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and reconstruction on the other remains controversial. Internal drainage is performed either into the duodenum as a choledochocysto-duodenostomy, or into the jejunum as a Roux-en-Y choledochocysto-jejunostomy, the latter being preferable.

The main advantage of internal drainage is the technical ease with which the operation may be performed, and the low operative morbidity and mortality. However, the ineffectual musculature and incomplete endothelial lining of a dilated cyst predisposes to stomal stenosis and resultant ascending cholangitis. The high morbidity and mortality previously associated with primary excision has been reduced by modern techniques, intensive care facilities and antibiotics. Excision also offers the added advantage of the elimination of the small, but real, risk of carcinoma developing in a choledochal cyst.[6] For these reasons, most recent reviews on this subject recommend excision and reconstruction with a Roux-en-Y jejunal loop in elective cases where a pre-operative diagnosis has been made.[1, 3, 7, 8, 9]

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Review

Nuclear magnetic resonance imaging in medicine

C S McKinstry

Accepted 2 July 1986

SUMMARY

Using the technique of nuclear magnetic resonance (NMR, MR, MRI), the first images displaying pathology in humans were published in 1980.[1] Since then, there has been a rapid extension in the use of the technique, with an estimated 225 machines in use in the USA at the end of 1985.[2] Considerable enthusiasm has been expressed for this new imaging technique,[3] although awareness of its high cost in the present economic climate has led to reservations being expressed in other quarters.[2] The aim of this article is to give an outline of the present state of NMR, and indicate some possible future developments.

HISTORY

The phenomenon of NMR was first described simultaneously by Bloch and Purcell in 1946,[4, 5] both scientists subsequently receiving the Nobel prize for their discovery. Following their initial description, NMR signals from small samples were obtained using small bore, high field magnets. Analysis of such signals allowed identification of nuclei within the sample and also differentiation of nuclei in different chemical environments; this technique of NMR spectroscopy is now a standard method of chemical analysis of small volumes but gives no spatial information. It has, in fact, been applied in humans although the technique is still at a very early stage.[6, 7]

Use of the technique for imaging in medicine required some method of spatial localisation as well as a magnet big enough to hold a patient. Also, whilst in theory any paramagnetic atomic nucleus may be studied, the relative abundance of hydrogen nuclei (protons) compared with all other species means that they are most suited to study using NMR. The first proton NMR image was published in 1973 by Lauterbur;[8] and human *in vivo* images followed in 1977[9, 10, 11] with the first pathology demonstrated in 1980.[1]

TECHNICAL ASPECTS

Physics

Only a brief description will be given here; fuller accounts are available elsewhere.[12, 13, 14] The phenomenon of NMR depends on the fact that nuclei containing an odd number of protons or neutrons behave as tiny magnets, i.e. they have a magnetic moment. Of those present in the body, the most numerous

NMR Unit, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS.

C S McKinstry, MB, FRCR, Senior Research Fellow.
(On leave from the Department of Radiology, Royal Victoria Hospital, Belfast).

are hydrogen (^{1}H), phosphorous (^{31}P), sodium (^{23}Na), carbon (^{13}C), fluorine (^{19}F) and potassium (^{39}K). The single proton nucleus of hydrogen is by far the commonest and also has the highest magnetic moment. The protons spin on their axes and, under certain conditions, when placed in a magnetic field, they can absorb and emit radiofrequency (RF) energy. This emitted energy can be detected by an appropriately tuned receiver coil and gives rise to the NMR signal.

For NMR imaging, the patient is first placed in a strong magnetic field, which is typically anything from 200 Gauss (0.02 Tesla) to 20,000 Gauss (2.0 Tesla). For comparison, the strength of the earth's magnetic field is 0.3 – 0.7 Gauss.[15] The long axis of this field is in the long axis of the patient (Fig 1) and is conventionally labelled the Z direction as shown. Protons in the body align with this field.

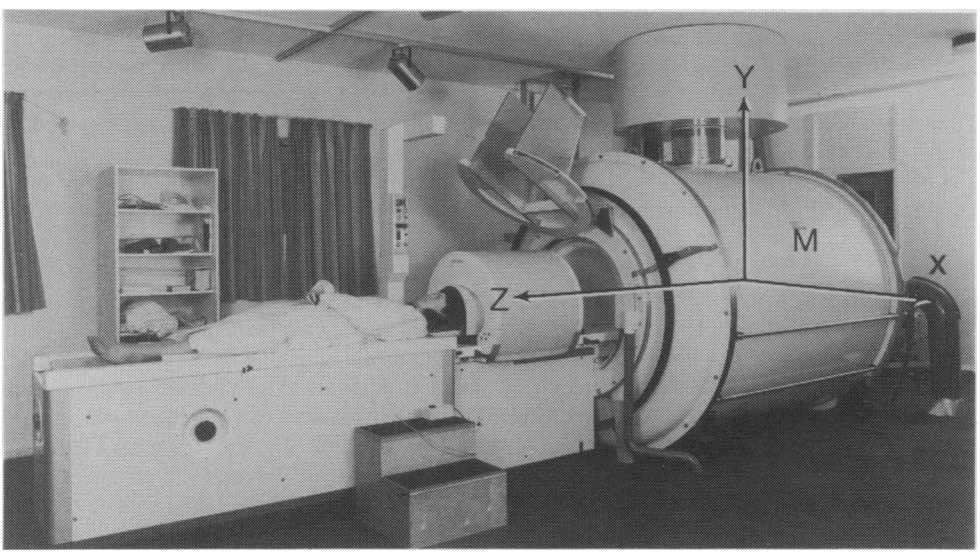

Fig 1. The NMR Scanner at the Hammersmith Hospital. Patient is in position for insertion into the circular cryomagnet (M). Relevant axes are shown (see text).

Within the bore of the magnet are transmitting and receiving RF coils; using a transmitted RF pulse of specific duration and frequency, the protons can be rotated 90° into the XY plane, and while spinning in this plane the receiver coil detects an RF signal. The strength of this signal will depend on the number of protons present (proton density, ρ). However, this signal decays rapidly; loss of coherence (phase) between the spinning protons occurs with a time constant T_2 (the spin-spin relaxation time), and the protons also return to the Z direction with a time constant T_1 (the spin-lattice relaxation time). By using different sequences of 90° and 180° pulses, the NMR signal can be made dependent to differing degrees on T_1 and T_2. A typical pulse sequence might last anything from 500msec to 2000msec and each sequence is repeated many times in order to build up the NMR image.

Selection of an anatomical slice is achieved by applying a magnetic field gradient in the Z direction so that only a 'slice' of protons responds to the transmitted RF pulse. Spatial localisation within the slice is achieved by applying X and Y gradients; image reconstruction is then carried out by computer using the

mathematical process of Fourier transformation. Flow effects can be seen on NMR because of the method of image formation. Blood which flows rapidly through the slice gives rise to no signal, because data is not retrieved from it, but slowly flowing blood may give rise to a signal ('paradoxical enhancement').[16] Quantification of flow is possible.[17]

Comparison with computed tomography (CT)

NMR sequences sensitive to T_1 and T_2 can produce images with greater soft tissue contrast than X-ray CT because of the wide range of these values for normal and pathological tissues. In CT, contrast depends on only one variable, the X-ray attenuation coefficient. However, because the relative brightness of tissues in the final NMR image may change drastically with the pulse sequence used, interpretation requires a knowledge of the physical principles involved if diagnostic information is not to be missed. Appropriate sequences must be chosen to highlight any pathology present. Transverse slices of similar thickness to X-ray CT can be obtained. However, by manipulation of the field gradients, direct sagittal and coronal images can also be obtained without moving the patient or the scanner, and oblique scans are also possible.

In CT, a single slice can be obtained in as little as two seconds, allowing breath-holding, for example in studying the chest and abdomen. In NMR, data acquisition time for a single slice is usually much longer, and may be anything up to 15 – 20 minutes for high resolution. This leads to problems with respiratory motion and patient throughput. However, it is now possible to image a number of sections simultaneously, reducing effective scanning time to levels comparable to CT.[18, 19] A method of respiratory gating without increased scan time is also available.[20]

Because of their low proton density, bone and calcium give a low signal on NMR; this is an advantage over CT in situations where artefacts from bone are a problem, for example in the posterior fossa and spine. However, bony abnormalities and calcified lesions are not well visualised with NMR. No ionising radiation is used in NMR, a major advantage especially in children and where repeated examinations are anticipated.

PRACTICAL ASPECTS

Insertion of the patient into the magnet causes claustrophobia in a small proportion of subjects. Some noise arises from the electronic gradient switching pulses but this is not usually a problem. Because of the presence of the very strong magnetic field, loose metallic objects must be excluded from the vicinity of the magnet, as must the vulnerable magnetic strip of credit cards. There is a theoretical risk of displacement of the clips used in treating intracranial aneurysms, and such patients must be excluded from study. Patients with cardiac pacemakers may also be at risk as some of these may be affected by the varying fields. No adverse effects have been demonstrated from NMR,[21] but limits on the field strength and magnitude of the varying fields and RF pulses have been set;[22] females in the first trimester of pregnancy are excluded from scanning.

CLINICAL IMAGING

All the images illustrated here were obtained on the NMR imager at the Hammersmith Hospital. This is a prototype Picker 0.15 Tesla superconducting scanner operating at a radiofrequency of 6.6 MHz.

Brain

In the early days of CT, the brain was the first organ to be studied using NMR, on account of its lack of physiological motion;[1, 23, 24, 25] consequently knowledge of the appearances of brain pathology is more advanced than for the rest of the body.[26, 27, 28, 29] Advantages of NMR over CT have been identified; these relate chiefly to the increased contrast sensitivity of NMR and lack of bone artefact. The latter is especially true in the posterior fossa.[30, 31]

Multiple sclerosis was one of the first conditions in which the high contrast sensitivity of NMR was demonstrated (Fig 2).[32] In a recent study, NMR demonstrated demyelinated plaques in 85% of patients with definite MS, compared with 25% on CT.[33] Plaques are typically seen in the periventricular white matter, centrum semiovale and posterior fossa, where they are not seen with CT. They have also been demonstrated in the cervical spinal cord.[34] A variety of other diseases of grey and white matter have also been studied.[27, 29, 35, 36, 37]

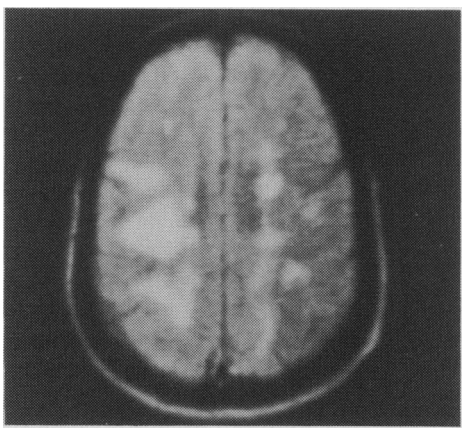

Fig 2. Transverse scan of brain in multiple sclerosis. White areas are demyelinating plaques

Cerebral tumours are well demonstrated by NMR (Fig 3),[38, 39] and the ability to provide direct sagittal and coronal studies is of value in showing their relation to other structures for planning of surgery and radiotherapy. Sagittal and coronal images of posterior fossa and brainstem lesions provide detailed information unobtainable by CT.[40, 41] In the cerebellopontine angle, the absence of bone signal may eliminate the need for CT contrast studies.[42, 43] Most tumours have an increased T_1 and T_2, but histological diagnosis on the basis of measured values has not proved possible. Benign tumours such as meningiomas may have a normal T_2 and only a moderate rise in T_1, giving rise to characteristic appearances on NMR.[44]

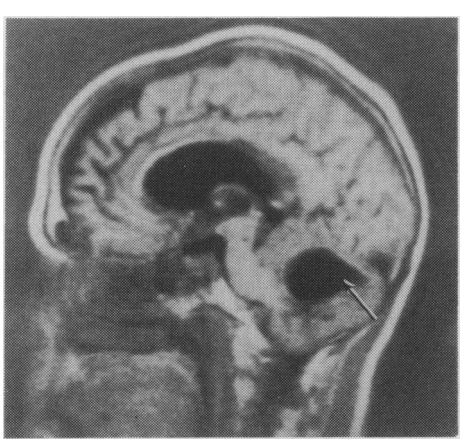

Fig 3 (a). Sagittal scan of brain. Large metastasis in cerebellum from bronchial carcinoma (arrow).

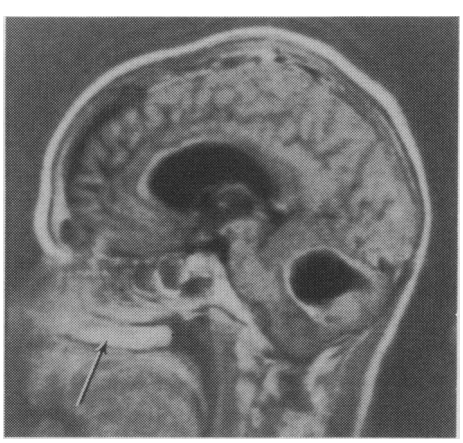

Fig 3 (b). Enhancement of tumour margin following intravenous Gd-DTPA. Note enhancement of nasal mucosa (arrow).

In cerebral infarction, increased T_1 has been visualised as early as six hours after onset.[45] Small ischaemic lesions can be seen, although their increased detection has led to difficulties in separating multiple lesion causing organic disease from lesions seen with ageing, which are also presumably ischaemic in nature.[46, 47] Intracranial haemorrhage shows a sequence of changes on NMR, with a short T_1 in the subacute stage which can allow differentiation from other pathology.[26] Subdural and extradural haematomas are well seen due to lack of signal from overlying skull.[48] Lack of signal from flowing blood is useful in demonstrating aneurysms and arteriovenous malformations.[49] A number of patients with infective conditions have been studied, and in some cases increased T_1 and T_2 lesions are seen.[27, 50]

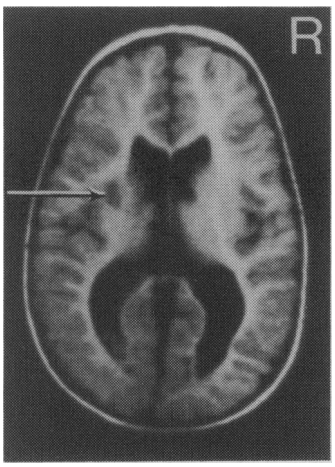

Fig 4. Transverse scan of baby at 20 months, following perinatal asphyxia. Small infarct (arrow) and delayed myelination on the left side (compare frontal lobes).

In children, a wide variety of pathology has been studied[51, 52, 53] and lack of hazard from ionising radiation is a particular advantage. In addition, NMR demonstrates the progress of normal myelination in childhood in a way impossible with any other technique. Deviations from this pattern following perinatal insults can be recognised (Fig 4).[52]

Spine

Excellent demonstration of the spinal cord and spine can be obtained using sagittal views; the cord and subarachnoid space are demonstrated without the use of contrast medium (Fig 5).[54, 55] Bone marrow in the vertebral bodies gives a high signal as does the nucleus pulposus of the intervertebral disc.[56] NMR can

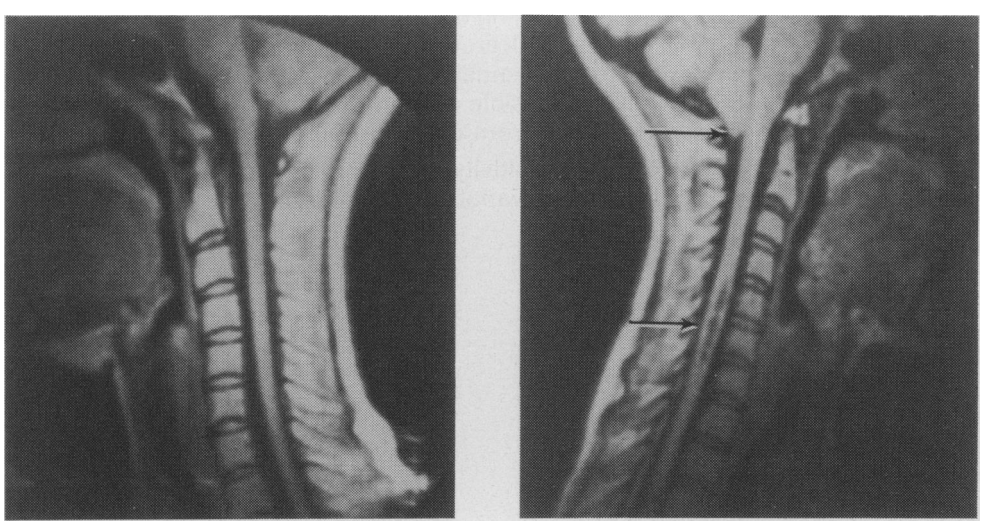

Fig 5 (a) Sagittal scan of normal cervical spine. (b) Syrinx in mid-cervical cord (lower arrow). There is also cerebellar tonsillar herniation (upper arrow) — Chiari I malformation.

therefore directly demonstrate cord abnormalities such as syringomyelia, in which the cystic cavity gives a low signal;[57] associated cerebellar tonsillar herniation can be assessed at the same time.[58] Tumours,[59] arteriovenous malformations,[60] demyelinating plaques and other abnormalities have been demonstrated.[54, 55] Disc herniation can be recognised with NMR.[61] In addition, loss of the normal signal from the nucleus pulposus may be an early signal of disc degeneration.[55, 62]

Musculoskeletal

Whilst cortical bone and calcium give a low signal on NMR, the technique has proved useful in defining the extent of bone tumours, especially within the marrow (Fig 6).[62, 63, 64] Direct coronal and sagittal scans can reveal the longitudinal extent of the tumour, which is of particular importance in planning surgery. NMR has also demonstrated marrow abnormality in leukaemia[65] and in the early stages of avascular necrosis, and may be useful in other joint disease.[62]

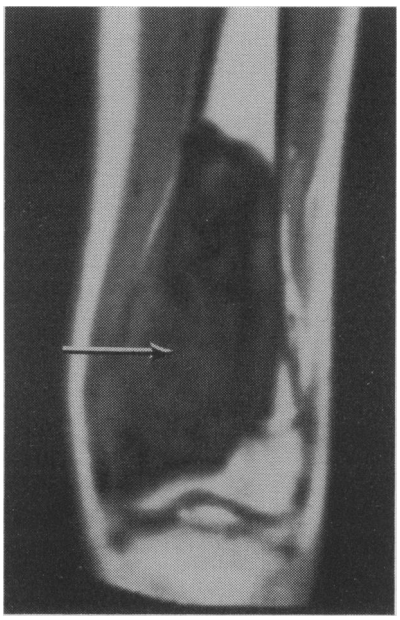

Fig 6. A coronal scan in a child with osteosarcoma of the lower femur (arrow). The tumour has broken through the epiphyseal plate inferiorly.

Abdomen

NMR imaging of the abdomen is hampered by respiratory artefact, although adequate images can be obtained. Respiratory gating[20] and special pulse sequences[66] can reduce this problem. In the liver, hepatic vessels can be identified without the use of contrast medium, and differentiation from bile ducts is possible (Fig 7a).[67, 68] This is valuable in assessing the spread of hepatocellular carcinoma prior to resection.[69] Initial studies indicated that most liver disease increased T_1 and that it might be possible to differentiate them on this basis;[70] however, this has not been confirmed.[67, 71] One possible exception is cavernous haemangioma, whose long T_2 may allow distinction from other tumours.[72, 73]

In focal liver disease, NMR has a sensitivity comparable with CT (Fig 7b).[74, 75, 76] In diffuse disease, changes are more variable. Cirrhosis may increase T_1, while in

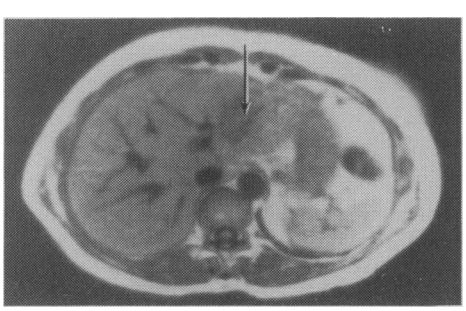

Fig 7 (a). Transverse scan of abdomen showing liver metastasis with area of low signal from calcification (arrow). Note low signal from vessels.

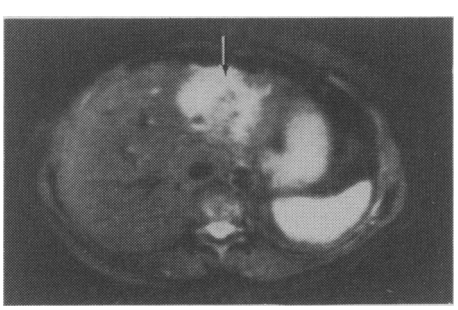

Fig 7 (b). Different pulse sequence highlights tumour (arrow).

haemochromatosis T_1 may be reduced: this has been ascribed to the paramagnetic properties of iron (see *Contrast agents,* below). However, in Wilson disease and primary biliary cirrhosis T_1 has been increased, presumably due to the cirrhosis associated with the copper deposition.[67] Fatty change has not been well visualised on NMR, although specialised sequences may show it.[76] In portal hypertension, portal vein flow has been assessed.[77]

In the kidney, NMR gives good distinction between cortex and medulla and can visualise Gerota's fascia, the adrenal glands and the renal vessels.[78] Loss of cortico-medullary differentiation has been seen in glomerulonephritis, renal failure, renal artery stenosis and transplant rejection.[78, 79] NMR can distinguish solid masses from cysts,[80] and has identified extension of hypernephroma into the renal vein and vena cava.[80, 81] The place of NMR in renal, adrenal and pancreatic disease remains to be established.[82]

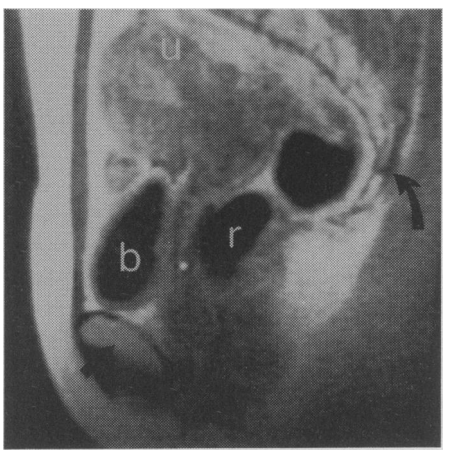

Fig 8. Sagittal scan of normal pelvis. b = bladder, r = rectum, u = uterine wall. Short arrow = pubic symphisis, curved arrow = tip of sacrum.

