. At these clinic conferences I was encouraged to relate my findings on the family I had seen, demonstrate physical signs, and commit myself towards a diagnosis in under five minutes, unaided by notes. The subsequent discussions of the possible diagnosis were always imaginative and suggestions for investigations plentiful, but it was to the senior physicians, and in particular Dr McKusick with his phenomenal memory, that attention focused in formulating the diagnosis. These conferences were a regular feature of all departments at Hopkins and provided a useful forum for the exchange of ideas and experiences between clinicians and were often used for impromptu student tutorials. After the genetics case conferences I helped counsel patients. It was rewarding to reassure a mother, recently widowed when her 34-year-old husband died of an aortic dissection due to the Marfan syndrome, that her 7-year-old daughter was unaffected. Explaining that her 5-year-old son, who already showed the typical tall, thin habitus, did have the Marfan syndrome and would have to avoid strenuous exercise with yearly follow-ups, including echocardiography, was more difficult.

Well-informed patients

Between clinics I would familiarise myself with the conditions I was scheduled to see, being directed towards the most recent journal articles, often written by staff at Hopkins. It was just as well, as the patients I saw were far more informed about their conditions than I was used to. Could this American characteristic be a trait determined by the environment of private medicine? One mother asked what would happen if her daughter with spondyloepiphyseal dysplasia congenita were to marry an achondroplast and have a family. No answer can

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yet be given for the combining of these two autosomal dominant causes of short stature, the former with a short trunk, the latter with shortened limbs, but the results are unlikely to be favourable. Currently, no treatment can be offered for modifying the responsible gene(s) themselves, but through its specialist departments the hospital is able to offer symptomatic relief for many of the problems resulting from these conditions. One orthopaedic surgeon, Steven Kopits, has devoted his career to alleviating the orthopaedic disabilities of dwarfism. He has devised operations for straightening bowed legs and preventing further spinal curvature that would otherwise produce paraplegia. In this way I gained introductions to various medical and surgical departments at Hopkins and from the specialty of genetics I was able to see a diversity of practice.

Many of the clinicians were also heavily committed to research work towards identifying these abnormal genes within the patient's genome and surveying the pleiotropic effects, apparently due to a single gene. I began a project that looked at a family in which several members in three generations had been affected by congenital inguinal hernias. Over the telephone to Pennsylvania I obtained an extensive family history which suggested a dominant pattern of inheritance. The contrast between laboratory and library study and then meeting people with these disorders provided a valuable insight and was a great stimulus to learning. During a short clinic visit I could only guess at the immense social problems of a family caring for a short-statured child and the burden that parents felt when identified as carrying a genetic disorder and having passed it on to their children.

"Funny-looking kids"

Daily, from early morning onwards, departments held seminars, research meetings, and teaching rounds at which attendance was encouraged by the provision of the staple diet: coffee, doughnuts, and journal reprints. I was spared seeing the sunrise over east Baltimore, enjoyed by the less fortunate city workers and surgical staff who were already working at 5 am. Attending paediatric genetics clinics, I saw children with inborn errors of amino-acid and carbohydrate metabolism. I was to discover that a major part of the case load was seeing FLKs (funny-looking kids). When a syndrome could not be reliably identified a full chromosome analysis was ordered in the search for new conditions, a rather costly item. Any suggestion of developmental delay necessitated a battery of tests, including full blood and urine screens for amino-acids and sugars, brain scans, and psychological evaluations. The enthusiasm of doctors there to publish papers was highlighted for me by the heated discussion over one particular FLK whose presenting complaints had never been described. There was no parental consanguinity to suggest the aetiology as a rare recessive or advanced paternal age, suggesting a possible new mutation. Chromosome studies had been normal, and the ironic end to this story was that the father of this unique FLK had been the tragic victim of a shooting some weeks earlier. This couple would have no more children, and the aetiology may never be known. Finding the whereabouts of a baby newly diagnosed as having homocystinuria, which occurs in only one in 190 000 births, and who was admitted to the PiCRU proved difficult. I knew that the PICU was the paediatric intensive care unit, but this was not to be confused with the paediatric research unit, the PiCRU. Funded by government grants, the PiCRU was the scene of many impressive patient work-ups (patient investigations).