Pelvis

Lack of respiratory motion makes the pelvis more suited to NMR scanning, and direct coronal and sagittal images are especially valuable in assessing the cervix and uterus and conditions of the bladder base (Fig 8).[83, 84, 85] NMR has shown promise in the distinction of bladder carcinoma from other conditions and in staging the tumour although the problems are encountered as on CT in staging nodal involvement.[86, 87] In the male, the prostate, seminal vesicles and ductus deferens can be demonstrated.[85] Prostatic enlargement is well seen on sagittal studies, although initial enthusiasm for the specificity of the findings in prostatic disease has not been confirmed.[88]

In the female, myometrium and endometrium can be distinguished and cyclical endometrial changes have been seen.[83] The cervix contains a band of low signal intensity and the ovaries are also seen. Benign and malignant gynaecological conditions have been studied, although more experience is required; NMR may have a role in staging of malignancy. The pregnant uterus in the second and third trimester has been studied and also a number of first trimester pregnancies scheduled for termination. Real-time ultrasound has obvious benefits; it is safe, inexpensive and not limited by fetal motion. Nevertheless, some possible advantages of NMR have been identified. The cervix and internal os are well visualised and their relationship to the placenta evaluated. Bladder distension is not necessary, and this may be an advantage over ultrasound in diagnosis of cervical incompetence.[89] The fetus is best seen in the last trimester when movement is least,[90, 91] and the demonstration of fetal fat by NMR may be of value in assessing intra-uterine growth retardation.[92]

Thorax

Mediastinal structures are well seen on NMR, vascular structures giving no signal due to flowing blood within them.[93] This is a major advantage over CT, which

requires intravenous contrast for vessel delineation. Difficulties arise in CT in distinguishing large benign lymph nodes from those involved by metastatic tumour, but NMR encounters the same difficulties[94, 95] and lack of visualisation of calcification of benign nodes is a disadvantage. NMR may be able to improve differentiation of central tumour from distally collapsed or consolidated lung.[96] Vascular structures are well delineated and a variety of lesions have been demonstrated, including aortic aneurysm, atheroma and dissection.[97, 98]

Gating data acquisition to the R-wave of the ECG gives good images of the heart (Fig 9).[99, 100] Details of cardiac muscle, chambers, valves and papillary muscles can be seen.[100] By varying the data acquisition delay after the R wave, a series of pictures of the slice can be built up in different phases of the cardiac cycle; by 'looping' these together a cine-type moving image of cardiac motion can be obtained. Orientation of the slice to the ventricular axes may allow assessment of ventricular volumes and function.[101] However, this is time-consuming, and multi-section and volume acquisition techniques are being developed. Echo-planar imaging can produce true real-time rapid images but resolution is, as yet, poor.[102] Following successful animal studies, acute infarcts in man have been successfully imaged as areas of increased T_1.[103, 104] Subacute and old infarcts appear as areas of thinned myocardium, and aneurysms and mural thrombus have been demonstrated.[99] Congenital disorders have also been studied.[105]

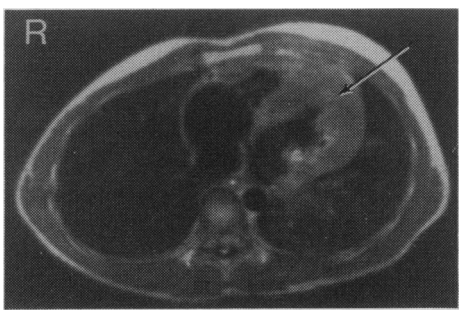

Fig 9. Transverse scan of thorax (ECG gated). Marked thickening of left ventricle in a patient with hypertrophic obstructive cardiomyopathy (arrow).

NMR images of the breast demonstrate normal ductal structures within the fatty stroma of the breast and can differentiate duct dysplasia, cysts and fibroadenoma from malignant lesions.[106] However, lack of visualisation of calcification, an important mammographic sign, is a disadvantage. NMR has obvious advantages as a possible alternative safe screening technique.

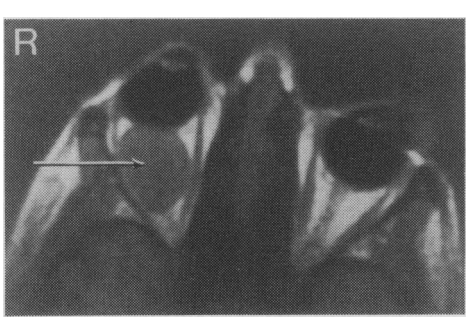

Fig 10. Surface coil study of orbits: right cavernous haemangioma (arrow).

OTHER TECHNIQUES

Surface coils

By placing a copper receiver coil close to the part being imaged, the NMR signal quality can be improved allowing increased resolution. This is of particular interest in small structures such as the orbit (Fig 10),[107] and may also be used in the inner ear, breast, spine and limbs.[108] The principle can, in fact, be extended to larger organs and, at the Hammersmith Hospital, surface coils are used for all examinations including the pelvis, abdomen, chest and brain.[109] Surface coils are now offered by most NMR manufacturers.

Contrast agents

To date, the most widely used contrast agent has been the intravenous agent gadolinium (Gd^{3+}) chelated to diethylenetriamine penta-acetic acid (DTPA). This is a paramagnetic ion which exerts local magnetic effects and reduces T_1 and T_2, thus altering or 'enhancing' the appearance of the tissue in the final image (Fig 3b). It behaves similarly to iodinated X-ray contrast media in not crossing the normal blood-brain-barrier and is excreted unchanged by the kidneys. Gd-DTPA improves differentiation between cerebral tumours and surrounding oedema[110,111] and may also improve detection of metastases.[111] Improved visualisation of spinal cord tumours has also been seen.[112] Enhancement has been observed in tumours of the liver[113] and kidney.[79]

CONCLUSION

NMR has already established itself as the imaging method of choice in several neurological conditions, while clinical experience is accumulating rapidly for the rest of the body. Study of phosphorous and of other spectra from human subjects *in vivo* has already identified some metabolic disorders, for example of muscle metabolism, although research is still at an early stage and the problem of spatial localisation with spectroscopy remains to be solved. This would be of great interest in, for example, monitoring the metabolism of tumours. Imaging using other nuclei such as sodium has also been achieved.

NMR is more costly than CT, and this together with doubts about its true role has led to a slower rate of diffusion than occurred following the invention of CT.[2] It will most likely prove to have a complementary role to CT rather than replacing it, and with increasing experience there is no doubt that NMR will find an established place as an imaging technique.

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Clinical and laboratory characteristics of patients with speckled pattern antinuclear antibodies

S A McMillan, Anne C Fay, A J Taggart, J D McCrea, S D Roberts, M W J Boyd, Jennifer K Nelson, Margaret Haire

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SUMMARY

Fifty patients whose sera contained a speckled antinuclear antibody (ANA) were interviewed and examined to determine if there was any relationship between their clinical manifestations and the presence of certain serological markers. The results suggest that speckled ANA is usually found in patients with definite connective tissue diseases, but a significant minority have incomplete or early stages of these diseases. Characterisation of the antibody to extractable nuclear antigen (ENA) and other serological markers does not normally assist in making a clinical diagnosis, but the detection of a speckled ANA should prompt further investigation and careful follow-up.

INTRODUCTION

Autoantibodies to nuclear antigens can be detected in a variety of ways. Immunofluorescent staining of tissue specimens and cultured cells can reveal antibodies reactive with nuclear components and various patterns of staining, i.e. homogeneous, nucleolar, speckled patterns have been identified and found to be diagnostically useful. In addition immunochemical tests using antigens extracted from cell nuclei (extractable nuclear antigens; ENA) can be used to identify a number of these antinuclear antibodies. A number of groups have reported the clinical significance of antibodies to extractable nuclear antigens (ENA), but these studies have generally been carried out on highly selected groups of patients

Immunology Laboratory, Belfast City Hospital.
S A McMillan, BSc, PhD, Principal Scientist.
Margaret Haire, MD, FRCPath, Consultant Immunologist.

Departments of Rheumatology, Musgrave Park Hospital and Royal Victoria Hospital, Belfast.
A J Taggart, MD, MRCP, Consultant Physician.
J D McCrea, MD, MRCP, Senior Registrar.
S D Roberts, MD, FRCP, Consultant Physician.
M W J Boyd, MD, FRCP, Consultant Physician.

Immunology Laboratory, Department of Microbiology and Immunobiology, The Queen's University of Belfast.
Anne C Fay, BSc, MB, MRCPath, Senior Registrar.

Department of Medical Computing and Statistics, The Queen's University of Belfast.
Jennifer K Nelson, BSc, Research Officer.

Correspondence to: Dr S A McMillan, Immunology Laboratory, Belfast City Hospital, Lisburn Road, Belfast BT9 7AD.

drawn from specialist clinics.[1,2,3] This selection tends to introduce a bias in favour of the speciality concerned. In an attempt to overcome this problem, we have examined the clinical and laboratory features of patients whose sera were received in a routine diagnostic immunology laboratory and gave a speckled antinuclear antibody staining pattern at a titre of one in 80 or greater, when tested by indirect immunofluorescence.

MATERIALS AND METHODS

Patients

Fifty consecutive patients on whom data were complete and who had significant titres of speckled antinuclear antibody (ANA) were selected for study. Of these 50 patients, 42 were female and eight male with a mean age of 45 years (range: 15 to 87 years). The duration of disease symptoms was between two and 31 years. Each patient was reviewed in person by a clinician (ACF, JDMcC or AJT) who completed a detailed questionnaire recording the time and nature of the onset of clinical symptoms and the course of the illness. Patients were examined for signs of disease with particular reference to the locomotor system and connective tissues. Systemic lupus erythematosus (SLE), progressive systemic sclerosis (PSS) and rheumatoid arthritis (RA) were all diagnosed according to criteria of the American Rheumatism Association (ARA).[4,5,6] The results of all previous investigations were recorded and a blood sample was taken for estimation of antibodies to double-stranded deoxyribonucleic acid (ds DNA), single-stranded deoxyribonucleic acid (ss DNA), histone, centromere, cardiolipin and extractable nuclear antigens (ENA). Rheumatoid factor (RF), complement components C3 and C4, immunoglobulins G, A and M were also measured.

Laboratory methods

Antibodies giving a characteristic speckled ANA pattern were detected by indirect immunofluorescence using 5 μm cryostat sections of rat composite tissue as substrate and fluorescein conjugated rabbit immunoglobulin to human kappa and lambda chains. The titres of antibodies in individual G and M immunoglobulin classes were determined using both fluorescein conjugated rabbit immunoglobulins to human IgG and IgM.

Antibodies to extractable nuclear antigens (anti-ribonucleoprotein, −Sm, −Ro and −La) were detected and identified using counterimmunoelectrophoresis (CIE) and various saline cellular extracts as previously described.[1,2,7,8] Antibody levels to double-stranded (ds) DNA were assayed using the Farr technique and a level of ds DNA antibody activity greater than 25 units/ml was considered as a positive result. Antibody to denatured single-stranded (ss) DNA was detected by CIE.[9] Anticentromere antibody was detected by indirect immunofluorescence using HEp 2 cultured cells as antigen.[10] Positive reference sera for antibodies to extractable nuclear antigens (ENA), ds DNA and centromere were obtained from the Centers for Disease Control, Atlanta, Georgia, USA. Antibody to histones was determined using indirect immunofluorescence and an acid-extraction histone-reconstitution assay.[11] Rheumatoid factor (RF) was assayed using the differential agglutination test[12] employing rabbit IgG as antigen and a quantitative latex assay which employed human IgG as antigen. The WHO International Reference preparation for rheumatoid factors was employed and a level of 30 IU/ml or greater was considered positive for this study. Antibody to cardiolipin was determined by a positive reaction against the Venereal Disease Research

Laboratory (VDRL) antigen with an accompanying negative reaction with the fluorescent treponemal antibody absorption test (FTA-ABS). Measurements of immunoglobulins G, A and M and complement C3 and C4 were assayed by laser nephelometry using internal standards (Beckman, UK).

Statistical analysis

Clinical and laboratory data were analysed using the 'Statistical Package for the Social Sciences' on a Vax computer at the Queen's University of Belfast. The statistical methods applied were the chi-squared test, the independent t-test and its non-parametric equivalent, the Mann-Whitney U test.

RESULTS

The majority of patients in the study group (40%) were diagnosed as systemic lupus erythematosus (SLE) with progressive systemic sclerosis (PSS) as the second most common diagnosis (18%). Patients with other connective tissue disorders comprised a further 22% of the total. The remainder (20%) had miscellaneous disorders, which included pulmonary fibrosis (with and without systemic hypertension), thrombocytopenic purpura, haemolytic anaemia and a bleeding tendency. Two patients had hypergammaglobulinaemia (IgG) and one had systemic hypertension (Table I). None of these patients was on any

TABLE I

Clinical diagnosis

Diagnosis	*Number*	*Number in group*
Systemic lupus erythematosus	15	
with Sjögren's syndrome	3	
with recurrent deep vein thrombosis	1	20 (40%)
with cutaneous vasculitis	1	
Progressive systemic sclerosis	4	
with Sjögren's syndrome	2	
with Sjögren's syndrome and rheumatoid arthritis	1	
with rheumatoid arthritis	1	9 (18%)
with polymyositis	1	
Mixed picture	4	4 (8%)
Vasculitis (small vessel)	2	
with Sjögren's syndrome	1	3 (6%)
Rheumatoid arthritis	1	
with Sjögren's syndrome	2	3 (6%)
Polymyositis	1	1 (2%)
Miscellaneous		
Pulmonary fibrosis	4	
Haematological disorders	3	10 (20%)
Hypergammaglobulinaemia	2	
Hypertension	1	
Total	50	50 (100%)

medication known to be associated with drug-induced lupus and in all cases antibodies to histones were not detected. Sjögren's syndrome, which was diagnosed clinically, was found in 18% of the patients. Sixty-two per cent of patients were receiving immunosuppressive therapy at the time of their review. These individuals were distributed evenly throughout the clinical groups irrespective of their antibody profile. Renal involvement was associated with antibody to ds DNA (50%) and decreased levels of C3 (67%). Twenty per cent of the patients with SLE and 22% of those with PSS had laboratory evidence of renal disease.

Antibody profiles

All the patients in the study had antibody to extractable nuclear antigens (ENA). The specificities of these antibodies are shown in Table II. The incidence of antibodies to ribonucleoprotein (RNP) alone, Ro and La, RNP, Ro and La, and Sm antigens were 54%, 24%, 14% and 8% respectively. Patients with antibody to Sm always had antibody to RNP and sometimes Ro. Antibodies to Sm and ds DNA were detected only in patients with SLE, whereas anti-RNP and anti-Ro with anti-La were present in a similar wide range of conditions. An important exception was PSS where all nine patients had antibody to RNP but none had antibody to Ro or La. All of these nine patients also had ss DNA antibody in their sera. Patients in the miscellaneous group had a higher percentage of antibodies to the mixture of RNP, Ro and La. Of the nine patients with Sjögren's syndrome, five (56%) had antibody to Ro and La. None of the 50 patients tested had antibodies to the VDRL antigen or to centromere. The SLE group had the highest incidence of IgG elevation and complement depression.

TABLE II

Antibody profiles of patients grouped according to clinical groups

Clinical group (patient numbers)	*ds DNA (8)*	*RNP only (27)*	*Ro/La only (12)*	*RNP/Ro/La* (7)*	*Sm** (4)*
Systemic lupus erythematosus	100	33	50	14	100
Progressive systemic sclerosis	0	26	0	29	0
Mixed picture	0	7	8	14	0
Vasculitis	0	4	17	0	0
Rheumatoid arthritis	0	7	8	0	0
Polymyositis	0	4	0	0	0
Miscellaneous	0	19	17	43	0

Figures within the table are percentages

*Antibody present to at least two of these antigens

**Sm positive (two patients Sm + RNP, two patients Sm, RNP + Ro)

Statistical findings

In view of the large number of possible associations of clinical features and serum markers, a comprehensive listing of these is not given – most were not significant.

Some of the more positive associations are shown in Table III. If values below the 1% level are considered to be clinically significant, then only xerostomia and the presence of an LE skin rash were significantly associated with particular antibodies. There was no significant association between the presence of antibody to RNP and Raynaud's phenomenon or the presence of antibodies to Sm antigen and renal or central nervous system disease.

TABLE III

Association between clinical features and the presence of serum markers

Clinical features	*Associated serum* marker*	*P value*
Eye problems at presentation	La	0.05
Joint features at review	RNP	<0.05
Signs/symptoms at any time:-		
1. Involvement of cervical spine (C1-3)	RF	<0.05
2. Involvement of cervical spine (C4-7)	RF	<0.05
3. Myalgia	RNP	<0.05
4. Dysphagia	RNP	<0.05
5. Radiological evidence of abnormal oesophageal motility	RNP	<0.05
6. Xerophthalmia	Ro	<0.05
7. Xerostomia	Ro	<0.01**
8. Xerostomia	La	<0.01**
9. Discoid LE skin rash	Sm	<0.01**

*Serum marker present at time of review

**Clinically significant

DISCUSSION

In general, these results are in keeping with previously published work. However, our patients had a much wider range of diagnoses than those drawn purely from rheumatological departments. Connective tissue disorders were diagnosed in 80% of patients but the remaining 20% had a variety of immunological, pulmonary, cardiovascular and haematological complaints. All the patients whose sera gave a speckled ANA staining pattern had antibody to ENA. Antibodies were not associated with a particular clinical diagnosis, with the exception of the association of SLE with antibodies to ds DNA or Sm. Antibody to RNP alone was detected in all nine patients with PSS. This is in contrast to a number of studies where very few of these patients (0 – 5%) had antibody to RNP.[13, 14] In a multicentre study on patients with PSS, serum antibodies to RNP characterised individuals with a PSS-overlap syndrome but did not occur in those with PSS alone.[5] In contrast, the follow-up to Sharp's original paper on mixed connective tissue disease reported that 45% of those with antibody to RNP finally developed PSS.[15] The nine patients in our study with PSS were among the oldest in the group and had the longest disease duration, so the length of follow-up may explain these discrepancies. Antibodies to Ro and La were detected in 56% of patients with Sjögren's syndrome which is consistent with previous reports. In

contrast, however, these antibodies were detected in 33% of patients with SLE who did not have Sjögren's syndrome. Other studies have shown antibody to La in only 2 – 3% of such patients.[3, 16]

The attempt to find statistically significant associations between clinical features and serological markers proved fruitless. Only xerostomia and a discoid LE skin rash were significantly associated with particular antibodies and these are unlikely to be of practical value. Despite this, our study demonstrates that the vast majority of patients with a speckled ANA do have significant disease and that the detection of this serological marker should prompt further investigation.

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Malignant melanoma over a fifty-year period: a histological evaluation

Maureen Y Walsh, H Bharucha

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SUMMARY

The incidence of primary cutaneous malignant melanoma is increasing in the developed countries. Cutaneous malignant melanomas diagnosed in our Department over a period of fifty years from 1930 to 1980 were examined to see if there was any change in their histological features. In 1930 and 1955, over 90% of malignant melanomas presented as tumours infiltrating deep into the subepithelial tissue. By 1980, 55% of tumours presented with deeply infiltrating lesions and only 20% occurred at a stage where adequate local excision could provide hope of a cure. There is thus a need for greater awareness among the medical profession and the public if we hope to be able to treat malignant melanomas at an early stage.

INTRODUCTION

Malignant melanoma is a malignant tumour arising from the melanocytes in the skin. It is the most common fatal illness seen by the dermatologist, and accounts for 1% of all cancer deaths.[1] The incidence of malignant melanoma of the skin is increasing in both sexes in developed countries, notably in fair-skinned people. It is thought that this increased incidence is related to an increase of intense and intermittent exposure to the sun. Associated with the increased incidence of malignant melanoma there have been reports of better overall survival, especially in areas like Queensland, where greater medical and public awareness ensure that the lesions are seen at an earlier stage of their development.[2, 3] This study is part of an ongoing multinational sixteen-centre project, funded by the International Agency for Research on Cancer of the World Health Organisation, to find out if there is a possibility that part of the rise in incidence is due to a change in the histological criteria used in the diagnosis of malignant melanoma.

The aim of the present study was to look at malignant melanoma presenting to our Department over a fifty-year period to see if there was any change in the histological features of the tumours and if the lesions present today at an earlier stage than they did in the past.

METHODS

Twenty lesions diagnosed as malignant melanoma were examined from the files of the Department of Pathology, Royal Victoria Hospital, Belfast, for each of three periods in 1930, 1955 and 1980. The cases were taken from the files in chronological order until 20 cases of primary cutaneous malignant melanoma were reached. In 1930 and 1955, where 20 cases were not available during the

Department of Pathology, The Queen's University of Belfast and The Royal Victoria Hospital, Belfast.
Maureen Y Walsh, MB, MRCPath, Senior Tutor/Senior Registrar.
H Bharucha, MD, MRCPath, Senior Lecturer/Consultant.
Correspondence to: Dr Walsh, Institute of Pathology, Grosvenor Road, Belfast BT12 6BL.

year, cases were taken from further years (i.e. 1931, 1956, etc.) until 20 cases were obtained. Secondary malignant melanomas occurring in the skin and non-cutaneous primary malignant melanoma were excluded from the study. The original reports were examined to obtain information about the age and sex of the patient and the site of biopsy. The original slides for the 1980 cases were available for review in the laboratory. For the periods 1930 and 1955 the original blocks were available and sections were recut. It was not known whether the blocks from the 1930 and 1955 cases had been taken from the deepest part of the tumour. If the blocks in the earlier years were not taken from the deepest part of the tumour, it can be assumed that both the Clark level and Breslow's thickness were greater than the values we obtained. The blocks in the 1980 cases were taken from the deepest part of the tumour.

In each case the following were noted:-

(a) sex of patient; (b) age of patient; (c) site of biopsy.

Microscopically the following features were recorded:-

(d) histogenetic type; (e) cross-sectional profile; (f) ulceration; (g) inflammatory infiltrate; (h) degree of pigmentation; (i) cell type; (j) evidence of regression; (k) vascular invasion; (l) evidence of pre-existing lesion; (m) elastosis; (n) Clark level; (o) tumour diameter; (p) tumour depth (Breslow's thickness); (q) number of mitoses/H.P.F. (X 40); (r) mitotic rate (mitoses/sq. mm); (s) prognostic index (tumour depth × mitotic rate) (p × r).

RESULTS

M:F Ratios

In each of the three time periods studied, the number of females was greater than the number of males and this is in keeping with the results in the literature.[4, 5, 6] There was a greater female to male ratio in the year 1980 of 2.3:1, compared with 1930 and 1955 when the ratio was 1.5:1.

Age

Malignant melanoma presented with a greater incidence from the fifth decade onwards in all three time periods. In the overall time studied there does not appear to be any change in the age group affected in the disease.

Site

The head and neck are the most common sites for the tumour to arise. The trunk, an area of relatively low sun exposure in this country, has a low incidence of tumour and there has been no change in the incidence over the period of the present study. (Table I).

TABLE I

Site of biopsy

	1930	*1955*	*1980*
Head and neck	6 (30%)	4 (20%)	8 (40%)
Trunk	2 (10%)	2 (10%)	3 (15%)
Upper limb	6 (30%)	5 (25%)	0 (0%)
Lower limb	3 (15%)	0 (0%)	7 (35%)
Site unknown	3 (15%)	9 (45%)	2 (10%)
	20 cases	20 cases	20 cases

Morphology

Almost half the tumours in the 1930 and 1955 groups and a quarter of the 1980 cases could not be classified by histogenic type.[7] The most common type of tumour was the superficial spreading malignant melanoma which accounted for 50% of the 1980 tumours and 40% of the 1930 tumours. Lentigo malignant melanoma only occurred in the 1955 and 1980 tumours, accounting for 5% and 15% respectively. (Table II).

TABLE II

Histogenic type

	1930	*1955*	*1980*
Lentigo malignant melanoma	0 (0%)	1 (5%)	3 (15%)
Superficial spreading malignant melanoma	8 (40%)	7 (35%)	10 (50%)
Nodular malignant melanoma	2 (10%)	3 (15%)	2 (10%)
Unclassifiable	10 (50%)	9 (45%)	5 (25%)
	20 cases	20 cases	20 cases

In the study, 45% of the 1930 tumours and 55% of the 1955 and 1980 tumours were predunculated. On average, over the time of the study, 50% of the lesions were ulcerated, had a light to moderate inflammatory cell infiltrate, and a mild to moderate degree of pigment, and these factors did not change over the period examined. The cell type predominant in the lesion did not show any significant change over the study period. Spindle cells were predominant in 55% (1930), 40% (1955) and 60% (1980) respectively. In none of the 60 malignant melanomas examined was there evidence of regression of the tumour.

Vascular invasion

Vascular invasion was noted in one case from both 1930 and 1980 and in two of the 1955 cases. When present, vascular invasion indicates a high risk of metastatic spread.[8]

Association with benign lesions

In the 1930 tumours, three of the malignant melanomas were associated with benign lesions: a compound naevus and two intradermal naevi. There was one case in the 1955 series where a compound naevus was associated with the malignant melanoma. Five of the 20 malignant melanomas of the 1980 cases were associated with the following lesions: lentigo, compound naevus, two intradermal naevi and a neurofibroma.

Elastosis

Elastosis due to sun damage was noted in 30% of the 1980 lesions and in 10% and 5% of the 1955 and 1930 lesions. All the cases of elastosis occurred in malignant melanomas arising in the head and neck.

Clark's levels

In 1930 no cases of Clark[7,9] level I (tumour confined to the epidermis) were recorded, and only 5% of cases in 1955 and 1980 had a Clark level I. In 1930, 80% of cases presented with Clark level IV and V (tumour involving the reticular

dermis and subcutaneous fat respectively), compared with 75% of cases in 1955, and 50% of cases in 1980. In 1980, 5% of these cases were at a Clark level V. (Table III).

TABLE III

Clark level

Level	*1930*	*1955*	*1980*
I	0 (0%)	1 (5%)	1 (5%)
II	2 (10%)	2 (10%)	2 (10%)
III	2 (10%)	2 (10%)	7 (35%)
IV	9 (45%)	12 (60%)	9 (45%)
V	7 (35%)	3 (15%)	1 (5%)
	20 cases	20 cases	20 cases

Thickness and diameter

The tumour thickness of each lesion was measured using the method described by Breslow.[10,11] In 1930, 95% of the tumours and, in 1955, 90% of the tumours had a Breslow thickness of more than 1.5mm. In 1980, 55% of cases presented with a Breslow thickness of greater than 1.5mm while 20% of cases had a Breslow thickness of less than 0.76mm and 25% were in the intermediate range of 0.76 – 1.5mm. (Table IV). In 1930, 65% of the tumours had a diameter greater than 11mm. In 1955, 45% of tumours had a diameter of more than 11mm and in 1980, 20% had a tumour with a diameter greater than 11mm.

TABLE IV

Breslow's thickness

	1930	*1955*	*1980*
<0.76mm	1 (5%)	1 (5%)	4 (20%)
0.76 – 1.5mm	0 (0%)	1 (5%)	5 (25%)
1.5 – 3mm	7 (35%)	8 (40%)	7 (35%)
>3mm	12 (60%)	10 (50%)	4 (20%)
	20 cases	20 cases	20 cases

Mitoses

The percentage of cases with fewer than one mitosis/5 high power fields was 20% in 1930, 55% in 1955, and 50% in 1980. There were 25% of 1930 cases, 20% of 1955 cases and 15% of 1980 cases with more than five mitoses/5 high power fields. The mitotic rate (number of mitoses per square millimetre) shows a slight fall over the period of the study.[11] In 1930, 20% of cases had a mitotic rate of nil compared with 40% in 1955 and 50% in 1980. (Table V).

Prognostic index

The prognostic index[12] (the product of tumour thickness and mitotic index) was less than 13 in 40% of cases in 1930, in 40% of cases in 1955 and in 65% of cases in 1980.

TABLE V
Mitotic rate

	1930	*1955*	*1980*
0	4 (20%)	8 (40%)	10 (50%)
1 – 5	7 (35%)	3 (15%)	4 (20%)
6 – 10	4 (20%)	5 (25%)	4 (20%)
11 – 20	4 (20%)	2 (10%)	1 (5%)
21 – 30	0 (0%)	2 (10%)	0 (0%)
31 – 40	1 (5%)	0 (0%)	1 (5%)
	20 cases	20 cases	20 cases

DISCUSSION

In both the 1930 and 1955 samples, cases had to be taken from more than one year to reach the required sample number in our study. This may be due to the increasing incidence of malignant melanoma, but in the earlier years malignant melanoma may have been removed and not submitted for histological examination. Over the fifty-year period of the study there has been little change in the sex, age and site on the body of the tumour of patients presenting with malignant melanoma. The predominant cell type showed little variation over the fifty-year period as did the presence or absence of ulceration.

Superficial spreading malignant melanoma was the most common histogenic type of tumour over the three periods examined. Lentigo malignant melanoma occurred only in the 1955 and 1980 samples and the incidence is higher in the latter. Lentigo malignant melanoma is a slow-growing tumour and perhaps this is why patients and doctors in 1930 appear to have ignored this lesion or at least tended not to remove it. Patients in earlier years with lentigo malignant melanoma may have presented at such a late stage in their tumour's development that accurate histogenic classification was not possible. Pedunculated tumours were most common in all the periods studied and did not show any significant variation over the fifty-year period. Vascular invasion showed no significant change over the period of the study. The association with a pre-existing lesion was more common in the 1980 cases than in the earlier years but the tumours arising in the earlier years were larger and may have destroyed any pre-existing benign lesion.

Solar damage to the skin was more commonly noted in 1980 cases than in earlier years, although the increasing number of lesions arising in the head and neck, especially the lentigo malignant melanoma type of tumour, could not have accounted solely for this. The occurrence of malignant melanoma with solar damage is increasing through the decades as seen in this series.

The number of patients in the series presenting with tumour confined to the epidermis (Clark's level I) is depressingly low: only 5% in both 1955 and 1980. There has been no change in the latter twenty-five years, when there has been an increasing awareness of the improved prognosis with early treatment of the lesion. More cases in 1980 than in earlier years were presenting with a Clark's level II or III, but it is depressing still to find 50% of cases in 1980 occurring with Clark's level IV or V, as compared with 80% in 1930 and 75% in 1955. Breslow's index of the thickness of the tumour showed a similar pattern. In 1930 and 1955

over 90% of tumours had a thickness of 1.5mm which is associated with a poor prognosis. In 1980, 55% of cases are still presenting with a thickness of greater than 1.5mm. Only 20% of cases in 1980 had a tumour thickness of less than 0.76mm, which is associated with a good prognosis.

Over the years of the study there was a steady decrease in the tumour diameter of the lesions, indicating that the tumours were presenting at a smaller size. There was a steady decrease from 25% in 1930 to 15% in 1980 of tumours with more than 5 mitoses/5 high power fields, and an increase in the number of cases with a low mitotic count. A prognostic index of less than 13 showed an increase in the number of cases from 1955 to 1980.

Gordon and Lowry found that over 75% of malignant melanoma present in Northern Ireland over the five-year period of 1974-1978 had a tumour thickness of greater than 1.5mm.[6] Our results support their finding that the majority of patients in Northern Ireland still present with malignant melanoma at a late stage with poor histological criteria and at a high risk of metastatic spread. The most likely reason for the large number of malignant melanoma presenting with poor histological criteria is lack of awareness, by both the public and the medical profession, of the importance of early diagnosis and treatment of these lesions. If patients with malignant melanoma are to present at a stage where local excision offers adequate cure and treatment, there is need for increased education of both the public and the medical profession.

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Subacute sclerosing panencephalitis in Northern Ireland: twenty years' experience

J I Morrow, K E Dowey, M W Swallow

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SUMMARY

Subacute sclerosing panencephalitis (SSPE) is a rare degenerative disease of the central nervous system that affects primarily children and adolescents. It is a late manifestation of measles virus infection. In a 20-year period (1965-85) there have been 26 cases of SSPE in Northern Ireland, a frequency of approximately one case per 1.2 million population per year. Males were affected more frequently than females. In other parts of the world the incidence of this disease has been dramatically reduced following effective measles immunisation programmes. The vaccination rate in Northern Ireland probably remains too low to have a similar effect.

INTRODUCTION

Subacute sclerosing panencephalitis (SSPE) was first recognised as a sporadic encephalitis with a subacute course in the early part of the 20th century. In 1933 Dawson described intranuclear inclusions and postulated a viral aetiology.[1] The term 'subacute sclerosing panencephalitis' was first used by Van Bogaert following careful studies of the white matter lesions.[2] In 1967 the role of the measles virus was postulated by Connolly, Allen, Hurwitz and Millar when they demonstrated measles antigen in brain cells and high titres of measles antibody in serum and CSF.[3] The first cases in Northern Ireland, also reported by Connolly, Allen, Hurwitz and Millar, were three patients who all became ill within a six-month period in 1965.[4]

SSPE is now recognised as a worldwide disease with an incidence in most studies of about one per million population per year.[5] However, even in North America where most epidemiological studies have been carried out, there has been some variation in incidence from state to state. This paper presents a retrospective study of all cases of SSPE known to the Regional Neurological Unit and the Regional Virus Laboratory at the Royal Victoria Hospital where all such cases would be expected to be referred.

CLINICAL FEATURES

During the period 1965-85 there were 26 documented cases of SSPE in Northern Ireland giving an overall incidence of 1.2 cases per million population per year. The disease had a definite predilection for males, boys being affected

Department of Neurology, Royal Victoria Hospital, Belfast BT12 6BA.
J I Morrow, MB, MRCP, Registrar.
K E Dowey, MB, MRCP, Consultant in Accident and Emergency Medicine, Belfast City Hospital.
M W Swallow, FRCP, Consultant Neurologist.
Correspondence to: Dr Morrow.

eight times more frequently than girls (23 males, three females). This male predominance has been a consistent finding in all reported series.

It has been stated that measles infection at an early age is a risk factor for the development of SSPE.[6] In this series, the age of measles infection was known in 19 cases. Three patients had measles under the age of two years, 13 between the ages of two and four years and only three over the age of four years, the average age of measles infection being 2.9 years. None of the cases had a history of measles vaccination. The age of onset of the encephalitis varied from three to 19 years with a mean of 10.8 years and there was a mean latent period between measles infection and the development of SSPE of 8.0 years, range two to 15 years. (Fig 1).

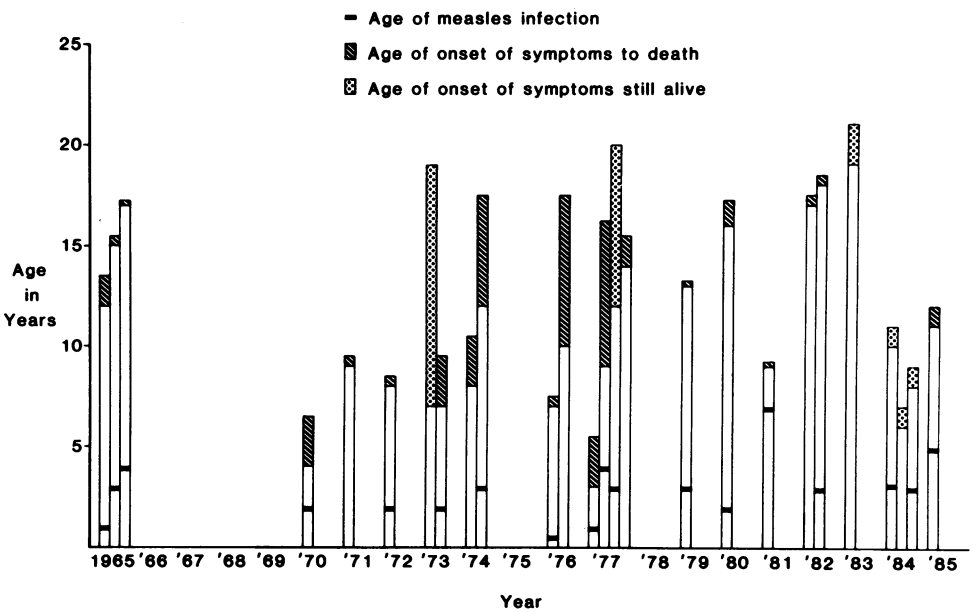

Fig 1. The age of onset of the encephalitis, and the age of measles infection in 26 patients with SSPE from 1965 to 1985.

The clinical course of the disease can be divided into four characteristic stages but there is no sharp demarcation between the stages, and the speed at which one merges into the next is variable. These stages are summarised in Table I. In this series, the first stage was most frequently characterised by intellectual impairment and changes in behaviour. The onset was often very gradual so that it was difficult to be specific about the exact time of onset of the illness. In several cases, signs were first detected by school teachers who noticed impaired intellectual performance. Deterioration in writing and school work was thought to be due, in six children, to difficulty in performing fine movements with the hands, and, in five others to some visual disturbance. Impaired powers of concentration and decreased intellectual ability followed in most cases, while 12 patients were noted to undergo personality change, most often becoming emotionally withdrawn.

Frequent falls were another common early symptom, and a history of trauma was obtained in 25% of cases. Although this was probably an effect of the disease,

the trauma was frequently cited by patient's relatives as the cause of the child's symptoms. In all cases the trauma was minor and on admission 21 of the 26 patients were noted to have unsteadiness of gait.

TABLE I

Clinical features of SSPE, in 26 patients, during the progress of the disease

STAGE 1 :	*MENTAL DISTURBANCES*	
	Intellectual deterioration	24
	Personality or behaviour changes	12
	Slurred speech	11
	Poor concentration	9
	Dressing dyspraxia	5
STAGE 2 :	*MOTOR DISTURBANCES*	
	Frequent falls/Unsteadiness of gait	21
	Myoclonic jerks	21
	Generalised/focal seizures	10
	Cortical blindness	8
	Difficulty performing fine movements with hands	6
	Other visual loss	5
	Urinary incontinence	7
	Choreform movements	2
	Facial weakness	1
STAGES 3 AND 4 :	*HYPERTONIA AND DECEREBRATION*	
	Absent speech	22
	Extrapyramidal rigidity	13
	Decerebrate rigidity	12
	Difficulty in swallowing	11
	Laryngeal spasms	3

The second stage was characterised by motor disturbances: myoclonic jerking occurred in 21 patients and generalised seizures in 10. At this stage the virus is thought to have spread to the white matter and focal deficits such as cortical blindness were sometimes apparent. This second stage lasted for a variable length of time, but in all cases the disease followed a progressive downhill course, and during the later stages there was further loss of higher cortical function with increasing lower limb spasticity. This progressed to severe extrapyramidal rigidity and finally complete loss of cerebral cortex function and akinetic mutism.

Twenty of the patients have died, usually from terminal lung infections. Six are still alive, at least three of whom appear to have gone into a state of remission, a previously recognised feature of the condition,[7] sometimes resulting in survival for many years despite severe disablement.

INVESTIGATIONS

EEG

All 26 cases had an electroencephalogram. The typical tracing of SSPE is a slow background activity of 4 – 8 c/s with periodic outbursts of high amplitude slow waves at approximately 3 c/s occurring at intervals of 10 – 15 seconds, which may be accompanied by generalised myoclonic jerking.[8] This type of tracing was seen in 25 of the 26 cases, but the timing of the investigation is important as in many cases the initial EEG was non-specific showing a generalised abnormality or even, as in three cases, a focal abnormality. (Table II).

TABLE II

Investigations

						Measles Ab Titre		*Typical*
		Typical	*Cerebrospinal fluid*					*histological*
Patient	*Sex*	*EEG*	*Protein*	*WCC*	*Lange*	*Serum*	*CSF*	*findings*
1	M	Yes	N	N	P	2048	128	Yes
2	M	Yes	N	N	N	1024	128	Yes
3	M	Yes	N	N	N	128	32	Yes
4	F	Yes	N	7	P	2560	256	Yes
5	M	Yes	.80	6	N	320	40	—
6	M	Yes	—	—	—	640	80	Yes
7	M	Yes	N	N	P	640	16	No
8	M	Yes	N	N	N	2560	—	Yes
9	F	Yes	N	N	?	640	32	Yes
10	M	Yes	N	N	N	2560	64	—
11	M	Yes	N	N	P	5120	128	—
12	M	Yes	N	7	P	5120	32	
13	M	Yes	N	N	N	2560	64	—
14	M	Yes	N	N	P	5120	64	—
15	M	Yes	N	N	N	2560	64	—
16	M	Yes	N	N	N	640	32	Yes
17	M	Yes	N	N	—	320	32	Yes
18	M	Yes	N	N	N	>10240	64	—
19	M	Yes	N	N	—	>10240	256	Yes
20	M	Yes	1.14	N	P	>10240	512	Yes
21	M	No	N	N	—	2560	16	—
22	M	Yes	(1) 0.94	20	N	160	16	—
			(2) 0.68	5	P			
23	M	Yes	N	8	—	2560	128	—
24	M	Yes	N	N	P	320	64	—
25	F	Yes	N	N	P	2560	64	—
26	M	Yes	N	N	—	1280	64	—

Protein N = < .45 g/l
WCC N = < 4 cells/µl
Lange P = Paretic

CSF

Every patient had CSF analysis carried out. In 19 the protein and cell count was within normal limits. A raised protein value was recorded in four cases, in five cases there was a modest lymphocytosis of 6 – 8 cells/μl, and a further case had 20 lymphocytes/μl on the first of two occasions when lumbar puncture was carried out. A paretic Lange curve was another relatively common finding (in 11 out of 21 cases measured).

An elevated CSF measles antibody titre at greater than 1:8 was found in 25 of the patients (in the other case the CSF antibody titre was not measured). It has been shown in these cases that measles virus antibody in the CSF is specifically raised when compared with polio type 2 antibody, indicating either a selective permeability of measles virus antibody through the blood brain barrier or measles virus antibody production within the CNS.[9]

HISTOLOGY

Six of the patients had a brain biopsy performed and nine had a post-mortem examination. Three of the biopsies showed features of encephalitis with congestion of the brain. In the later stages there was nerve cell degeneration with loss of nerve fibres and glial replacement. Two cases were more specific in demonstrating inclusion bodies or measles antigen using immunofluorescence. The final case demonstrated only slight congestion of the cortex but was otherwise normal.

Post-mortem examination was performed in nine cases. While the brains appeared macroscopically normal, on microscopy extensive perivascular infiltration in both grey and white matter was found, together with degeneration and loss of neurones. In all but one case, intranuclear inclusion bodies and/or measles antigen were demonstrated. The neuronal loss was accompanied by gliosis, but with little destruction of myelin, both of which features are characteristic of this condition. (Fig 2).

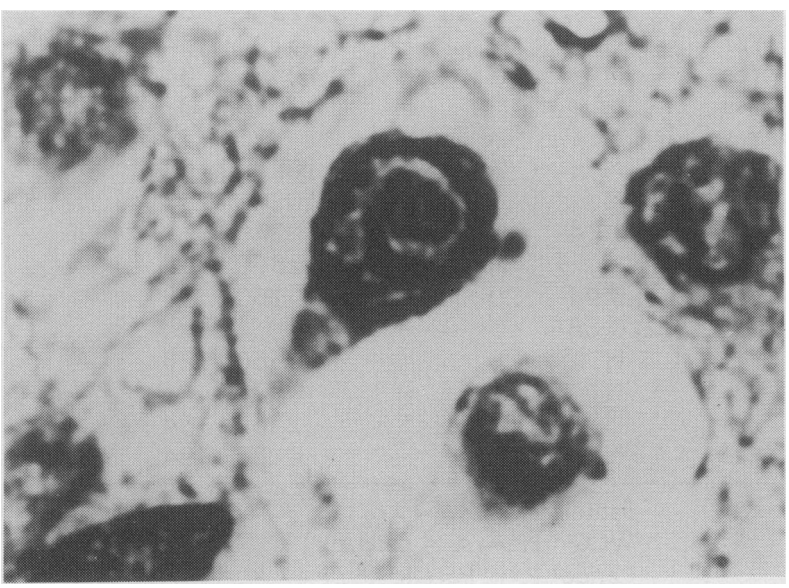

Fig 2.
Neurone with intranuclear inclusion body in SSPE, ×400. (Courtesy of Professor I V Allen).

TREATMENT

A small group of patients survived for several years and spontaneous remissions have been reported.[7] Over the last 20 years, several agents have been advocated to treat SSPE: steroids were used in two cases with little or no affect. Anti-viral therapy with amantadine (two cases), vidarabine (one case) and interferon (three cases, administered in the Hospital for Sick Children, Great Ormond Street, London), did not prove helpful in our cases although there have been reports of their efficacy from other centres.[10]

Following an observation in-vitro that the measles virus is susceptible to heat,[11] hyperpyrexial therapy was administered to five patients. This was performed by raising the body temperature to 40.5C for 18 hours on two occasions one week apart and then for 24 hours two weeks later. There was no apparent benefit. It has been suggested that patients with SSPE have a deficiency of cellular immunity and that this might be restored by small amounts of transfer factor;[12] also that plasmaphoresis might reduce the high titres of measles antibody. One of our cases therefore underwent a combination of these proposed therapies, but there was no beneficial effect.

Two of our patients received isoprinosine, a drug which is thought to have an immunomodulating effect, and which current research suggests may be more effective than any other form of therapy in reducing the mortality and morbidity of SSPE.[10] It did not alter the outcome. Palliative measures continue to have an important part to play in management, particularly the use of anticonvulsants, nutritional supplements, physical aids and good nursing care.

CONCLUSION

SSPE remains a distressing condition. It runs a progressive course with a high mortality rate and those that survive do so with profound neurological deficits. Although the measles virus has long been held to be responsible for the disease, only recently has it been more fully understood how the virus produces its effect so late after the acute infection. It is suggested that the virus enters the host at a vulnerable immunological period, then appears to escape the natural host reaction and enters the central nervous system. The CNS being a relatively protected site immunologically, the virus survives. For some still poorly understood reason the virus is defective and cannot mature into complete virions in the brain. This failure to produce virion progeny by the persistently infected cells distinguishes SSPE from acute measles virus infection and, as a result, virus antigen is not exposed to the extra-cellular space where it may be recognised and destroyed by the host immune response. Only when the cell dies and the virus is extruded does an antibody response occur.

There is so far no effective therapy. In the United States of America a decline in measles infection occurred between 1964 and 1968, and this was reflected by a similar fall in SSPE from 1971 onwards.[5] These changes appeared to correlate with the measles immunisation programme which began in 1964. Although a small number of cases of SSPE have been reported in previously immunised individuals, it has not been shown that the vaccine was responsible and the risk of developing SSPE after measles infection is 10 times greater than after vaccination.[13] To date, there does not appear to have been a similar reduction in the incidence of the disease in Northern Ireland and this is probably a reflection of our low vaccination rate which is currently around 15%. The best hope for control of the disease locally lies in achieving high levels of vaccination against measles.