A system of consults

Hopkins operates a system of consults whereby specialists are asked to see inpatients and give their opinions. In this way patients may get the benefit of several ultraspecialists. One 87-year-old man with persistent gastrointestinal bleeding, despite a colectomy to try and remove the area of the bleeding, was admitted under the care of his gastroenterologist. A malignancy was not thought to be the cause, and consults were duly obtained from a physician in internal medicine, a cardiologist, a haematologist, a radiologist, an anaesthesiologist, and a surgeon. When the diagnosis of Osler-Weber-Rendu telangiectasia was under consideration the genetics team moved in. After I had seen the patient I reported back to my department, and we agreed that in the absence of any cutaneous telangiectases or relevant family history we could not confirm that this was a case of Osler-Weber-Rendu telangiectasia. As the days went by barium was introduced to both ends of his gastrointestinal tract, endoscopes followed, searching deeper and deeper, contrast media were injected into arteries, and, finally, the surgeon's knife was introduced. It was a tribute to this man, himself a survivor of a plane crash in the first world war, and the standard of critical care provided by the hospital, that he went home cured, but minus a segment of small bowel. The final contribution by the genetics department to exclude a familial cause was to suggest endoscoping the man's family, now extending to great-grandchildren, in a search for possible intestinal angiomas, an exercise of rather questionable value.

Different practices

My travels on to the wards of Johns Hopkins were opportunities to compare their system to English practices. Interns (their equivalent of housemen) wearing white uniforms were indistinguishable from the nursing staff and the meaning of some of their language was obscure. "D/C IV stat. RTND ASAP," for example, ordered the drip down immediately and a return to normal diet as soon as possible! I admired interns for their willingness to perform their patients' blood counts and to Gram-stain urine and sputum samples on the wards, though I hesitated over their enthusiasm to draw arterial blood samples q2 (every two hours) on respectably pink patients with chest infections. Listening to protracted debates between residents (equivalent to our registrars) over whether the greater accuracy of the calcium concentration obtained from the extensive M12 profile justified the increased cost over the cheaper, but more restricted M6 profile was a continual source of amazement to me. Overall, the American practice that I observed seemed to be more concerned with ruling out possible differential diagnoses before making a final pronouncement than I was used to. Whether this was for medicolegal or for teaching purposes, in view of the hospital being an academic centre, I could not decide. I thought that even at the London teaching hospital that I attend we take a more pragmatic approach in diagnosis and treatment with similar results. Medical students at Hopkins worked very hard, staying up one night in three with their intern, and were always eager to learn how to "drop" central lines. For me, Hopkins will always be the archetypal teaching hospital, where I was encouraged to voice opinions and accept responsibility, where consultants would approach me to see patients with them and were always willing to answer my questions.

Central Baltimore, like other large American cities, has suffered as the more affluent communities have moved out to the suburbs. Areas around the Johns Hopkins Hospital near the city centre are not considered safe to walk through at night, though the immediate hospital blocks are closely policed. When not working I did feel restricted within the hall of residence opposite the hospital, but the gymnasium, swimming pool, tennis courts, and cafeteria were compensations. Within a week of my arrival, however, generous hospitality had been extended, and the recently redeveloped harbour area was only a short drive away. This area of shops, restaurants, and bars is the centre of much activity in the evenings. Great efforts are being made to revitalise the down-town areas, and a new underground railway is nearing completion. Washington DC, an hour from

Baltimore, offers all the museums and monuments a tourist could want.

Bar Harbor, Maine

It was with regret that I left "Balamer," as the locals pronounced it, for the final part of my elective. I had arranged a place on a two-week lecture course on mammalian genetics in Bar Harbor, Maine, 700 miles (1100 km) to the north. A flight took me to Boston, a city that claims a medical school to rival Hopkins. A six-hour drive took me into the beautifully clear area of Maine, mercifully free of the humidity that blankets Baltimore in the summer. Seeing miles of forest, broken only by lakes, was a refreshing sight after the endless grey of cities on the East Coast. The course was held at the Jackson Laboratory, a centre for research into molecular biology, neoplasia, and the aging process, using the hundreds of specially inbred strains of mice raised there. The laboratory lies a short bus ride outside the town of Bar Harbor. This charming coastal resort of white-washed timber buildings clusters around the village green, offering fine eating places between the artists' studios and galleries.