We are grateful to the following colleagues for allowing us to report on cases under their care: Dr J H D Millar, Dr J A Lyttle, Dr S A Hawkins, Dr V H Patterson. Also to Dr J H Connolly of the Regional Virus Laboratory for his help and advice, and Professor Ingrid Allen for the histological data. Some of the autopsy examinations were carried out in the middle of the night in order to obtain fresh material. The five children treated by hyperpyrexia were under the care of the Intensive Care Unit at the Royal Belfast Hospital for Sick Children.

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Northern Ireland twin study 1983

P F McMullan

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SUMMARY

Two hundred and fifty-three twin deliveries in Northern Ireland during 1983 were studied. A high perinatal mortality rate of 57 per 1000 births was found, over four times greater than the overall perinatal mortality rate for Northern Ireland in that year. The main cause of these losses remains premature delivery which is frequently complicated by fetal growth retardation. Serial ultrasound scanning in the third trimester is considered mandatory in order to reduce the incidence of undiagnosed fetal growth retardation in twins.

INTRODUCTION

The antenatal diagnosis of a twin pregnancy seldom fails to create great excitement, coupled with a sense of foreboding in the patient concerned. This latter reaction is usually due to the thought of the many problems to be faced in rearing a set of twins. The patient is usually unaware of the more imminent problems associated with the antenatal course and delivery of a multiple pregnancy. Human multiple pregnancy has always been associated with a high perinatal mortality rate. Since the incidence of twin pregnancy in the developed world is falling, and is currently only 1 per cent of all births, a clearer picture of the overall situation can be obtained by studying a regional population rather than any single hospital population. This study reports on all twin pregnancies delivered in consultant maternity units in Northern Ireland during the year 1983.

PATIENTS AND METHODS

The case records of all patients with a recorded delivery of twins in any of the 18 consultant maternity units in Northern Ireland during 1983, at a gestational age of 24 weeks or greater, were studied. Details were recorded on a computer-compatible form which included information about the mother's previous medical and obstetrical history, details of the pregnancy including complications and hospital admissions, as well as information about labour, delivery and the neonatal period.

RESULTS

Twin pregnancies numbering 253 were studied.

Antenatally — Seventy per cent of patients had attended a booking antenatal clinic by 20 weeks' gestation but only 56 per cent of all the twins were diagnosed by this stage. Sixteen patients (6.4%) remained undiagnosed in labour. Ten of these patients had never had an ultrasound scan and the other six had a scan

Craigavon Area Hospital.
P F McMullan, MB, MRCOG, Senior Registrar.
Correspondence to: Dr P F McMullan, Consultant Obstetrician, Dunfermline Maternity Hospital, Dunfermline, Fife, Scotland.

which had failed to pick up the twin pregnancy. On 34 occasions (13%) the first ultrasound scan failed to pick up the presence of a twin pregnancy. One hundred and sixty-one patients (63%) required admission to hospital during the antenatal period, the commonest indications being for rest, or because of suspected pre-term labour or pre-eclampsia (Table I). Some patients suffered more than one antenatal complication. Eighty-three patients (33%) were admitted for rest in the absence of any established complication at some stage during the pregnancy, but only 49 (19%) were admitted at any point between 26 and 34 weeks' gestation.

TABLE I

Antenatal complications

	Number of patients	*Percentage of twin pregnancies*
Premature labour (less than 37 weeks)	79	31%
Mild pre-eclampsia	37	15%
Anaemia (less than 9.5 grams %)	20	8%
Threatened abortion	18	7%
Urinary tract infection	14	5%
Severe pre-eclampsia	9	4%
Antepartum haemorrhage	8	3%
Hydramnios	7	3%
Essential hypertension	4	2%
Other	4	2%

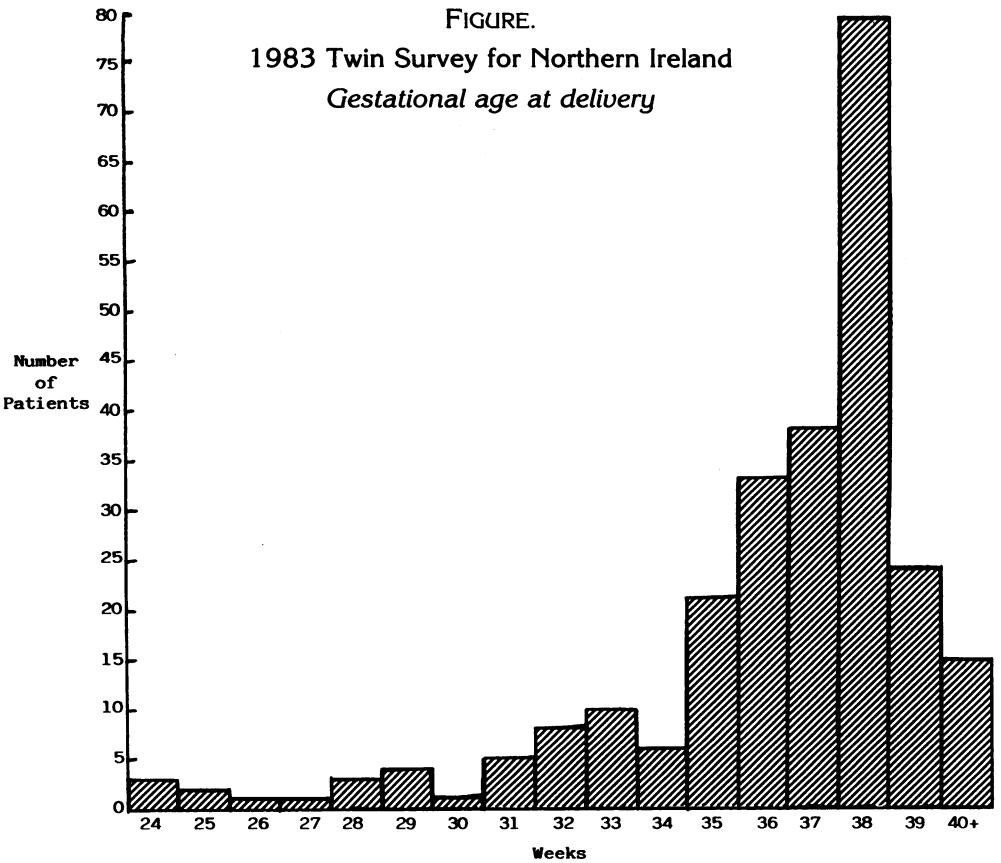
Delivery — The mean gestational age at delivery in spontaneous labour was 36 weeks (range 24 to 41 weeks). Thirty-one per cent of labours were pre-term, and 30% were induced. Forty-three per cent of all babies were delivered normally, 12.8% required an assisted cephalic delivery and 28% were delivered as vaginal breech deliveries. The Caesarean section rate was 15% and included three sections for the second twin only (Table II, Figure).

TABLE II

Mode of delivery

	Twin 1		*Twin 2*	
Normal delivery	145	57.3%	75	29.7%
Barnes Neville forceps	27	10.7%	23	9.0%
Kiellands forceps	4	1.6%	2	0.8%
Vacuum extraction	3	1.2%	6	2.4%
Assisted breech	34	13.4%	50	19.8%
Breech extraction	3	1.2%	56	22.2%
Elective Caesarean section	22	8.7%	22	8.7%
Emergency Caesarean section	15	5.9%	18	7.1%

FIGURE.
1983 Twin Survey for Northern Ireland
Gestational age at delivery



Outcome — Four hundred and sixty-four babies were born alive and were still alive at one year. Eighteen were born dead, but five of these died before 28 weeks' gestation. Twenty-two died within the first year after delivery (Table III).

TABLE III
Outcome

	Twin 1	*Twin 2*
Alive and well	235	230
Stillborn	11	7
Died day 0 – 6	5	11
Died day 7 – 28	1	1
Died day 29 – 365	1	3
5 min. APGAR less than 5	10	14
Intubated	6	14
Went to Special Care Baby Unit	79 (32.6%)	89 (36%)
Major abnormality	1	6
Minor abnormality	7	6

One fetus papyraceous was excluded from the statistical analysis. The perinatal mortality rate was 57 per 1,000 total births compared with an overall perinatal mortality rate for Northern Ireland in 1983 of 13 per 1,000 total births. The perinatal mortality rate for twin 1 was 48.2 per 1,000 and for twin 2 was 67.7 per 1,000. Thirty-two per cent of first twins and 36% of second twins required transferral to the Special Care Baby Unit. Sixty-six per cent of all the babies admitted to the Special Care Baby Units required to stay there longer than one week, and 20% remained there for longer than four weeks.

When the cause of perinatal death is studied using the Aberdeen classification,[16] 23 of the 29 deaths fall in the 'premature, cause unknown' category. Fourteen of these were due to immaturity alone and nine were associated with fetal growth retardation. Twenty-seven per cent of all the babies were born growth-retarded. Seven deaths in the immature group occurred at less than 28 weeks' gestation.

DISCUSSION

When McClure reported in 1937 on multiple pregnancies delivered at the Royal Maternity Hospital, Belfast, the stillbirth rate alone was 111 per 1,000 births, the neonatal losses not being recorded at that time.[1] This rate was approximately three times the overall rate for stillbirths in the hospital. Fifty years on, the overall perinatal mortality rate has fallen faster than that for multiple pregnancies. The high perinatal mortality rate in this study is in agreement with figures from many other studies in which the rate lay between 55 and 125 per 1,000 births.[2, 3, 4, 5] The association with prematurity is also a common feature. Late diagnosis of twins has been shown greatly to increase the perinatal mortality rate[6] and so the 13% failure to pick up twins at first scan is disappointing. It is also interesting to note that in 10 of the 20 patients who never had a scan the twins remained undiagnosed throughout the antenatal period. There has been conflicting evidence as to the value of admitting twin patients electively for rest in an effort to prevent pre-term labour. Laursen[4] showed a prolongation of pregnancy but these findings have not been confirmed in other studies.[7, 17] Only 19% of patients in this study were admitted for rest at any time during the relevant period of 26 – 34 weeks, which seems to reflect the present uncertainty as to the value of this socially unpopular practice. A definitive trial is still awaited in the hope that it may help to reduce fetal loss from uncomplicated pre-term labour.

The commonest cause of perinatal death at over 28 weeks' gestation in this study was pre-term labour complicated by fetal growth retardation. Growth retardation in one twin may be difficult to pick up clinically as it is often masked by the presence of the other well-grown twin. It may be further complicated by feto-fetal transfusion rather than by the more common placental insufficiency. Serial ultrasound scanning should therefore be mandatory in all twin pregnancies. Biparietal diameter assessments may help used on their own[8] or when used as part of a predictive screen for growth retardation using many variables.[9] Other ultrasound measurements may give more reliable indications of poor fetal growth. Neilson[10] found that the product of the crown-rump length and the trunk area identified all growth-retarded fetuses whereas, in an earlier study, 44% had been missed on biparietal measurements alone. A report by Giles et al on the use of continuous wave Doppler ultrasound to study umbilical waveforms in twin pregnancies suggests that the technique is not difficult and allows identification of the small-for-gestational-age twin in both intrauterine growth failure and the twin-to-twin transfusion syndrome.

The 15% Caesarean section rate in this study is very low in comparison with the comparable 1983 Scottish twin survey in which a section rate of 27% was found.[5] Even higher rates are reported from Europe with Papiernik reporting a 40% rate in a recent French study.[12] These higher rates reflect a significant move away from vaginal breech delivery particularly for the first twin, as advocated by several authors.[13, 14, 15] This requires closer study for this population group before any such major alteration in management is recommended.

Multiple pregnancy can be a cause of much delight but is still too often a cause of unexpected tragedy. It should not be regarded as a variant of normal pregnancy but rather as an abnormal pregnancy requiring high-risk monitoring throughout the third trimester by serial ultrasound assessment.

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The first hysterectomy in Northern Ireland?

R Blaney

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Considering that even today abdominal hysterectomy constitutes a major surgical operation, it is not surprising that it was not practised until late in the last century. One of the important indications is extensive fibroid disease and according to Bland-Sutton, writing in 1905, 'the successful removal of a uterus beset with fibroid ranks, in some circumstances, among the greatest enterprises of modern surgery'.[1]

The first successful abdominal hysterectomy in Ireland was carried out on 6 June 1878 when Thornley Stoker in Dublin removed the uterus and one ovary from a patient suffering from a large uterine tumour.[2] However, the operation came to Belfast from Birmingham by the influence of Lawson Tait, the great pioneer of gynaecological surgery. One of his pupils Dr John St Clair Boyd brought the technique home and operated on a 38-year-old unmarried woman in the Ulster Hospital for Children and Women (then situated at Fisherwick Place, on the site of the present ABC Cinema) on 18 July 1889. In the published details of the case Dr Boyd explains that the symptoms of pain and swelling in the left iliac region which had been progressive for four-and-a-half years had led to the diagnosis of a tumour.[3] Dr Calwell gave the anaesthetic. He was assisted at the operation by Professor Sinclair and also present were Professor Dill and Dr Strafford Smith. Briefly the operation was described as follows. Laparotomy showed that, contrary to the expectations, the swelling was due to a soft oedematous myoma of the uterus, and that hysterectomy was indicated. In order to facilitate the supravaginal amputation of the uterus a corkscrew was wound into the tumour and the mass pulled up through the abdominal incision. The broad ligaments were tied with silk and the whole secured at its lower part by Tait's temporary or rope clamp. The mass was prevented from slipping back into the abdominal cavity by the use of two transfixing pins through the lower segment pedicle. Below the pins a Koeberlé's *serré-noeud* clamp was applied and screwed tight. The uterine body with its enclosed myoma was then cut off above the point where it had been transfixed, the temporary clamp removed by cutting the rope, the abdominal incision closed with silk sutures, and the stump, which apparently had been stitched to the wound, was dressed with perchloride of iron and glycerine. The operation lasted 55 minutes. The patient was ambulant by the seventeenth day and was discharged after 35 days, wearing an abdominal belt.

In commenting on his operation Dr Boyd recounts that it was conducted on the same principle as he had seen used by Lawson Tait who had 'performed it thirty-three times consecutively with a successful result'. He also describes the operation as exactly similar to Porro's operation, as far as it concerns the uterus. The careful details of the operation and the presence of such senior colleagues mark the importance of the occasion. However, from the internal evidence in the

Department of Community Medicine, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.
R Blaney, MD, FFCM, FFCMI, DPH, Acting Head of Department.

paper it appears that this was not an elective hysterectomy. How then did the senior colleagues come to be present? The answer is clearly that all the colleagues were members of staff at the hospital and that when Boyd found that he had unexpectedly met with the opportunity of demonstrating this new operative technique it was a simple matter of calling on his colleagues who were on the premises at the time. Thomas Sinclair who assisted him was Professor of Surgery; William Calwell who gave the anaesthetic was consultant physician to the hospital, as was Strafford Smith; and Robert F Dill was Professor of Midwifery.

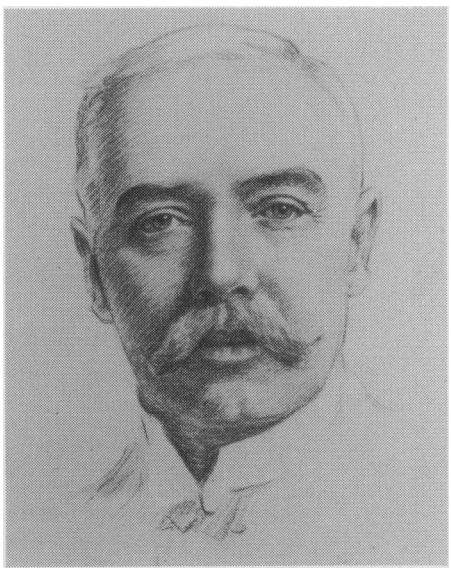

Fig 1. Dr John St Clair Boyd (1858-1918).

John St Clair Boyd, described by Robert Marshall as 'our principal gynaecologist in those days',[4] had just joined the staff of the hospital a little earlier in the year. Immediately after registration, on 29 October 1886, he had spent six weeks on the wards of the Edinburgh Royal Infirmary[5] and from there went to work with Lawson Tait in Birmingham. A publication relating to a case treated in June 1887 has been identified.[6] He must have spent the best part of a year in Birmingham and returned to Belfast in 1888 to take up an appointment as Assistant Surgeon in the Belfast Hospital for Sick Children, then located in Queen Street. When in the following year he joined also the staff of the Ulster Hospital he would presumably have had available to him the instruments necessary to carry out the Porro/Tait hysterectomy. In Arnold's *Catalogue* there are more than twenty surgical devices carrying Lawson Tait's name.[7] Among these are his myoma screw (Fig 2) and his *serré-noeud,* but strangely enough Boyd used Koeberlé's *serré-noeud* (Fig 3).

With regard to St Clair Boyd's subsequent career, he became most closely associated with the Samaritan Hospital which he first joined on 12 December 1890 as a locum for McMordie.[8] His permanent appointment began on 6 December 1892. The minutes of the hospital record that on 28 February 1894 he carried out a Caesarean section and that the baby survived.[9] No further details are available but it must be concluded that this was another pioneering operation in Belfast. Two years previously Tait had reported on what is now called the Tait-Porro operation used for performing Caesarean section in cases of placenta praevia.[10]

Outside of his surgical activities Boyd was involved in many of the cultural activities in Belfast.[11] In 1893 he joined the Belfast Naturalists' Field Club and became Secretary of the Microscope Section.[12] The Club was much affected by the Celtic Revival and Boyd read a paper to the Club on the subject of the Irish language[13] and later a report on the Celtic Class.[14] Such was his ability and enthusiasm for the subject that he was elected President of the newly formed Belfast Gaelic League on 19 August 1895. He was also closely associated with the Queen's University Gaelic Society founded by Sir William MacArthur.

Unfortunately his health began to fail while he was still relatively young and for this reason he resigned from the Samaritan Hospital in November 1905 while still only 47 years of age. He retained the title of Honorary Consulting Surgeon until his death on 10 July 1918.

I wish to thank the following for their help: Mr M J Armstrong, Mr Joseph Clint, Dr Alun Evans, Mr Gerald Kemp, Mr George Murnaghan, Mr John F O'Sullivan, Colonel Gerald Parker, Professor Jack Pinkerton.

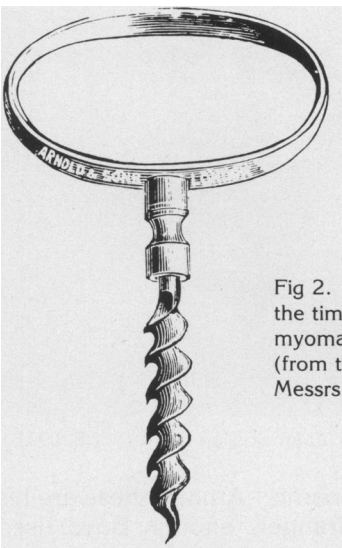

Fig. 2226.

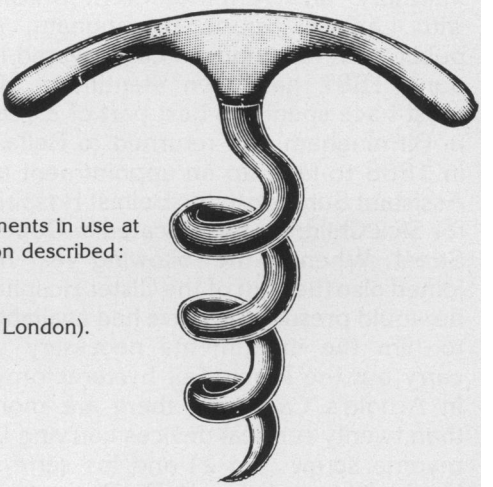

Fig. 2227.

Fig 2. Surgical instruments in use at the time of the operation described: myoma screws. (from the catalogue of Messrs Arnold & Sons, London).

Myoma Screw (Lawson Tait's), nickel-plated, Fig. 2226 . . **0 2 6**
Ditto (Greig Smith's), ditto Fig. 2227 . . **0 10 0**

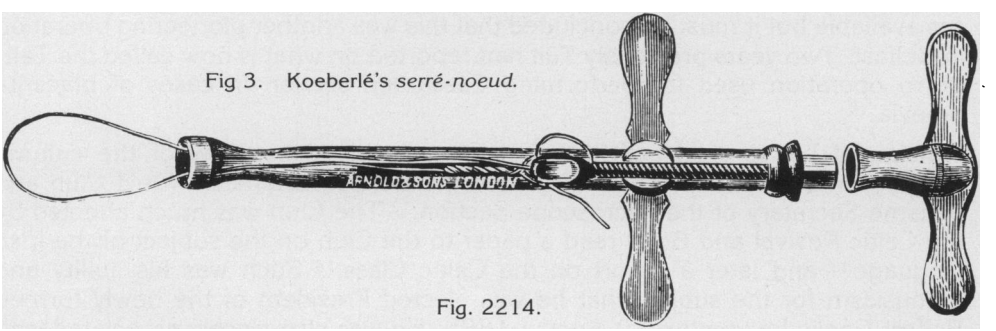

Fig. 2214.

Fig 3. Koeberlé's *serré-noeud.*

Serré-Noeud (Koeberle's), nickel-plated, Fig. 2214 . . . **0 19 0**

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Gastrointestinal hormones in alcoholic patients with and without liver disease

W W Dinsmore, M E Callender, A H G Love, K D Buchanan

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SUMMARY

To assess the effects of both alcoholism and liver disease on gastroenteropancreatic hormones, fasting and post-prandial concentrations were analysed in the following four groups: (1) Alcoholic subjects with liver disease; (2) Alcoholic subjects without liver disease; (3) Control subjects with liver disease; (4) Control subjects without liver disease.

Liver disease was associated with increased fasting serum glucose, plasma insulin, pancreatic polypeptide, gastrin and vasoactive intestinal polypeptide. Alcoholism in the absence of liver disease did not influence either the fasting or post-prandial concentrations of serum glucose, plasma gastrin, insulin, pancreatic polypeptide, gastric inhibitory polypeptide, N- and C-terminal glucagon or vasoactive intestinal polypeptide. Alcoholism with liver disease depressed plasma gastric inhibitory polypeptide concentrations. The results suggest that the abnormalities in gastroenteropancreatic hormone in alcoholics are likely to be related to liver disease which is often concurrent.

INTRODUCTION

Alcohol is known to have widespread effects on the small intestine[1] and chronic alcohol abuse is often associated with liver disease.[2] While there are a few studies available which examine the effect of either alcoholism or liver disease on gastroenteropancreatic hormones,[3-16] there are none which attempt to separate the effects of alcoholism from the effects of the frequently concurrent liver disease which in itself will distort the results due to decreased liver metabolism, blood flow and porto-systemic shunting.

Accordingly, the aim of the present study was to assess fasting and post-prandial concentrations of gastroenteropancreatic hormones in alcoholics and control groups, both with and without liver disease. The four groups studied were: (1) Alcoholics with liver disease (2) Alcoholics without liver disease (3) Patients with non-alcoholic liver disease (4) Normal volunteers. From these four groups it was hoped to draw conclusions regarding the effects of both alcoholism and liver

Department of Medicine, Institute of Clinical Science, The Queen's University of Belfast, Grosvenor Road, Belfast BT12 6BJ.
W W Dinsmore, MD, MRCP, Registrar.
A H G Love, BSc, MD, FRCP, FRCPI, Professor of Medicine.
K D Buchanan, PhD, MD, FRCP, Professor of Metabolic Medicine.
Royal Victoria Hospital, Belfast BT12 6BA.
M E Callender, MRCP, Consultant Physician.
Correspondence to: Dr W W Dinsmore, Royal Victoria Hospital, Belfast BT12 6BA.

disease on fasting and post-prandial glucose, and release of the gastroenteropancreatic hormones studied, which were gastrin, insulin, pancreatic polypeptide (PP), gastric inhibitory polypeptide (GIP), glucagon N, glucagon C and vasoactive intestinal polypeptide (VIP).

MATERIALS AND METHODS

Thirty-two alcoholic subjects (all less than 70 years), with alcohol consumption of greater than 150g/day for five or more years, were divided into a group of 13 patients (12 male and one female) with liver disease, and a group of 19 patients (18 male and one female) without liver disease. Of the 13 patients with liver disease eight had a liver biopsy and the remaining five were diagnosed as having liver disease on the basis of five to seven liver function tests which were greater than three standard deviations from the mean, (increased serum gamma glutamyl transferase, aspartate transaminase, alanine transaminase, alkaline phosphatase, bilirubin, or a reduction in the prothrombin time and serum pseudocholinesterase). The 19 patients without liver disease had all liver function tests (including gamma glutamyl transferase) and were within normal limits, (two standard deviations from the mean). Patients with intermediate liver function tests were excluded from the study. The study had approval of the Research Ethical Committee of the Faculty of Medicine, The Queen's University of Belfast. Liver biopsy was not performed on the 19 patients without evidence of liver disease. All alcoholic patients had an alcohol intake estimated from their history of alcohol consumption during the previous five years and particularly during the preceding week.

Two control groups were used in the study. A group of 17 normal volunteers (14 male and three female) from the staff and students of the hospital, all less than 70 years old, were studied. They did not have any systemic illness, were on no medication and their individual alcohol consumption was less than 10g/day. A further control group of 10 patients (six male and four female) with non-alcoholic liver disease were studied. These patients, all of whom had a liver biopsy, included three with primary biliary cirrhosis, three with chronic active hepatitis, three with idiopathic cirrhosis and one with methotrexate-induced cirrhosis.

Alcoholic patients were studied within 48 hours of admission to hospital. All subjects were fasted overnight from 10 pm prior to study. At 9 pm on the day of study each subject had an intravenous cannula secured in a forearm vein, and an initial blood sample was taken for glucose and gastroenteropancreatic hormone analysis. After 15 minutes a second fasting sample was taken from all subjects, before a standardised meal was given. The meal used in this study consisted of 60g ham, 60g white bread, 15g butter, 100ml orange juice and one cup of tea. This contained 50g carbohydrate, 18g protein and 20g fat and had an energy value of 450 kcalories. This meal was given at time 0 minutes and blood samples were taken at times, 15, 30, 45, 60, 90 and 120 minutes. The cannula was flushed out after each sample with physiological saline (0.9% NaCl). The first 3ml of each sample was discarded to prevent contamination with saline. All hormone samples were immediately transferred to cooled heparinised tubes and kept on ice before centrifugation at the end of the study. All blood samples were analysed for glucose insulin, gastrin, gastric inhibitory polypeptide (GIP), and pancreatic polypeptide (PP). In addition the fasting samples were analysed for N-terminal glucagon, C-terminal glucagon and vasoactive intestinal polypeptide (VIP). All hormones were analysed by radioimmunoassay using methods

previously established in the Department of Medicine, The Queen's University of Belfast.[17-20] The results were analysed non-parametrically using the Wilcoxon rank sum test.

RESULTS

The mean age of the patients with alcoholic liver disease was 46 years (range 28-65 years); that of the patients without alcoholic liver disease 43 years (range 21-69 years); of those with non-alcoholic liver disease 57 years (range 21-69 years), and of the normal volunteers 45 years (range 19-69 years). There were no significant differences between any of these groups.

The mean estimated daily alcohol consumption of the alcoholics with liver disease was 235g/day (range 150-400g/day) and that of the alcoholics without liver disease was 300g/day (range 150-750g/day) (N.S.). Only one patient with non-alcoholic cirrhosis drank alcohol (10g/day). The mean alcohol consumption in the normal volunteers was 5g/day (range 0-10g/day). The alcoholics with liver disease had been drinking for a mean of 19 years (range 5-34 years) and the alcoholics without liver disease had been drinking for a mean of 18 years (range 5-42 years).

Fasting gastroenteropancreatic hormone and glucose analysis

The results of fasting gastroenteropancreatic hormone and glucose analysis are presented in the Table. These fasting results are the average of the two fasting samples taken for each subject.

The fasting serum glucose concentrations were higher both in the alcoholics with liver disease and in the patients with non-alcoholic liver disease when compared with the normal volunteers ($p<0.01$). The patients with non-alcoholic liver disease had higher mean fasting gastrin concentrations than either the alcoholics with liver disease ($p<0.005$) or the normal controls ($p<0.05$). The patients with non-alcoholic liver disease had higher fasting plasma insulin concentrations than either the normal volunteers ($p<0.05$) or the alcoholics with or without liver disease ($p<0.05$).

The patients with alcoholic liver disease had higher fasting plasma PP concentrations than either the subjects with non-alcoholic liver disease ($p<0.05$) or the normal volunteers ($p<0.05$). The alcoholics with liver disease had lower fasting plasma GIP concentrations than the normal volunteers ($p<0.05$).

There were no significant differences noted in fasting plasma N-terminal glucagon or C-terminal concentrations in any of the groups. The patients with non-alcoholic liver disease had higher fasting plasma VIP concentrations than either the alcoholics with liver disease ($p<0.05$) or normal controls ($p<0.005$).

Post-prandial changes in gastroenteropancreatic hormones and glucose

There were significantly higher post-prandial serum glucose concentrations at 120 minutes in the alcoholics with liver disease (6.6 SE $\pm$ 0.8 mmol/l) than in the alcoholics without liver disease (4.9 $\pm$ 0.4 mmol/l, the patients with non-alcoholic liver disease (5.4 $\pm$ 0.8 mmol/l, or the normal controls (4.3 $\pm$ 0.2 mmol/l).

There were significantly lower post-prandial insulin concentrations in the alcoholics with liver disease (40 $\pm$ 8mU/l) than in either the alcoholics without liver disease at 45 minutes (69 $\pm$ 7mU/l), the patients with non-alcoholic liver

TABLE

The fasting plasma gastrin, insulin, pancreatic polypeptide (PP), gastric inhibitory polypeptide (GIP), N-terminal glucagon, C-terminal glucagon, vasoactive intestinal polypeptide (VIP), and fasting serum glucose concentrations in 13 alcoholic patients with liver disease, 19 alcoholic patients without liver disease, 10 patients with non-alcoholic liver disease and 17 normal controls.

(mean ± standard error)

	Gastrin ng/l	*Insulin mU/l*	*PP ng/l*	*GIP ng/l*	*Glucagon N ng/l*	*Glucagon C ng/l*	*VIP ng/l*	*Glucose mmol/l*
Alcoholics with liver disease n = 13	51±18	13±1	125±23	37± 6	177±23	123±14	90±24	4.7±0.4
Alcoholics without liver disease n = 19	72±11	10±1	95±18	63±16	185±15	113± 8	99±15	4.3±0.2
Patients with non-alcoholic liver disease n = 10	110±22	21±6	139±40	79±26	260±42	157±16	153±17	4.8±0.3
Normal volunteers n = 17	73±12	11±1	70±14	59± 6	204±11	125± 9	87±11	4.0±0.1

disease at 60 minutes (42 ± 9mU/l and 87 ± 19mU/l) or the normal volunteers at 30 minutes (32 ± 6mU/l and 68 ± 8mU/l).

There were lower plasma gastrin concentrations in the alcoholics with liver disease than in the patients with non-alcoholic liver disease at 45 minutes (49 ± 20ng/l and 160 ± 60ng/l, respectively) and at 60 minutes (54 ± 22ng/l and 140 ± 61ng/l). There was no significant difference in post-prandial plasma gastrin at the recorded times between the alcoholics with and without liver disease and the normal volunteers. There were no significant differences in post-prandial plasma concentrations of PP or GIP, between any of the groups.

DISCUSSION

In this paper alcoholics were defined as patients who have consumed more than 150g alcohol per day (approximately 15 measures or two bottles of wine) for five or more years before inclusion in the study. While this definition is arbitrary, most authorities would agree that the patients included were likely to have dependence or harm as a result of their alcohol consumption. The slightly higher mean alcohol consumption in the alcoholics without liver disease than the group with liver disease was not significant, and may be related to a decreased ability in the latter group to metabolise alcohol.

There was evidence of post-prandial glucose intolerance in both groups with liver disease in keeping with previous studies.[3] This may be due to a combination of hepatic resistance to the action of insulin and the porto-systemic shunting of both the carbohydrate load and insulin.[3,4] As there was no elevation of the fasting serum glucose concentration in the alcoholics without liver disease, the present data suggests that liver disease was responsible for glucose intolerance noted in alcoholism. Although the patients with non-alcoholic liver disease had fasting hyperinsulinism, plasma insulin concentrations in either alcoholic group were similar to that recorded in the normal volunteers and these findings are in agreement with previous work.[4,5] There is a suggestion in the present study that the elevation of fasting plasma insulin concentration is associated with the presence of liver disease (in the subjects with non-alcoholic liver disease) rather than the presence of alcoholism itself as has previously been reported.[6] There was a lower post-prandial insulin response in patients with alcoholic liver disease compared with normal controls, which contrasts with the post-prandial hyperinsulinism associated with alcoholic liver disease in previous studies.[6] These differences could possibly be related to the severity of the liver disease, patients with more severe liver disease having decreased hepatic metabolism of insulin and increased porto-systemic shunting of insulin.

The fasting and post-prandial plasma gastrin concentrations were elevated in the patients with non-alcoholic liver disease, confirming previous work in patients with cirrhosis.[7] Alcoholism, either with or without liver disease, did not affect plasma gastrin concentration.

The fasting plasma PP concentration in both groups with liver disease was higher than in the normal controls, in agreement with previous reports in both alcoholics[9] and subjects with liver failure.[8] PP is known to be a strong inhibitor of pancreatic secretion.[9] Because up to 40% of alcoholics may have pancreatic exocrine insufficiency, even in the absence of clinical evidence of chronic pancreatitis,[10] some authors have suggested that pancreatic insufficiency may be a result of elevation of PP concentrations.[5] However, there was no elevation in PP in the

alcoholic subjects without liver disease, and therefore liver disease rather than the presence of alcoholism may be the predominant influence in increasing the fasting plasma concentrations of PP.

The reduction in fasting plasma GIP in alcoholics with liver disease when compared with the normal volunteers was not observed in the subjects with non-alcoholic liver disease, suggesting that alcoholism in combination with liver disease reduces GIP concentrations. While the significance of this in unclear, GIP is known to inhibit gastric acid production in animal experiments[11] and therefore the present reduction in GIP may play a role in the hyperacidity associated with alcohol ingestion.[12, 13]

N-terminal glucagon release is thought to be a measure of both enteroglucagon and pancreatic glucagon, and C-terminal glucagon is thought to be a measure of pancreatic glucagon. There were no differences noted in either N- or C-terminal glucagon concentrations as a consequence of either alcoholism or liver disease which is in agreement with previous studies.[5]

An elevation of fasting plasma VIP concentrations in patients with non-alcoholic liver disease compared with controls has been shown previously.[14, 15, 16] Alcoholism without liver disease, however, had no apparent effect on fasting plasma VIP concentrations. It has been suggested that the elevation of VIP in subjects with liver disease is due to porto-systemic shunting, and this elevation in VIP, while small, may nevertheless be related to some of the features of liver disease including diarrhoea and cutaneous vascular changes.

The purpose of this study was to clarify the changes in gastroenteropancreatic hormones related either to chronic alcohol ingestion or to liver disease. There was no difference in fasting or post-prandial hormone release in the alcoholic group without liver disease compared with that found in the normal volunteers, indicating that alcoholism without hepatic complications does not influence gastroenteropancreatic hormone release.

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Neonatal duodenal obstruction with emphasis on cases with Down's syndrome

S R Potts, W I H Garstin

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SUMMARY

In the past 31 years, 47 cases of duodenal obstruction were admitted to the Royal Belfast Hospital for Sick Children. Thirty-six per cent of these had Down's syndrome. The crude mortality was 48% but this figure was reduced to 33% in the last five years of the study. The combination of duodenal obstruction, Down's syndrome and any other abnormality carried an 89% risk of mortality.

INTRODUCTION

Duodenal atresia occurs in approximately 1/1,500 live births. Treatment of neonatal duodenal obstruction in isolation should have a successful outcome. However, this remains a dangerous condition because of the association with abnormalities in other systems, particularly cardiac and renal. The association with Down's syndrome produces the major difficulty both pre- and post-natally. This review was therefore undertaken to establish the relative prognosis of Down's syndrome with duodenal atresia.

METHODS

The hospital records for the period 1954-1985 inclusive were examined and the following details documented for each period: gestational age, birth weight, date of birth, sex, presence of Down's syndrome and other congenital abnormalities, condition on admission, details of surgery and any subsequent complication.

RESULTS

The period under study was 1954-85 inclusive. There were 47 cases recorded, 24 boys and 23 girls. Down's syndrome was present in 17 cases (36%) — 12 boys and five girls. The crude mortality for the group as a whole was 47%, and 65% for the Down's syndrome sub-group. In the last five years of the study, five of the 15 cases (33%) did not survive. The mean gestational age was 36.5 weeks for non-Down's cases, and 37 weeks for Down's, whilst the mean birth weight was 2.58 kg for both groups. All the survivors under 2.5 kg and less than 34 weeks' gestation were born in the last 10 years. Table I shows the frequency and mortality with a subdivision for Down's syndrome over two 10-year and one

Royal Belfast Hospital for Sick Children.
S R Potts, FRCS, Senior Surgical Registrar.
W I H Garstin, FRCS, Surgical Registrar.
Correspondence to: S R Potts, FRCS, Royal Manchester Children's Hospital, Hospital Road, Pendlebury, Manchester M27 1HA.

TABLE I

Duodenal obstruction: total cases, Down's syndrome cases and survival, 1955 – 1985 inclusive

	1955 – 64	*1965 – 74*	*1975 – 85*
Total cases	10 (3)	13 (7)	24 (15)
Down's syndrome	2 (0)	3 (1)	12 (5)

Figures in brackets denote number surviving.

11-year consecutive periods. It will be seen that 12 of the 17 cases of Down's syndrome appeared in the most recent period, presumably therefore giving them the maximum chance of survival. The gradual increase in the number of cases presenting at the Royal Belfast Hospital for Sick Children is probably due to a change in the referral pattern rather than to any increase in the population incidence of duodenal obstruction.

TABLE II

Surgical profile

Site of obstruction	*Pre-ampullary*	*Post-ampullary*	*Annular pancreas*	*Incomplete obstruction*	*No information*
Total	9	30	10	9	8
Alive	8	14	4	9	7

Operation	*Duodeno-duodeno-stomy*	*Duodeno-jejuno-stomy*	*Gastro-jejuno-stomy*	*No surgery*
Total	22	18	4	3
Alive	15	10	0	0

Table II shows the distribution of surgical pathology and the operative management with an indication of survival in each group. Gastro-jejunostomy was performed only prior to 1960. No surgical complication contributed to the death of any patient in the series, and the only early complication was wound infection in three cases.

TABLE III

Duodenal obstruction with or without other congenital abnormalities

Non-Down's group		*Down's group*	
Isolated	With anomalies	Isolated	With anomalies
19 (13)	11 (6)	8 (5)	9 (1)

Figures in brackets indicate number surviving.

The associated anomalies in other systems are shown in Table III. At least one additional abnormality was present in 42.5% of cases. There was only one survivor from nine Down's syndrome babies who had at least one additional anomaly.

DISCUSSION

Our review of duodenal atresia in a captive population over a period of 31 years has shown a gradual improvement in survival, an increase in cases referred, and the early abandonment of gastro-jejunostomy in favour of duodeno-duodenostomy/jejunostomy. The major factor in improved survival of these children lies in the development of neonatal intensive care rather than the development of surgical technique. It was evident that many of the cases in the first 10 years of the study were severely dehydrated on transfer to the specialist centre: aspiration pneumonia and sepsis frequently were complicating factors. These observations have been noted in other larger series.[1] Aspiration pneumonia and sepsis will affect any neonate in whom vomiting is allowed to go unchecked and this brings to light one of the diagnostic pitfalls with duodenal atresia. Preampullary atresia occurs in approximately 30% of cases,[2] and does not produce bile-stained vomitus. Hence babies in this group tend to be managed as feeding problems initially. The gravest situation is when malrotation with midgut volvulus produces duodenal obstruction with the classical 'double bubble' on plain abdominal X-ray. This situation requires urgent laparotomy unlike duodenal obstruction *per se* which demands only elective intervention.[3]

Following surgical correction of duodenal atresia, the proximal duodenum remains dilated and atonic for three to four weeks, so that the anastomosis does not function efficiently. Nasogastric suction must be effective throughout to prevent further vomiting and aspiration, and some workers prefer a gastrostomy in this situation. Feeding is best carried out via a transanastomotic tube.

From a technical standpoint the only complications were three wound infections, which compares favourably with the 15% complications rate reported in many series.[4] Special reference should be made to obstruction associated with annular pancreas which occurs in 25 – 30% cases.[5] No attempt should be made to resect this area since damage to the biliary and pancreatic ducts is inevitable: a standard bypass is therefore indicated.

Similar to other reported series,[1, 2, 4, 5] the Down's syndrome babies comprised 36% of the study and presented with the same distribution of birth weight and gestational age as the rest of the group. The crude mortality was 65% in the Down's sub-group and 47% in the remainder.[5] However, mortality in Down's cases rose to 89% when one other abnormality was present, whilst in the non-Down's group mortality was 66% in the same situation. The 42.5% occurrence of associated abnormalities in the series is similar to that in other studies.[1, 2, 6] This high association of a second and often serious abnormality undoubtedly contributes to the elevated mortality figures.

Management of Down's syndrome babies requiring surgery produces predictable controversy. Attention should therefore be given to their comparative prognosis with non-Down's babies requiring operation. In this area, correction of duodenal atresia and cardiac lesions[7] most commonly cause difficulty, the former because it sets a precedent for treating any one child and the latter because of its magnitude. It is interesting to note that only one correctable renal lesion was

recorded in the Down's group. This was a unilateral hydronephrosis, the other two cases of renal lesions being a single agenetic kidney. Review of the literature shows a 5% association of renal anomalies in duodenal atresia encompassing the full spectrum of urinary tract pathology and therefore tending to be less significant in the management of a Down's baby than duodenal atresia with or without a cardiac lesion.

In this retrospective study, it is evident that, comparing crude and corrected mortality of Down's and non-Down's babies with duodenal obstruction, the Down's group have an overall reduced prognosis. Whilst such an observation should be considered when planning the management of a Down's syndrome baby and when counselling the parents, it does not form a basis for a policy of non-treatment.[8]

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Effect of a meal on blood pressure in the elderly

M Power, R W Stout

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SUMMARY

As post-prandial hypotension may be a cause of falls in older people, blood pressure was measured for one hour following a test meal in 22 elderly patients. There was a small fall in both systolic and diastolic blood pressure but no change in heart rate. Although the changes were small and no symptoms occurred, post-prandial hypotension might be important in elderly patients who had other abnormalities in blood pressure regulation.

INTRODUCTION

Increasing age is associated with changes in blood pressure regulation particularly in relation to posture.[1] Postural hypotension is one of the many causes of falls in the elderly.[2] It has been suggested that a post-prandial reduction in blood pressure may occur in the elderly and cause symptomatic hypotension and falls.[3] However, the published data has come from studies of severely disabled institutionalised patients[3] or of those with idiopathic orthostatic hypotension.[4] To study whether post-prandial hypotension occurs in a wider range of elderly people we measured the blood pressure after a test meal in a group of hospitalised elderly patients who did not have postural symptoms and who had a variety of degrees of disability.

PATIENTS AND METHODS

The study sample comprised a group of 22 patients in the geriatric medical unit, Belfast City Hospital. All subjects gave informed consent. There were 10 males, age 83.4 ± 5.9 (mean ± SD), range 68 – 95, and 12 females, mean age 78.8 ± 8.2, range 70 – 92. They comprised 13 patients undergoing short and medium stay rehabilitation and nine receiving continuing care. The majority of patients were ambulant, most with the assistance of a helper or a walking aid, and none was acutely ill. None had experienced syncope or any 'funny' turns either related or unrelated to meals. Six patients were being treated with anti-hypertensive medication and some were on sedation at night. Medication was omitted on the day of the study. All patients ate a normal breakfast on the morning of the test meal.

Geriatric Medical Unit, Belfast City Hospital.
M Power, MB, MRCP, Registrar.
Department of Geriatric Medicine, The Queen's University of Belfast.
R W Stout, MD, FRCP, Professor of Geriatric Medicine.
Correspondence to : Dr M Power, Department of Geriatric Medicine, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL.

At 12.00 midday on the test day, the patients ate a standard test meal within a 15-minute period. The test meal comprised 24% protein (21g), 42% fat (24g) and 34% carbohydrate (45g) — total 508 kCal. The patients remained seated throughout the study period and systolic and diastolic blood pressure and heart rate were recorded 15 minutes before the meal was begun and at five-minute intervals for one hour after the meal had been completed. On a later date, similar measurements of heart rate and blood pressure were made on nine of the same patients in the absence of a meal. Blood pressure was recorded automatically using a Roche Arteriosonde 1217. The data was examined by analysis of variance.

RESULTS

No patient complained of symptoms related to hypotension during the test. The mean readings for systolic and diastolic blood pressure fell after the meal while the heart rate remained unchanged (Fig 1). The maximum fall in mean systolic blood pressure was 8.3 mmHg and in mean diastolic blood pressure was 7.1 mmHg. The maximum change in mean heart rate was a reduction of 1.1 beats per minute.

Analysis of variance showed that all systolic blood pressures from 25 minutes after the meal to the end of the test, and all diastolic blood pressures from five minutes after the meal to the end of the test were significantly lower than the pre-prandial blood pressure. There was no significant change in mean heart rate. There were no differences between the responses of those on drugs or between patients with differing degrees of mobility. Blood pressure measurements taken at five-minute intervals for one hour in the absence of a meal in nine of the same subjects showed no significant change from the basal levels (Fig 2).

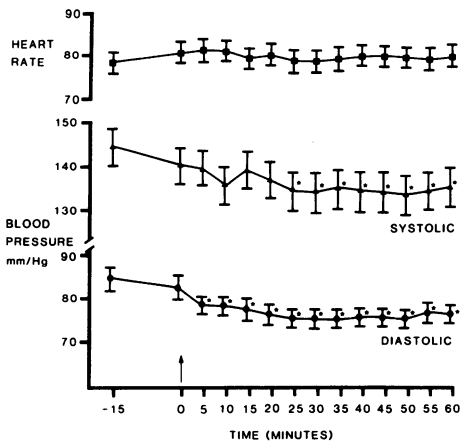

Fig 1. Mean (± SEM) heart rate, systolic and diastolic blood pressures during the test period. The arrow indicates when the meal was administered.