Held annually, the course content changes to reflect current interests, and this year the conference centred on progress in DNA sequencing and the interpretation of gene maps. The international group of speakers covered topics including protein structure, developmental genetics, evolution, chromosomal sex determination, HLA, and immunoglobulin genes. Workshops were held in the afternoon between the morning and evening blocks of lectures. I tried my hand at cutting out chromosomes from a metaphase spread and forming a karyotype. My inexperience coupled with windy gusts and what I still maintain were blunt scissors turned what should have been a trisomy 21, Down's syndrome, into a monosomy with a "Sellotape-induced" translocation! Biochemical screening necessitated learning to appreciate the various smells of samples of urine. The sweet smell of maple syrup urine disease later led me to discover and enjoy waffles with real maple syrup for breakfast. At the "mouse clinic" one morning examples of mouse mutants that mimic human disorders were shown. I was introduced to the reeler, the staggerer, and the stumbler mouse strains as examples of central nervous system abnormalities, but to see the achondroplastic mouse with its severely shortened limbs was truly astonishing.

Fortunately, a few days of rain maintained reasonable attendance on the course, but otherwise I found myself spending afternoons in the nearby National Park. Groups of geneticists were to be found hiking over mountains, descriptively called the Bubbles, swimming in the warm fresh water of Echo Lake, and cycling along the ocean front. I had my first attempt at deep-sea fishing, landing a three-foot (0·9 m) sand-shark among other sea creatures, but no dinner. Throughout the course new friendships were made, and the relaxed atmosphere was fostered by a week end cocktail party at High Seas, a stately mansion built on the ocean cliffs. Now owned by the Jackson Laboratory and accommodating summer students, High Seas was built in 1912 in anticipation of the arrival of the owner's future bride, sailing from England. Looking out over the Maine coastline to see the Atlantic waves driving on to the granite rocks, we learnt that she never arrived from her voyage on the *Titanic*. After the Bar Harbor course I spent a few days in New York, seeing relatives and friends. I will pause only to suggest that an elective in pathology or psychiatry spent on 42nd Street would not be dull! I flew to Gatwick and, as I took the train to London, the newspaper headlines were reporting the continuing industrial action within the health service. My memorable elective was over and I knew I was home . . . but the temptation was to go back.

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Would there be any contraindication to maintaining a hypomaniac patient on haloperidol for a short period while she is being stabilised on lithium?

There is increasing evidence that combined use of lithium and haloperidol provides more effective control of manic syndrome than either drug alone. This combination may be given to achieve control in states of acute manic excitement in which the main feature is excessive psychomotor activity. The onset of action of haloperidol is more rapid than that of lithium. Once the control is attained the dose of haloperidol may be decreased gradually and if possible the drug should be discontinued. Patients should then be maintained on lithium preparations alone; its effects as a prophylactic agent in the treatment of both unipolar and bipolar affective illnesses have recently been shown in several double-blind studies. "Stabilisation" when two drugs are used must be carried out under proper clinical control (inpatient treatment). Furthermore, the diagnosis of an affective illness should be firmly established and particular attention paid to underlying neurological, metabolic, or any other abnormality. Treatment with lithium and haloperidol might lead to side effects of the type seen during treatment with either of these drugs alone in a few properly selected patients. The combination of lithium and haliperidol should not be administered to patients with signs and symptoms of brain organicity, and special precautions should be exercised in elderly patients. Lithium should be avoided in association with some diuretic treatment, low salt diet, dehydration, vomiting and diarrhoea, and pregnancy. Whenever possible renal function should be assessed before lithium is given. It is also advisable to assess thyroid function before starting treatment with lithium. Haloperidol should be avoided in patients showing signs of basal ganglia disorders. Lithium preparations have a narrow therapeutic/toxic ratio and should therefore not be prescribed unless facilities for monitoring its plasma concentrations are available. The dose should be adjusted to achieve plasma concentrations of 0·6-1·2 mmol/l.

Recently there have been single cases reported where the patients treated with a combination of lithium and haloperidol developed severe neuromuscular side effects (rigidity, ataxia, tardive dyskinesia), and some even had permanent neurological sequelae. In most of these cases high doses of both drugs had been used. Some patients had also developed impairment of consciousness and hyperthermia. These uncommon side effects were thought to be due to high concentration of both drugs. There was a poor selection of patients with inclusion of elderly patients and possibly patients with organic brain syndrome. In some of the patients who developed "irreversible brain damage" both drugs were continued for several days after serious physical deterioration was recognised. These reports have created a negative view about concomitant administration of lithium and haloperidol. They have also generated several retrospective and prospective inquiries. The conclusions from these is that the combination of lithium and haloperidol is therapeutically useful and safe when administered to properly selected patients in moderate doses and under strict clinical scrutiny.—J RUCINSKI, senior psychiatric registrar, London.

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