* Indicates points of statistically significant change ($p < 0.05$) in blood pressure compared with the basal level.

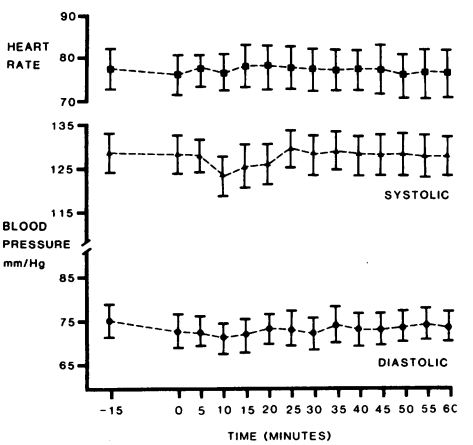

Fig 2. Mean (± SEM) heart rate, systolic and diastolic blood pressures in control subjects who did not take a meal.

DISCUSSION

This study shows that in a hospitalised group of elderly patients there is a statistically significant drop in both systolic and diastolic blood pressure, but no change in heart rate, after eating a meal. This confirms the results of previous studies.[3,4] The clinical significance of this fall in blood pressure is doubtful. Although statistically significant, it was small, and none of the patients experienced any symptoms during the test period. It is possible that, if blood pressure is already low, a meal might result in a further decrease to a symptomatic level. On the other hand, postural hypotension in the elderly is more common in those with hypertension.[1] There is considerable intra-individual variability in blood pressure in the elderly, so that any change occurring after a meal must be interpreted cautiously.

The mechanism of the post-prandial fall in blood pressure is unknown. Detailed study of a patient with autonomic neuropathy and profound post-prandial hypotension suggested that a gastro-intestinal hormone might be involved.[5] Although the hormone was not identified, treatment with somatostatin prevented the post-prandial fall in blood pressure. The fact that heart rate did not alter suggests that the post-prandial fall in blood pressure might be due to decreases in stroke volume or unpaired peripheral vasoconstriction.[1]

Our results demonstrate that elderly patients with varying degrees of severity of disability have a small drop in blood pressure after a meal. Although this did not appear to be clinically important in these patients, it might be significant in elderly patients who have other abnormalities in blood pressure regulation.

We gratefully acknowledge the help of the patients and staff of the Geriatric Medical Unit, Belfast City Hospital — in particular Dr RJG Cuthbert and Dr AB Stevens who helped with the blood pressure measurements, statistical assistance from Dr JD Merrett, and the preparation of the manuscript by Miss Andree Best.

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Rates of admission to six Northern Ireland psychiatric hospitals of patients with primary alcohol-related diagnoses

S A Compton, O Daly

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SUMMARY

The rate of admissions to psychiatric hospitals of patients with primary alcohol-related diagnoses (PARD) has increased from 1971 to 1983 and they now account for 19.7% of all admissions. There is a wide variation in admission rates between hospitals, and the use of the Mental Health (NI) Act 1961 to admit these patients formally varies up to twelvefold.

INTRODUCTION

Until recently it was assumed that there were large regional variations in alcohol-related problems in Britain between north and south [1] and also between different regions in Scotland.[2] These assumptions were based on officially recorded levels of alcohol-related mortality, crimes and alcohol admissions. Crawford et al [3] suggested that patterns of alcohol consumption did not differ in a manner consistent with the much higher rate of alcohol-related problems recorded in certain regions. They further suggested [4] that the differences in psychiatric admissions for alcohol dependence, abuse and psychosis could be largely explained by admission policies.

The use of Mental Health Acts in Britain for the formal admission to psychiatric hospitals of people with primary alcohol-related diagnoses also seems to vary. There is scant literature on the use of the Mental Health (NI) Act 1961 and of the position in England and Scotland which have similar but not identical acts. Szmukler, in a community study in London in 1976-1978 showed alcoholic admissions under the English act to be less than 1% of all compulsory detentions,[5] and McKechnie et al showed in Scotland in 1974-1979 a figure of 15.4%.[6] In Australia, alcoholics account for just under 7% of all compulsory detentions.[7]

Nosologically, abuse of or addiction to alcohol occupies an uncertain place in psychiatry and after many years the concept of alcoholism as a disease is falling out of favour, to be recategorised as a social and political problem.[8] Dependence on alcohol without concomitant mental illness is mentioned clearly in the new

Holywell Hospital, Antrim.
S A Compton, MB, MRCPsych, Consultant Psychiatrist.
Purdysburn Hospital, Saintfield Road, Belfast.
O Daly, MB, BCh, BAO, Senior House Officer.
Correspondence to : Dr S A Compton, Holywell Hospital, 60 Steeple Road, Antrim, Co. Antrim, BT41 2RJ.

Mental Health (NI) Order 1986 as a condition which may not be used as a reason for compulsory admission, i.e. it is not a mental illness. This Order becomes law on 1 August 1986.

It was decided therefore to ask three questions with regard to Northern Ireland practice for primary alcohol-related diseases.

1. Have the number of admissions increased in recent years?
2. Have the rates of admissions varied between hospitals?
3. Does the use of the Mental Health (NI) Act 1961 to admit patients vary throughout the Province?

METHOD

The study years were 1971 to 1983. Northern Ireland is divided into six catchment areas, each serviced by its own general psychiatric hospital. Two of these hospitals have alcohol treatment units which deal exclusively with alcohol-related problems. In addition, three of these areas have in-patient psychiatric facilities within general hospitals and these are affiliated to the general psychiatric hospital in the area. Admission figures to these general hospital units have been included with those of their respective general psychiatric hospitals in this report. A description of the hospitals included is given in the Table.

There are two autonomous psychiatric units within general hospitals in the Greater Belfast area — Windsor House (at the Belfast City Hospital) and the unit at the Mater Infirmorum Hospital. These units have been excluded from the study because they do not have a defined catchment area population. Attendance at psychiatric day hospitals, of which there are two in Belfast, and of day patients and out-patients have not been included as the criterion of inclusion in the study was: 'Do these people require in-patient treatment?' The regional unit for drug and alcohol dependence in Shaftesbury Square was excluded because it is not a general psychiatric unit and it does not have a defined catchment area. It is recognised that each of the above omissions will limit any inferences which can be drawn from the results.

The International Classification of Diseases was used to define the number of admissions. The categories included were:

1971-1980	Alcoholism and alcoholic psychosis ICD8 No. 291, 303
1981-1983	Alcoholic psychosis, alcohol dependence syndrome and non-dependent use of alcohol ICD9 No. 291, 303, 305.O.

The data for admissions for the years 1971-1983 in the above categories was obtained from the DHSS (NI) which analyses the Mental Health Record forms (MHR4) completed on every admission to a psychiatric unit or hospital. The primary diagnosis only was used, and alcohol-related problems secondary to other mental illnesses were not counted.

RESULTS

The Table shows the percentage change in catchment population, total psychiatric admissions and admissions with primary alcohol-related diagnoses from 1971 to 1983.

There has been a considerable shift in the distribution of the population in Northern Ireland over these years and this Table attempts to show the changes in admissions in context. No matter what happened to catchment populations or

psychiatric admissions in general, all hospitals showed an increase in admissions between 1971 and 1983 ranging from 18.3% to 261.1%. These increases were much greater than any relative or absolute increase in psychiatric admissions.

TABLE

1971-1983: changes in catchment populations, total admissions and alcohol-related admissions for six psychiatric hospitals

Hospitals (see below)	*% Change in catchment population*	*% Change in all psychiatric admissions*	*% Change in all alcohol admissions*
A	+13.8	+57.61	+132.89
B	−22.58	−14.73	+18.27
C	+7.84	−6.40	+65.67
D	+13.38	+8.05	+62.30
E	+11.32	+19.93	+126.44
F	+9.23	+57.73	+261.11

Description of hospitals

A. Downshire Hospital and Ards Hospital.	County psychiatric hospital with an alcohol unit. Associated in-patient psychiatric facilities in a general hospital.
B. Purdysburn Hospital.	General psychiatric hospital with a predominantly urban catchment area.
C. Tyrone and Fermanagh Hospital.	County psychiatric hospital with an alcohol unit.
D. Holywell and Whiteabbey Hospitals.	County psychiatric hospital. Associated in-patient psychiatric facilities in a general hospital.
E. Gransha Hospital.	General psychiatric hospital with a mixed urban and rural catchment area.
F. St. Luke's and Craigavon Hospitals.	County psychiatric hospital. Associated in-patient psychiatric facilities in a general hospital.

Selecting three years which represent the overall trends, the rates of first admissions to the six hospitals in 1971, 1977 and 1983, per 100,000 population, are shown in Fig 1. Wide variation in the rates can be seen — there was a threefold difference between the lowest (Holywell) and the highest (Gransha) in 1971, and the same pattern of variation persisted in 1977 and 1983, although the absolute rates were higher in the later years.

The rates of formal admissions per 100,000 population, under the Mental Health (NI) Act 1961, for the same hospitals and years as shown in Fig 2, also show wide variations. In each year the lowest formal admission rate was to Holywell Hospital and the highest rate was to Gransha Hospital. All except Gransha Hospital had a lower rate in 1983 than in 1971.

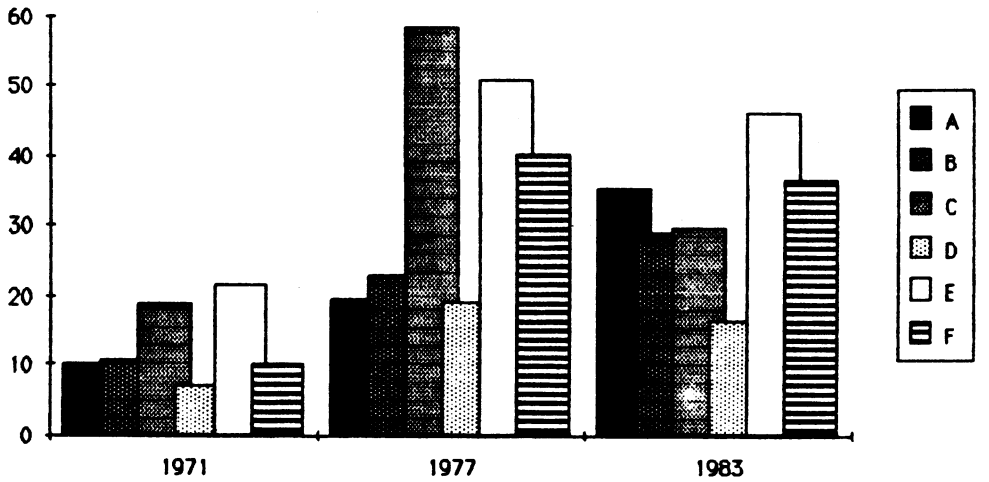

Fig 1. Rates of first admission with primary alcohol-related diagnoses per 100,000 population: by hospital.

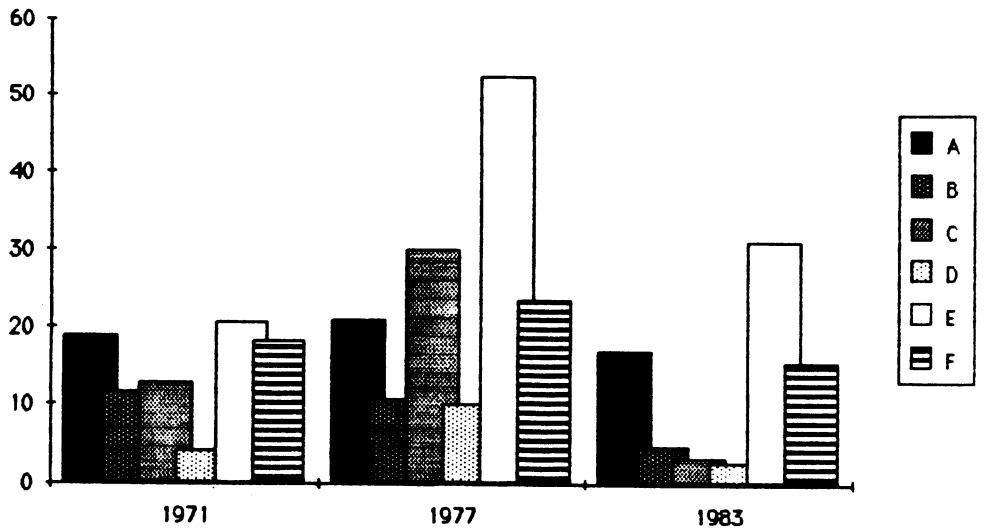

Fig 2. Rates of all formal admissions with primary alcohol-related diagnoses per 100,000 population: by hospital.

DISCUSSION

It is clear that there has been a definite increase in admissions with primary alcohol-related diagnoses since 1971, with a peak in most hospitals in 1977. This is not simply a result of an increase in all psychiatric admissions. The number of admissions between 1971 and 1983 has increased by 68.4% compared with an increase in Scotland between 1971 and 1981 of 33.6% [9] and an increase in England between 1972 and 1982 of 63.4%.[10]

In 1983, 19.7% of all admissions to general psychiatric hospitals in Northern Ireland were with primary alcohol-related diagnoses. The corresponding figures for England and the Republic of Ireland in 1982 were 9%[10] and 26%[11]

respectively. It is possible that the increase in the number of these admissions is a reflection of the increase in alcohol consumption as documented by WHO [12] and others.[13]

Poikolainen in Finland showed that an increase in alcohol consumption of 100% was mirrored by a doubling in the number of admissions for alcoholism and alcoholic psychosis.[14] Furthermore, liver cirrhosis mortality increased by 50% in this period in Finland. This has been described as a sensitive indication of alcohol consumption and the number of deaths due to cirrhosis has indeed increased steadily since World War II along with alcohol consumption.[13, 15] In the period 1971-1983, deaths due to cirrhosis of the liver have increased by 33%.[16] No figures are available for average amounts of alcohol consumed in Northern Ireland. Other explanations for the increase could be a change in admission policy of the hospitals, or a change in public opinion with respect to alcohol abuse — it could either be more acceptable to enter a psychiatric hospital for treatment or else more people believe that alcohol problems are caused by mental illness.

It is also clear that admission rates vary between hospitals, on average by a factor of threefold, between the lowest and the highest. This is similar to the threefold difference in 1982 for admission rates between the Regional Health Authorities in England with the lowest and highest rates.[10]

There are also wide variations in the use of the Mental Health Act, but these are not restricted to primary alcohol-related diagnoses. For all psychiatric diagnoses in 1983, the admission rate for all formal orders under the Act varied from 28 per 100,000 in the Tyrone and Fermanagh catchment area to 103.5 per 100,000 in the Gransha catchment area, which is a 3.7-fold difference.

It is difficult to explain these variations between hospitals both in the rate of admissions and the use of the Mental Health Act. Two local community surveys [17, 18] did not show any significant differences in prevalence rates for alcohol abuse between the four area boards, so this cannot explain the differences. The availability of specialised resources might affect the admission rate in either direction; however, this theory would appear to be negated by the considerable variation in admission rates between the Downshire Hospital and the Tyrone and Fermanagh Hospital, both of whom have specialist alcohol treatment units.

The admission policy of a hospital could also affect the use of formal orders,[4] but there are no studies which look specifically at compulsory detention and alcohol-related diagnoses.

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Gliadin antibody detection in gluten enteropathy

R G P Watson, S A McMillan, Clare Dolan, Cliona O'Farrelly, R J G Cuthbert, Margaret Haire, D G Weir, K G Porter

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SUMMARY

Circulating antigliadin antibody has been described in patients with gluten enteropathy although the prevalence varies in different studies. It has been suggested that the investigation for antigliadin antibody might be useful as a screening test. The object of the present study was to evaluate two different techniques for assaying these antibodies — an indirect immunofluorescent method and an enzyme-linked immunosorbent assay (ELISA). Antibodies were assayed in the sera of 102 patients in whom jejunal biopsies were also obtained. The specificity of both tests was greater than 95%, and the correlation between the presence of antibody and histology was significant ($p < 0.005$), though the sensitivity of each test was less than 70%.

INTRODUCTION

Detection in patients with gluten-sensitive enteropathy of circulating antibody to gluten or to one of its components, gliadin, might obviate the need for jejunal biopsy in diagnosis. However, the prevalence and specificity of tests for antibody have varied in different studies. In part, this may be due to differences between adults and children,[1] the use of different laboratory techniques,[2, 3] and the assessment of different fractions of anti-gliadin antibodies. The IgA fraction has been shown to be more specific than IgG or IgM[4, 5, 6] and, more recently, antibody to α gliadin was described as being more sensitive and specific for coeliac disease than antibody to other wheat proteins tested.[7, 8] So far, no assay has yet proved to be an entirely satisfactory screening test for gluten enteropathy.

Department of Gastroenterology, Belfast City Hospital, Belfast.
R G P Watson, BSc, MD, MRCP, Senior Registrar.
K G Porter, BSc, MD, MRCP, Consultant Physician.

Immunology Laboratory, Belfast City Hospital, Belfast.
S A McMillan, BSc, PhD, Principal Scientist.
R J G Cuthbert, MB, MRCP, Senior House Officer.
Margaret Haire, MD, FRCPath, Consultant Immunologist.

Departments of Immunology and Clinical Medicine, Trinity College, Dublin, and St James's Hospital, Dublin.
Clare Dolan, BSc, Research Fellow.
Cliona O'Farrelly, BSc, PhD, Research Fellow.
D G Weir, MD, FRCPI, Regius Professor of Medicine.

Correspondence to : Dr R G P Watson, Queen Elizabeth Medical Centre, Edgbaston, Birmingham B15 2TH.

The purpose of the present study was to assess the sensitivity and specificity of the immunofluorescent method used in the Immunology Laboratory, Belfast City Hospital, and to compare results with those obtained with an enzyme-linked immunosorbent assay (ELISA) for α gliadin antibody, developed in St James's Hospital, Dublin.

PATIENTS AND METHODS

From June 1982 to July 1985 all patients undergoing jejunal biopsy at the Gastroenterology Unit of the Belfast City Hospital also had a fasting blood sample taken for assay of antibody to gliadin. The biopsy was obtained by Crosby capsule which was placed endoscopically at a distance of 30cm from the pylorus.[9] The study group comprised 102 patients (61 females, 41 males); their age range was 15 – 89 years, their mean age 46.8 years. Fourteen patients were referred with dermatitis herpetiformis, and four patients who had repeat biopsies during the period were also included in the series giving a total of 106 jejunal specimens with corresponding blood samples. The jejunal biopsies were examined and reported by the Histopathology Department of the Belfast City Hospital. Antibody to gliadin was assayed at the time each blood sample was received in the IgG, IgA and IgM classes using an immunofluorescent method described by Unsworth et al,[3] and antibody in any immunoglobulin class at a titre of 1/10 or greater was considered positive. The sera were also stored at $-20°C$ and at the end of the study period those available were sent to St James's Hospital, Dublin, for assay of α gliadin antibody using an enzyme-linked immunosorbent assay (ELISA).[7] Testing was carried out without knowledge of the jejunal biopsy appearance, previous results of antibody testing or diagnosis.

RESULTS

Jejunal biopsy findings

In accordance with accepted criteria,[10] jejunal biopsies reported as total atrophy, sub-total atrophy or as severe partial atrophy were considered significant. With lesser degrees of atrophy (mild or moderate) they were considered to be of uncertain significance. In the study group 30 patients had total, sub-total or severe partial atrophy, 17 had mild or moderate partial atrophy and 59 had normal histology. Of the 14 patients with dermatitis herpetiformis, five had significant jejunal atrophy, six mild or moderate partial atrophy and three were normal.

Incidence of antibodies to gliadin

Of the 30 patients with significant jejunal histology, 20 (67%) had antibody to gliadin in IgG, IgA or both immunoglobulin classes detected using the immunofluorescent method. Immunoglobulin G class antibody to gliadin was detected in 19/30 (63%) patients whereas only 10/30 (33%) had IgA antibody, and IgM class antibody was not detected in any of the samples. Sera for the ELISA assay of α gliadin antibody were only available in 28 of these 30 cases and antibody (IgG class) was detected in 18 (64%) (Table I). There were 16 patients whose sera were positive with both assays and eight patients in whom both were negative.

TABLE I

Titres of IgG and IgA class antibody to gliadin measured by immunofluorescence and the presence of IgG antibody to α gliadin detected by ELISA in patients with significant jejunal mucosal atrophy

Patient number	Antibody to gliadin measured by Immunofluorescence IgG	IgA	ELISA IgG
1	160	–	+
2	160	10	+
3	–	20	+
4	–	–	–
5	–	–	–
6	–	–	–
7	40	–	–
8	40	10	+
9	80	10	–
10	10	20	+
11	10	–	+
12	10	–	+
13	40	10	+
14	160	40	NA*
15	20	–	+
16	40	–	+
17	–	–	+
18	20	–	+
19	–	–	–
20	80	–	+
21	10	–	+
22	–	–	+
23	–	–	–
24	–	–	–
25	40	10	+
26	20	10	+
27	–	–	–
28	80	80	NA*
29	–	–	–
30	20	–	+
Number positive	19 (63%)	10 (33%)	18 (64%)

*NA = Not available.

For the cases with mild or moderate partial atrophy two out of 17 had detectable gliadin antibodies using the immunofluorescent method, and the ELISA test for α gliadin antibody was positive in two different cases (Table II). The incidence of

positivity in this group of patients, using both methods, was less than in the group with significant histology ($p < 0.005$ using Chi square analysis).

TABLE II

Incidence of antibody to gliadin measured by immunofluorescence and ELISA in relation to jejunal histology

Histology	*Number of patients with antibody to gliadin measured by* *Immunofluorescence*	*ELISA*
Total, sub-total or severe partial atrophy	20/30 (67%)	18/28 (64%)
Mild or moderate partial atrophy	2/17 (12%)	2/17 (12%)
Normal	1/59 (2%)	3/59 (5%)

For the 59 subjects with normal histology, one was positive using both the immunofluorescent and ELISA methods. A further two cases were positive with the ELISA test alone. The percentages positive with both methods were less than for the group with significant histology ($p < 0.005$).

The sensitivity of each test was expressed as the percentage of cases positive in the significant histology group, hence the immunofluorescent method was 67% and the ELISA method 64% sensitive. The specificity was expressed as the percentage of cases which were negative in the normal histology group. For the immunofluorescent method this was 98.3% compared with 95% for the ELISA test.

DISCUSSION

This study has demonstrated that there is excellent correlation between the presence of circulating gliadin antibodies and severity of jejunal mucosal atrophy. The ELISA test for antibody to gliadin was similar in detection rate to the currently used immunofluorescent test for gliadin antibodies. It could be argued that storage of sera may in some way have impaired the sensitivity of the ELISA test, but, as a check, the immunofluorescent tests were repeated at the end of the study period on the same stored sera and these showed no difference from the original results.

Although the specificity of both tests was high, their sensitivities were unacceptably low (67%, 64% respectively) with one-third of patients with gluten enteropathy being undetected. Previous studies indicate that detection of gliadin antibodies is more likely amongst children than amongst adult patients with coeliac disease.[1,6] In our study the age range of patients with significant jejunal mucosal atrophy was 17 to 81 years, mean age 45 years, and therefore our conclusions can only be applied to an adult population.

In a previous study of a group of patients with coeliac disease, in the Republic of Ireland, the detection of α gliadin antibody by the ELISA technique had a sensitivity of 82% and a specificity of 85%.[7] This higher incidence of both true positives and false positives may reflect genetic differences between the populations in different parts of Ireland.

In the group with mild or moderate villous atrophy, it is probable that some of these cases did not have gluten sensitivity. However, four of the biopsies in this group were repeat tests taken after a gluten-free diet and showed significant histological improvement compared with their initial biopsies. Also a further patient from this group showed significant improvement in a subsequent biopsy after a gluten-free diet. These five patients were therefore definitely gluten-sensitive, but only one had detectable antibody (by immunofluorescence). Although the number of patients was small, this observation tends to emphasise the association of detectable antibody with severe histological changes and not with gluten sensitivity *per se.* This is in keeping with a number of prospective studies which have demonstrated that antibodies to gliadin tend to disappear in patients who take a gluten-free diet and who show histological improvement.[2, 5, 7]

The specificity of both tests was very favourable but there were a small number of false positives in the group with normal histology. One patient who had Crohn's disease had antibody with both assays. Such false positives have been described in Crohn's disease and in various other conditions including ulcerative colitis and postenteritis syndrome.[6]

The presence of antibodies to gliadin in IgA class have been described as being a better indicator of gluten enteropathy than those in IgG class[4, 5, 6] but this was not evident from the present study, when their incidence was lower. In our hands, measurement of IgA antigliadin antibodies alone would be less useful than both IgG and IgA. As guidance to the clinician we have shown that a positive test for gliadin antibody with the currently used immunofluorescent method is highly specific. There is a strong chance that a positive result indicates gluten enteropathy. However, a negative result does not exclude it, and the present sensitivity makes it unsuitable for use as a single screening test.

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Posterior fossa haemangioblastomas in Northern Ireland: a clinico-epidemiological study

C P Chee, I C Bailey

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SUMMARY

A retrospective study of 25 patients who presented with posterior fossa haemangioblastomas to the Northern Ireland Regional Neurosurgical Centre over the past 25 years has been carried out. The epidemiological and clinical features and the results after operative treatment are presented and compared with other series. Posterior fossa haemangioblastomas were more common in female than in male patients and solid tumours accounted for 40% of all cases. While only two patients had associated polycythaemia, five patients (20%) were found to have persistent leucocytosis pre-operatively, while 24% had von Hippel-Lindau complex including two patients who were operated upon for an associated spinal haemangioblastoma. Of particular interest was a patient who had neurofibromatosis. There was no perioperative deaths. Patients with solid tumours fared badly in the long term compared with those who had a cystic type.

INTRODUCTION

Haemangioblastomas account for 7.3% to 12% of all tumours arising in the posterior cranial fossa.[1, 2, 3, 4, 5] Considerable interest has been expressed in their epidemiology, the concurrence of polycythaemia[6, 7, 8] and von Hippel-Lindau complex.[9, 10] Many studies have been published from centres in Europe and the USA but no cases have previously been reported from Northern Ireland. We have therefore reviewed all the posterior fossa haemangioblastomas treated in this centre between 1960 and 1985 with special emphasis on the epidemiology, their association with von Hippel-Lindau complex and various haematological changes. An attempt was made to compare the results of operation with nine other series.[1, 2, 4, 11, 12, 13, 14, 15, 16]

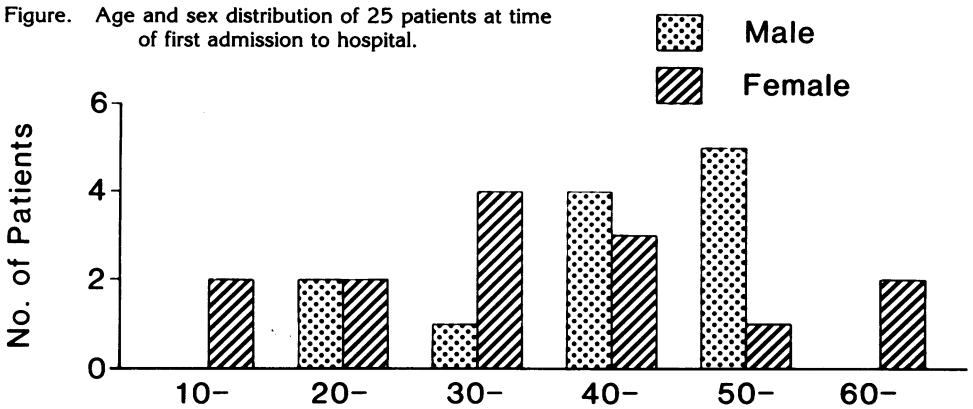
Polycythaemia indicates a haemoglobin level greater than 18g% or a peripheral red blood cell count of more than 6.5×10^6 per ul.[7, 8] The von Hippel-Lindau complex is defined by Jeffreys as a 'clinico-pathological syndrome in which at least one haemangioblastoma of the neuraxis occurs with at least one intra-abdominal example of the following — cysts of the kidney, pancreas or liver, renal carcinoma or phaeochromocytoma. The term may also be applied to cases with haemangioblastoma of the retina and another haemangioblastoma within the neuraxis. The complex may be sporadic or familial'.[6]

Department of Neurosurgery, Royal Victoria Hospital, Belfast.
C P Chee, FRCS (Ed), FRCS (Glasg), Senior Neurosurgical Registrar.
I C Bailey, FRCS, Consultant Neurosurgeon.
Correspondence to : Mr C P Chee, Department of Neurosurgery, Royal Victoria Hospital, Belfast BT12 6BA, Northern Ireland.

PATIENTS

All the 25 patients admitted to the Regional Neurosurgical Centre, Belfast, with posterior fossa haemangioblastoma were evaluated. There were 11 male and 14 female patients — a sex ration of 1 : 1.3. The age group of highest frequency was the sixth decade for male but the fourth for female patients (Figure). A study of both the ABO and Rhesus blood group distribution in 20 of these patients did not reveal any significant difference when compared with that of the general population.[17, 18]

Figure. Age and sex distribution of 25 patients at time of first admission to hospital.



The presenting symptoms and signs during the first admission are presented in Tables I and II. The average length of time that elapsed between initial symptoms and referral to hospital ranged from one month to five years with an average of 13 months. Sixteen patients (64%) presented with features of raised intracranial pressure. Papilloedema was detected in 36% of the patients which is lower than the reported incidence of 56% to 90%.[1, 2, 4, 13, 14, 15]

TABLE I ·

Symptoms of 25 patients with posterior fossa haemangioblastomas

Symptoms	*Number of patients*	*%*
Headache	20	80%
— occipital	6	24%
— frontal	6	24%
— hemispheric/global	8	32%
Vomiting	12	48%
Blurring of vision	4	16%
Diplopia	3	12%
Vertigo	3	12%
Mental changes	3	12%
Unsteady gait	15	60%
Tinnitus	2	8%
Neck stiffness	5	20%
Epilepsy	1	4%

TABLE II

Neurological signs of 25 patients with posterior fossa haemangioblastomas

Symptoms	*Number of patients*	*%*
Papilloedema	9	36%
Cerebellar deficit	12	48%
— nystagmus	6	24%
— dysmetria	4	16%
Ataxia	13	52%
Cranial nerves palsy	5	20%
Corticospinal tract involvement	3	12%
Occipital tenderness	2	8%

Six patients had haemangioblastomas elsewhere (four retinal and two spinal) leading to a diagnosis of von Hippel-Lindau complex in 24% of the whole group. The four patients with retinal angiomas had a strong family history of this condition. One other patient had an associated neurofibromatosis (von Recklinghausen disease).

Two patients (8%) had polycythaemia and both were found to have solid posterior fossa haemangioblastomas at operation. In five instances (20%), there was a persistent leucocytosis of more than 11,000 per ul without any focus of infection being discovered. One of these, a 52-year-old woman with a cystic cerebellar tumour had a leucocytosis of more than 25,000 per ul for more than six months before the cerebellar lesion was found. Her bone marrow examination did not reveal any abnormality.

Skull X-rays carried out on 10 patients did not reveal any abnormality. Electroencephalography (EEG) was normal in six patients and abnormal in seven, but correct localisation of the lesion was only found in two instances. Radioisotope scans were normal in five patients and abnormal in three, two giving a correct tumour location in the posterior fossa. Although vertebral angiography was performed in only nine cases it always gave the exact situation of the tumour. Prior to 1980, ventriculography was the only definitive diagnostic procedure achieved in nine patients. Since computed tomographic (CT) scanning became available in 1979, 13 cases of posterior fossa haemangioblastomas were diagnosed with its help. Four cases during the last two years were diagnosed by CT scan alone while in others angiography and ventriculography were used as adjunctive investigations.

Surgery was carried out on all the patients. As one later developed a second tumour, a total of 26 procedures was completed. Cystic haemangioblastomas were found in 15 cases situated in the cerebellar hemispheres. The size of these cysts ranged from 10 to 30 ml and that of mural tumour nodules between 0.5 and 2cm diameter. All of these tumours were removed totally. Solid tumours were found in 11 cases (42%), most of which were in the floor of the fourth ventricle or upper cervical cord. Two of the solid cerebellar masses were extirpated, two others partially removed, and the remainder biopsied and given radiotherapy. (Table III).

TABLE III

*Site and consistency of posterior fossa haemangioblastomas**

Site	Number		
	Cystic	*Solid*	*Total*
Right cerebellar hemisphere	11	2	13
Left cerebellar hemisphere	4	1	5
Vermis	0	1	1
Floor of fourth ventricle	0	5	5
Upper cervical cord	0	2	2
Total	15	11	26

*One patient presented with a solid upper cervical cord tumour six years after total removal of a right cerebellar cystic tumour.

All 25 patients have been followed up for periods varying from nine months to 14 years, with a mean of four years. Ten patients have died. The cause of death (Table IV) shows that five died suddenly, suggesting that the tumour had invaded the cardiac or respiratory centre, but post-mortem examination was not carried out. In two others, a medullary infarct was confirmed at autopsy.

TABLE IV

Ten cases of posterior fossa haemangioblastomas who died during follow-up

Case	*Year of death*	*Age at first admission*	*Sex*	*Site and consistency*	*Circumstances of death*
1	1963	65	F	(R) cerebellar, cystic	Sudden death, 3 years
2	1965	15	F	Upper cervical cord, solid	Sudden death, 2 years
3	1971	50	M	(L) cerebellar, solid	Features of increased ICP, 3 years after partial removal
4	1971	38	F	Vermis, solid	Medullary infarct following reoperation, 3 years
5	1973	43	F	(R) cerebellar, cystic	Sudden death, 3 years
6	1974	41	F	(R) cerebellar, cystic	Sudden death, 12 years
7	1976	42	M	(L) cerebellar, solid	Aspiration pneumonia following reoperation, 1 year
8	1980	51	M	Upper cervical cord, solid	Aspiration pneumonia, 4 months
9	1981	34	F	Floor of 4th ventricle, solid	Sudden death following revision of shunt, 1 year
10	1981	11	F	(R) cerebellar, cystic	Medullary infarct following reoperation for upper cervical solid tumour, 6 years.

Eight of the 15 patients who remain alive have sustained neurological improvement following surgery. Six out of these eight patients had cystic tumours. In five of the 15, the neurological picture was unchanged by surgery. Two were made worse, one requiring a feeding gastrostomy for bulbar palsy.

TABLE V

Results of surgery in 10 series of posterior fossa haemangioblastomas

	Percentage of all cases						
	Total cases	*Cystic*	*Solid*	*Multiple Tumours*	*Post-op death*	*Alive and well 3/12 post-op*	*Incapac-itated*
Cushing and Bailey (1928)	11	63	37	0	37	54	?
Davis (1946)	22	100	0	0	23	32	?
Perlmutter et al (1950)	25	100	0	0	8	68	20
Olivecrona (1952)	70	79	21	4	14	60	7
Silver and Hennigar (1952)	40	85	15	10	20	?	?
Krayenbuhl and Yasargil (1958)	45	86	14	?	9	64	8
Mondkar et al (1957)	108	70	30	9	15	86	?
Stein et al (1960)	19	80	20	0	30	52	0
Jeffreys (1973)	67	70	30	7	15	80	7
Chee and Bailey (1985)	25	60	40	4	0	60	8

DISCUSSION

In this study posterior fossa haemangioblastomas affected female patients more commonly than males, unlike any other series reported where there was a male to female preponderance of 2:1.[1, 4, 9, 11, 13, 14, 15, 16, 18, 20] Some comparisons with other series are shown in Table V. Clinical symptoms may appear at any age group but predominantly between the fourth and sixth decades of life. There was no significant difference in their ABO and Rhesus blood group distribution compared with that of the general population.[17, 19]

The clinical manifestations can usually be explained on the basis of the tumour location and slow growth characteristics. A triad of headache, vomiting and ataxia or ataxia, papilloedema and nystagmus[20] were found in a large proportion of these patients and any such symptoms should arouse suspicion of this type of lesion. The non-specific triad of headache, vomiting and papilloedema was present in only one-third of the patients. On average, 13 months elapsed between a patient first experiencing a symptom referrable to the nervous system and arrival at hospital compared with a range of seven to 12 months in other series.[1, 4, 11, 14, 15]

Various conditions have been observed in association with posterior fossa haemangioblastomas. Von Hippel-Lindau complex was found in 24% of our cases. One patient also had neurofibromatosis. Two patients with solid tumour had erythrocytosis but, to our surprise, five patients had persistently elevated peripheral white cell counts pre-operatively for which no other cause was found, highlighted by one woman having a leucocytosis of more than 25,000 per ul for six months before the cerebellar tumour was found.

Since the introduction of computed tomographic scans, the pre-operative diagnosis and localisation of this posterior fossa lesion has been made easier and more accurate. The presence of a posterior fossa cyst with a mural tumour nodule which enhances after injection of contrast is almost pathognomonic of a cystic cerebellar lesion.[21] However, in certain cases, angiography is still advisable to outline the vascular supply of the lesions, the mural nodule and the anatomy of

main vessels. Angiography in our series gave 100% correct localisation of the tumour, similar to that reported by Jeffreys.[1] Electroencephalography and radioisotope scans were of limited value in making a correct diagnosis and localising these tumours. Plain skull X-ray may be useful but did not reveal any abnormality in 10 cases. Ventriculography has now been superseded by CT scanning as a primary method of investigation. Solid tumours accounted for 40% of our cases — a higher incidence than usually found. Seven cases (64%) were located in the floor of the fourth ventricle and upper cervical cord.

The post-operative death rate in other series was 8% to 37%. Our results compare favourably in that no patient died during operation or the early post-operative period. This may reflect the introduction of the operating microscope for all cases, a more conservative approach to solid tumours (especially those involving the floor of the fourth ventricle and upper cervical cord) and advances in neuroanaesthesia and resuscitation. Nonetheless, 8% of the patients were incapacitated following the operation although 60% were alive and well at three months. In our experience, cystic tumours have a better outcome after surgery than solid tumours which is in agreement with other reported series.[22, 23]

We would like to thank our colleagues in the Neurosurgical Department for permission to review their cases.

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Case report

Methyldopa-induced connective tissue disorder

M J P Power, J G McConnell, I C Taylor

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Several drugs are known to cause a lupus-type syndrome.[1] Methyldopa causes positive anti-nuclear antibody reactions, but only two previously reported cases of a methyldopa-induced lupus-type syndrome have been described.[2,3] We report a case of this syndrome which failed to resolve fully on withdrawal of the drug, and which has features of a mixed connective tissue disorder (MCTD).

CASE HISTORY

A 78-year-old woman presented in March 1985 with myalgia, arthralgia, loss of energy and postural dizziness. Drug therapy prior to admission was methyldopa 500 mg three times daily and cyclopenthiazide 500 µg daily, which she had taken for four years for 'hypertension', and naftidrofuryl oxalate 100 mg three times daily.

On examination she had severe postural hypotension (supine blood pressure 140/80 mmHg, erect 80/40 mmHg), generalised muscle tenderness, marked leg oedema and ascites. The ESR was 106 mm/hour, Hb 11.7 g/dl, WCC $13.1 \times 10^9/l$ (eosinophils $2.22 \times 10^9/l$), urea and electrolytes normal, total protein 49 g/l, alkaline phosphatase 62 u/l, aspartate transaminase 28 u/l, alanine transaminase 13 u/l and gammaglutamyltransferase 5 u/l. Plasma protein electrophoresis showed generalised hypergammaglobulinaemia. Serum creatinine was 123 µmol/l, creatinine clearance 30 ml/min, urinary protein output 0.14 g/24 hours. Serum C_3 and C_4 complement levels were normal. Anti-nuclear antibodies (ANA) were present, titre 1:320 (IgG class, diffuse pattern) but antibodies to double-stranded DNA and to ribonucleoprotein were negative. The chest X-ray showed a moderate right-sided pleural effusion.

All her drugs were stopped and, at review one month later, her postural hypotension had resolved. The ESR was 30 mm/hour, the WCC $10.9 \times 10^9/l$ (eosinophils $0.26 \times 10^9/l$) and the total serum protein had risen to 63 g/l. The pleural effusion had resolved radiologically and the ascites had cleared. At this review, she had severe Raynaud's phenomenon and complained of 'taut, tight skin' on hands and feet. There was a violaceous rash on the extensor surfaces of elbows and knees and around the eyes suggestive of dermatomyositis. There were discrete telangiectatic areas over the hands, and the skin appeared

Geriatric Medical Unit, Ulster Hospital, Dundonald, Belfast BT16 0RH.
M J P Power, MB, MRCP, Senior Registrar.
J G McConnell, MD, MRCP, Consultant Geriatrician.
I C Taylor, MD, MRCP, Consultant Geriatrician.
Correspondence to Dr Power.

thickened, tight and shiny over hands, forearms and knees. A skin biopsy showed oedema only and was negative for immunofluorescent antibody staining. Despite this, the clinical appearances were typical of sclerodermatous change. Barium swallow demonstrated oesophageal hypomotility and pooling of barium in the erect position suggesting systemic involvement. X-rays of both hands were negative for soft tissue calcification.

COMMENT

A drug-induced lupus-type syndrome was first associated with hydrallazine in 1953.[4] Since then, over 30 drugs have been implicated,[5] the commonest being hydrallazine and procainamide.[1] As far as we are aware, this is only the third reported case of methyldopa-induced lupus-type syndrome.

In contrast with systemic lupus erythematosus, drug-induced lupus is commoner in older patients and tends to run a benign clinical course. Renal and neurological involvement is rare and the clinical syndrome usually remits following withdrawal of the offending drug. Our patient had certain unusual features of the drug-induced lupus syndrome. Although her pleural effusion and ascites resolved spontaneously following drug withdrawal, she rapidly developed severe Raynaud's phenomenon and cutaneous features of scleroderma and dermatomyositis. These have persisted for nine months following withdrawal and she remains positive for ANA. This contrasts with most reported cases of drug-induced lupus in which symptoms and signs have remitted promptly following drug withdrawal. However, in one of the two previously reported cases the positive ANA persisted for three months following drug withdrawal, though in this case the clinical syndrome itself resolved rapidly within two weeks of drug withdrawal.[2] The fact that the positive ANA can persist indicates that the drug-induced auto-immune condition can also persist. It is therefore possible that our patient's condition persisted and evolved into a sclerodermatous condition following withdrawal of the methyldopa. The combination of arthralgia, myalgia, Raynaud's phenomenon, oesophageal hypomotility and cutaneous features of scleroderma and dermatomyositis raises the possibility of mixed connective tissue disease despite the fact that serum was repeatedly negative for ribonucleoprotein antibodies.

Seroconversion to positive ANA has occurred in the known cases of methyldopa-induced lupus syndrome after variable periods of drug exposure. Breckenridge et al showed that ANA positively rises with duration of treatment.[6] In the two previously reported cases, the duration of treatment before seroconversion was two years and one year respectively[2, 3] and in our patient it was four years. The development of ANA and the lupus-type syndrome in patients taking methyldopa is therefore probably dose-related. Inhibition of suppressor T cell functions by methyldopa has been demonstrated and may be one of the factors responsible.[7]

This patient demonstrates some unusual features of methyldopa-induced lupus syndrome and is only the third reported case. The clinical presentation and progress raises the possibility of an associated mixed connective tissue disease. We cannot recommend the use of methyldopa as an anti-hypertensive agent in the elderly because of its association, in our experience, with central nervous system depression, postural hypotension, haemolytic anaemia, cholestatic jaundice and now a lupus-type syndrome.

We thank Dr M Haire for supplying the autoantibody measurements, and Dr G Allen for dermatological advice.

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Case report

Intrapericardial bowel hernia with cardiac tamponade

A O'Brien, M Brotherston, P Bateson

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An intrapericardial hernia resulting from an episode of blunt trauma six years prior to injury presented as acute intestinal obstruction accompanied by acute cardiac tamponade. This occurred three months following elective repair of a totally separate left diaphragmatic hernia. Both hernias were presumed to have resulted from the same traumatic incident, as both were devoid of hernial sacs. This is the second such case in which acute tamponade has been documented, and in both cases reduction of the hernia was followed by prompt resolution of tamponade.

CASE HISTORY

A 58-year-old semi-skilled labourer was the front-seat passenger in a car involved in a frontal collision with another vehicle in 1978. He received an injury to the left lateral chest wall. He complained of severe left lower chest pain exacerbated by breathing. On examination, there was bony crepitus on springing the left lateral chest wall. There was poor entry to the left base which was dull to percussion. A chest X-ray revealed fractures of the left fifth to seventh ribs in the anterior axillary line with a small left basal effusion. A basal chest drain was inserted but removed after 24 hours following only minimal serosanguinous drainage. He was discharged from hospital four days later with only minimal left thoracic discomfort. At review over the next six months, he was noted to have a slowly resolving left basal effusion associated with persistence of left chest discomfort.

By 1980, he had been complaining of increasingly severe upper gastrointestinal symptoms, including heartburn, vomiting and, on one occasion, possible haematemesis, following which he was referred for oesophagogastroscopy. This showed a hiatus hernia, mild gastritis and a normal duodenum. He was prescribed cimetidine with minimal relief of symptoms.

In 1983, he was admitted to hospital with acute, severe central abdominal pain associated with diarrhoea, both of which symptoms settled spontaneously. It became evident that he had been suffering from increasingly severe intermittent epigastric pain, with pain referred to the left shoulder, of being 'short of breath

Department of Surgery, Altnagelvin Area Hospital, Londonderry.
A O'Brien, FRCSI, Surgical Registrar.
M Brotherston, FRCSI, FRCSEd, Surgical Registrar.
P Bateson, FRCSI, Consultant Surgeon.
Correspondence to: Mr A O'Brien, FRCSI, University Department of Surgery, St. James's Hospital, James's Street, Dublin 8.

after a large meal' and of both orthopnoea and dyspnoea on exertion. He was hypertensive (190/110), and on auscultation of the left chest, pulmonary air entry was minimal whilst bowel sounds were readily audible. Chest radiography revealed cardiomegaly and marked elevation of the left hemi-diaphragm. Diaphragmatic screening confirmed the presence of a left diaphragmatic hernia, and barium meal revealed a gastric volvulus. ECG showed mild inferior ischaemic changes.

On exploration through a left eighth interspace thoracotomy, an oval defect, measuring some 12cm in its longitudinal axis, was found in the centre of the left hemi-diaphragm, orientated anterolaterally. Greater omentum, most of the stomach, splenic flexure and several loops of small bowel had herniated through the defect into the chest. There was no peritoneal hernial sac. Following division of widespread adhesions, the viscera were readily reduced into the abdomen and the defect repaired with interrupted linen. He made a rapid, uneventful recovery. At review two months later, his only complaint was of postprandial epigastric fullness. A barium meal demonstrated oesophageal reflux on posturing, but was otherwise normal. A chest X-ray was normal except for persistent cardiomegaly.

In 1984, he was re-admitted with classical symptoms and signs of acute intestinal obstruction, evident on erect and supine abdominal X-rays. Anteroposterior and lateral chest X-rays revealed an air-filled loop of bowel situated in the anterior mediastinum (Figure). From the time of his admission to that of finding an intra-pericardial hernia at laparotomy, there was a progressive fall in systolic blood pressure from 140mmHg to 60mmHg, with a rise in pulse rate from 80/min to 120/min, despite adequate intravenous fluid replacement. On exploration, the previous diaphragmatic repair was found to be both intact and distant from a circular defect, measuring some 3cm in diameter, with a thickened fibrous rim, situated in the central tendon of the diaphragm. A loop of proximal ileum had herniated through the defect into the pericardial sac. There was no peritoneal hernial sac. The bowel was readily extracted from the pericardial sac by gentle

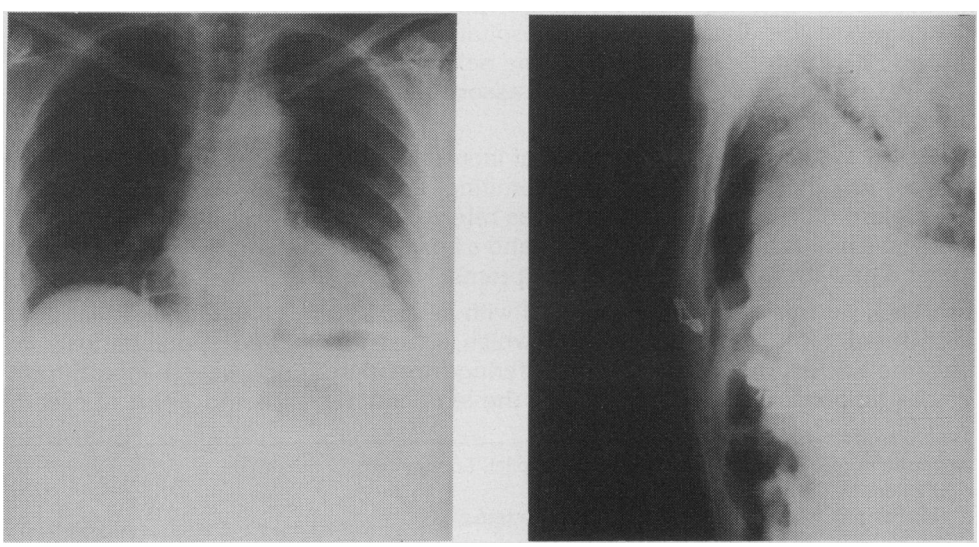

Fig (a) and (b). Anteroposterior and lateral chest X-rays showing air-filled loops of bowel in the anterior mediastinum.

traction, following which the systolic blood pressure promptly rose to 120mmHg. The defect was repaired with an expanded polytetrafluroethylene sheet. Once again, the patient made a rapid recovery.

Since then he has remained very well. His dyspepsia has been minimal, his anti-hypertensive therapy has been discontinued and there has been a marked improvement in the cardiomegaly.

COMMENT

Thirteen cases of intrapericardial hernia resulting from blunt trauma have been reported.[1-9] Ages ranged from 18 to 72 years. Ten were male. The injuries were received in road traffic accidents in 10 cases. The main site of bodily impact was the chest in eleven cases, seven of which had sustained fractured ribs. Four patients had pelvic fractures, one sustained a ruptured bladder while another had a splenic injury requiring splenectomy.

While five cases were diagnosed within one week of injury, five others were not diagnosed until at least one year after injury. Indeed one case remained undiagnosed until 23 years later.[4] The more common cardiorespiratory symptoms prior to dignosis were exertional dyspnoea and palpitations, while the more common abdominal symptoms were those of vague discomfort, cramps and pain. Initial chest X-rays were normal in nine cases, and intrathoracic bowel gas shadows were seen in only one case, but by the time of diagnosis, precordial gas shadows were evident in all. Handley and Havill reported the only previous case of acute cardiac tamponade due to such a hernia in 1975.[8]

In six cases, surgical approach was left thoraco-abdominal, in five by laparotomy alone. One case had bilateral thoracotomies. In four cases, the defect extended beyond the periphery of the central tendon. The absence of a hernial sac, considered to be pathognomonic, of a traumatic rupture, was specified in 10 cases. The pericardium was found to contain a portion of stomach which had undergone a volvulus to allow the greater curvature to enter the defect in 10 instances, taking with it transverse colon and greater omentum in five. As in this case, small bowel was the herniating organ in the remaining three. The defect could be primarily sutured in eleven cases, one was repaired with a pericardial rotational flap, and one with fascia lata.

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Case report

Rumination in adults – a rare cause of gastro-oesophageal regurgitation in two patients

J S A Collins, F N Brennan, R J E Lee, A H G Love

Accepted 1 September 1986.

Rumination is the effortless regurgitation of previously ingested food from stomach to mouth, usually followed by chewing and re-swallowing. It is usually not accompanied by nausea or abdominal discomfort and ceases when the gastric contents become acid to taste. The onset of symptoms may occur at any time during life and are frequently associated with emotional disturbance or psychiatric disorder. In most cases, the rumination is involuntary leading to embarrassing results for patient and close contacts. This case report details the clinical features of two patients who presented at a gastroenterology clinic with this condition in 12 months.

CASE 1

A 33-year-old housewife first attended in October 1985 complaining of the frequent, effortless regurgitation of partly-digested food over a period of 15 years. The problem had started during her teenage years and had become more frequent over the past five years, with rumination episodes occurring up to 30 times daily. The peak period during the day seemed to be after her evening meal. She denied heartburn, abdominal pain or vomiting and admitted that the involuntary regurgitation was often pleasurable. Dietary factors appeared to have no influence on the condition. She worked part-time as a shop assistant and there was no history of recent psychological stress or past psychiatric illness. In the family history, one sister aged 24 years also ruminated and the patient's nephew aged 14 years had recently developed the habit. While the patient herself had not previously sought medical advice, her husband had precipitated the consultation when he complained about her halitosis.

On examination she was overweight at 81kg but otherwise physically normal. Regurgitation could not be exhibited at will. Further investigations of oesophageal function were performed. Oesophagoscopy and barium swallow were normal. Oesophageal scintigraphy showed no evidence of gastro-oesophageal reflux and oesophageal motility studies were normal. Prolonged ambulatory pH monitoring was performed using a 'Digitrapper' probe sited 5cm above the lower

Department of Medicine, The Queen's University of Belfast.
J S A Collins, MB, MRCP, Senior Registrar/Senior Tutor.
F N Brennan, MB, MRCPI, Registrar.
R J E Lee, Senior Registrar/Senior Tutor.
A H G Love, MD, FRCP, Professor of Medicine.
Correspondence to: Dr J S A Collins, Department of Medicine, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.

oesophageal sphincter, which had previously been located using a 'pull-through' technique. Only one episode of reflux with pH < 4.0 was noted in the supine position during the 20-hour study. In the prone position there were six episodes of pH < 4.0, and lasting less than two minutes during sleep. Rumination episodes, as noted on the system's event marker had occurred 37 times between 0800 hrs and 2330 hrs but were not accompanied by pH fall at any time.

CASE 2

A 24-year-old postgraduate male university student first presented in May 1985 complaining of recurrent regurgitation of partially-digested food for 18 months. He could not recall previous episodes in childhood. The episodes had started prior to the patient's final degree examinations. They were most frequent in the evening 30 – 60 minutes after the evening meal, but no dietary provoking factors could be recalled. He had no heartburn, nausea or vomiting and denied psychological stress. There was no relevant past or family history. On examination he was of normal weight at 69.5kg and physically normal. Oesophagoscopy, barium swallow and oesophageal manometric studies showed no abnormality. Prolonged ambulatory oesophageal pH monitoring was again performed for 21.5 hrs using a 'Digitrapper' probe. Although eight supine episodes of acid reflux with pH < 4.0 were recorded, none was associated with rumination episodes which had been noted 14 times from 0900 – 1135 hrs on the event marker.

Both cases had no response to a trial of metoclopramide therapy. In the first case, neither increasing the starch content nor increasing the size of her evening meal reduced rumination episodes. Both patients refused to undergo formal psychiatric examination, and their condition remains unchanged to date.

DISCUSSION

Rumination, derived from the Latin verb *ruminare,* meaning 'to chew the cud', was first described in adults by the Italian anatomist Fabricius ab Aquapendente in the early 17th century. Several accounts of the condition have appeared during the early 20th century,[1-3] but due to its rarity in adults, few cases have been documented in the literature in the past 20 years.[4, 5]

The two cases described here are typical of the disorder described in the previous accounts. The regurgitation appears to be effortless, often involuntary and completely unassociated with heartburn, nausea or vomiting.

The condition may be first noticed at any time during life[2] or present as a clear result of a life stress event. It appears to be especially prevalent in mentally retarded individuals who reside in institutions, with an incidence of 8.0% quoted in one hospital in the United States.[6] In these individuals, chronic rumination may result in severe weight loss, dehydration and a significant morbidity.[6] In normal adults there are no serious sequelae to health but the act of rumination often causes acute embarrassment to the patient and may disturb the family.[5]

Although rumination has been closely studied in animals, the sequence of physiological events is poorly understood in man. In most ruminators, as in these two cases, radiological studies have been reported as normal. Fluoroscopic regurgitation of barium has been observed very infrequently, during screening, probably because of involuntary suppression of rumination by the patient, and retrograde oesophageal peristalsis has not been observed in man. The first manometric study in ruminators was reported by Brown in two adults.[5] As in our

two cases, he could not exhibit an abnormality in either the resting pressure of the lower oesophageal sphincter or peristaltic pressures. It would appear that lower oesophageal sphincter incompetence is not a prerequisite for rumination.

There are no detailed previous reports of prolonged ambulatory pH monitoring on these patients. Interestingly, both patients in this report had no evidence of acid reflux during their numerous episodes of rumination, indicating that the regurgitated food is of neutral to alkaline pH. This finding explains their lack of oesophageal symptoms, and supports the theory that regurgitation of low pH gastric contents deters rumination.[5] With the classical history described in these two cases we conclude that prolonged pH monitoring has no role to play in their investigation, unless there is other clinical evidence of reflux disease.

Most authors have concluded that psychological factors are important in the pathogenesis of this disorder. Dambassis has stated that 'the tendency to rumination is a universal phenomenon in infants, and its persistence into adult life indicates the somatic projection of psychic conflicts as well as emotional immaturity or regression'.[7] In neither of our two cases was there obvious psychological abnormality, although in Case 2 the disorder may have been triggered by pre-examination stress. This contrasts with Case 1 who had a long history of rumination and had developed it as a pleasurable habit. Both patients were reluctant to undergo further psychiatric evaluation.

Unfortunately, medical management of rumination has been unsatisfactory. Antiemetic drugs have been found to be unhelpful,[8] but recent studies on dietary manipulation have shown some benefit in mentally subnormal individuals, particularly with reference to the starch content of the ingested foodstuff. By adding 15 – 20oz of extra starch in the form of potatoes or rice to the daily dietary intake of four retarded subjects, Rast et al showed significant differences in reducing rumination frequency.[9]

In conclusion, rumination is a rare, poorly understood cause of gastro-oesophageal regurgitation in adults. The diagnosis must be made on the typical history in most cases. This report of two patients stresses the importance of recognising this disorder and shows that sophisticated oesophageal function tests are not indicated, as they are unlikely to reveal any abnormalities in such patients.

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Case report

Near death due to inhalation of slurry tank gases

M Spiers, O C Finnegan

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Slurry tank storage facilities are playing an increasing role in mechanised farming. Accidental poisoning from gases produced in such tanks is a recognised hazard, and multiple fatalities have been reported.[1,2] The principal constituents are methane, ammonia, carbon dioxide and hydrogen sulphide. The most dangerous of these is hydrogen sulphide which acts in a similar manner to cyanide, with reversible inhibition of the respiratory enzyme cytochrome oxidase. Concentrations above 200 parts per million (ppm) produce direct irritant effects on exposed surfaces, and pulmonary oedema on prolonged inhalation.[3] Higher levels (above 500 ppm) depress the central nervous system, with paralysis of the respiratory centre, and almost instantaneous loss of consciousness. The familiar smell of 'rotten eggs' is not a reliable warning sign as paralysis of the olfactory nerve makes the gas odourless at lethal levels.

Most reported cases have been associated with agitation of slurry prior to, or during, emptying procedures, although toxic exposure to hydrogen sulphide can also occur in sewers, mines and the chemical industry. The problem was exacerbated in 1985 by the wet summer and autumn, which made fields unworkable. Large quantities of slurry therefore remained undisturbed for long periods and subsequently more gas than usual accumulated beneath a hard crust, to be released when the tanks were eventually emptied.

CASE HISTORY

A 31-year-old farm labourer, previously in good health, was preparing to empty a tank containing approximately 6,000 gallons of slurry. This had been undisturbed since the autumn one year previously. The surface crust had been broken and the contents agitated by a tractor-driven mechanical pump prior to removal to a tanker. His workmates noticed him slumped over the drainage slats above the slurry tank inside the cowshed. Help was summoned and he was dragged outside within three minutes. The patient was noticed to be blue, pulseless and unconscious, with very weak respiratory efforts only. No attempts at cardiopulmonary resuscitation were made. Two cows in the cowshed died immediately and a calf was later destroyed.

Coleraine Hospital, Mountsandel Road, Coleraine, Co. Londonderry, BT52 1JA.
M Spiers, BM, Senior House Officer.
O C Finnegan, MRCP, Consultant Physician.
Correspondence to Dr Finnegan.

On arrival of the ambulance about 20 minutes later, he was unconscious with no palpable carotid or femoral pulses, but there was still shallow respiration. The pupils were only moderately dilated. Oxygen was administered, and after several minutes he vomited and gradually regained consciousness. On admission to hospital the patient was orientated in person, time and place. He was not cyanosed. Blood pressure was 150/90mmHg, and his pulse irregularly irregular at 70 beats per minute. He had good bilateral air entry with normal breath sounds. Tone, power and reflexes were normal. The electrocardiogram confirmed atrial fibrillation, but was otherwise normal. The chest radiograph was normal, with no evidence of pulmonary oedema. Sinus rhythm returned within an hour of admission. Subsequent electrocardiograms and cardiac enzymes were normal. He made a rapid recovery and was discharged after two days. At follow-up one month later, he was in perfect health.

COMMENT

The reported case highlights the danger of working with slurry in a confined space. The toxic effects of slurry gases have been well documented[3] and, although no qualitative or quantitative gas analysis was made at the scene, the clinical picture is consistent with inhalation of a high concentration of hydrogen sulphide. The sudden loss of consciousness was presumably due to paralysis of the respiratory centre with resulting hypoxia. Grand mal fits and long-term neurological sequelae have been reported,[4] but despite collapse and unconsciousness our patient had no permanent ill effects. Supraventricular and sinus tachycardias have been associated with hydrogen sulphide intoxication, but we are not aware of atrial fibrillation being previously reported as a clinical complication. This arrhythmia was probably due to cardiac hypoxia although ventricular irritability would be a more expected finding. There was no indication in the patient's history, examination or investigations to suggest any pre-existing heart disease or paroxysmal tachyarrhythmia. There was no clinical or radiographic evidence of pulmonary oedema, and his initial cyanosis responded to administration of oxygen by the ambulance crew. The absence of pulmonary oedema can be explained by the sudden collapse and apnoea protecting the lungs from further toxic exposure.

Our patient must be considered lucky to have survived this episode. His rescuers were also at considerable risk when dragging him clear without breathing apparatus, but in so doing they undoubtedly saved his life. After removal from the toxic environment, further management of hydrogen sulphide is mainly supportive, with the need for oxygen administration, cardiopulmonary resuscitation and mechanical ventilation being determined by the severity of intoxication. Inhaled or intravenous nitrite has been suggested as a measure to protect and reactivate cytochrome oxidase,[5] but the need for its early, and probably pre-hospital, administration limits its efficacy. The resulting formation of methaemoglobin is, moreover, not without its own hazards.

Including this case, there have been 14 slurry tank accidents reported to the Department of Agriculture in Northern Ireland in the 17 years prior to the end of 1985.[6] Six incidents involved cattle only (with more than 35 deaths), and five involved a total of nine people, all of whom recovered, apart from one believed to have permanent brain damage. The three remaining incidents produced four human deaths. One of the victims entered the slurry tank attempting to rescue his colleague. The cause of death was in one case asphyxia by slurry gases, and in

three drowning in slurry probably preceded by asphyxia. Ten of the reported accidents occurred in 1985. This recent increase can be explained by the freak weather experienced in the Province that year. Hydrogen sulphide should be considered as lethal as cyanide, and clear advice has recently been given to the farming community to minimise the risks of accidental exposure when emptying slurry tanks.[7]

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CORRIGENDUM

C.A.T. scan pictures shown in Fig 1 of "Acquired Immune Deficiency Syndrome in Northern Ireland" (Vol 55, No 1, page 81) were of different levels of the brain. This was due to a mistaken submission with the final draft by R. D. Maw and W. W. Dinsmore. Comparable levels were, of course, taken and reported as showing cerebral involution.

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Case report

Capgras syndrome

Shelagh M Rea, Diana G Patterson

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The Capgras syndrome, an uncommon psychiatric syndrome, was originally described in 1923 by Capgras and Reboul-Lachaux who termed it 'l'illusion des sosies' (the illusion of doubles). In this syndrome, the patient believes that a person, usually a close relation, has been replaced by an exact double. This delusion assumes a central dominating role in the symptomatology even in the presence of other psychotic features. It occurs in the setting of clear consciousness and is a delusional misidentification in which perception is not impaired and memory is intact.[1] We report a case in which there is a cultural influence on the content of the delusions reflecting the current political scene in Northern Ireland.

CASE HISTORY

A 30-year-old single male office worker, who had assaulted his mother, was admitted to a psychiatric hospital as a formal patient. In a belligerent manner, he related his belief that his mother and two brothers had been murdered and replaced by 'lookalikes'. He stated that on two occasions he had been told by a member of the security forces, who had identified himself to him in a public bar, that his family had been murdered and replaced by lookalikes. These lookalikes were to observe him as it was believed that he was involved in a terrorist organisation. The patient had no links whatsoever with any organisation. Further enquiry revealed that the patient could perceive slight differences between the appearance of his elder brother and that of the lookalike. The latter had straighter hair and the tone of his voice was different. The patient also believed that there were electronic devices around his home gathering intelligence for the security forces and that it was common in Northern Ireland for key figures of organisations to have been replaced by lookalikes for intelligence purposes. The patient's speech was quite coherent and there was no evidence of thought disorder. His affect was angry and tense with no sign of depression or elation. He denied hallucinatory experiences. Results of physical and neurological examination were normal and all investigations, including EEG and isotope brain scan, were unremarkable. He was commenced on trifluoperazine and showed marked improvement. His delusions became well encapsulated. His detention was not extended and when he took his own discharge from hospital, he was considered fit to return to work. Unfortunately he refused treatment with a long-acting depot phenothiazine but agreed to attend the outpatient clinic.

Tyrone and Fermanagh Hospital, Omagh, Co. Tyrone, BT79 0NS.
Shelagh M Rea, MB, MRCPsych, Senior Registrar.
Diana G Patterson, MD, MRCPsych, Consultant Psychiatrist.
Correspondence to: Dr Rea.

The patient is the second son in a family of four siblings. His mother had had a psychiatric admission for depression. He first received psychiatric treatment in the form of psychotherapy for a chronic anxiety state at the age of 20 years. A year later his father died and he briefly took charge of the family farm until his elder brother returned from England to take over. The patient found alternative employment but felt jealous of his brother, who assumed a dominant role in the family, and was favoured by the mother. Eight years later, when his elder brother married and the patient moved to accommodation with his mother in a nearby town, he became disturbed. He believed that he was being doped with drugs and that he was under surveillance by the security forces. He was admitted to hospital where a diagnosis of a paranoid psychosis was made and he was treated with chlorpromazine. On discharge his compliance with treatment was poor and five months later he developed the symptoms of the Capgras syndrome.

COMMENT

In many ways this patient is typical of others that have been reported with this syndrome. The patient developed an elaborate systematised delusion involving doubles of close relations with perception of slight differences in the physical appearance in the case of the elder brother. Usually the double is an exact replica, but Merrin and Silberfarb review 14 cases in which the double differed slightly in appearance from the original person.[2] The most common accompanying diagnosis is schizophrenia but cases have been described in which the diagnosis has been schizo-affective psychosis or affective psychosis. A marked paranoid tendency has been found in almost all cases irrespective of diagnosis.[3] In recent years, many papers have suggested an organic basis to the Capgras syndrome.[3, 4, 5] The type of organicity included cerebral atrophy, head injury, alcoholism and toxic delirium. However, Berson suggests that, while organic factors may be present and may even be the basis of the psychotic state, it is unlikely that organic factors alone can be held causally accountable for the content of the delusion of doubles, primarily because of the selectivity of the delusion.[6]

The psychodynamic explanation for the Capgras syndrome is that it is basically a love-hate conflict resolved by directing ambivalent feelings on to an imagined double. One can only speculate on the dynamic antecedents in this case but they may be related to the patient's changing position in the family and a complicated relationship between him and his mother.

There is no specific treatment for this syndrome and therapy must be directed towards the accompanying condition. The prognosis of the delusion of doubles does not necessarily follow the course of the associated psychosis. Treatment must also include helping to improve the relationship between the patient and the persons implicated and helping the relatives to gain insight and perhaps change their attitude towards the patient.[7]

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BOOK REVIEWS

Cell, tissue and disease: the basis of pathology. By Neville Woolf. 2nd ed. (pp 503. Illustrated. Paperback £8.50). London: Baillière Tindall, 1986.

It seems almost by accident that Professor Woolf provides, in his preface, a useful definition of the term 'General Pathology'. This book, he claims, is primarily about how diseases happen. Generations of pathologists have struggled with this remit in the attempt to produce an intelligible and reasonably comprehensive text. The first problem is that most medical students are thrown into this subject with little or no background knowledge of the terminology or of the clinical features of disease. The second problem is the weight of tradition and precedent which largely indicates what topics will and will not appear on the Contents page of such a book. Professor Woolf has resolved these problems as well as anyone is likely to do within the format of a pocket-book of 500 pages.

This is a readable book. The subject order is partly dictated by tradition and partly by logic, from cell injury and inflammation through to oncogenesis. After Chernobyl, the author may regret the calculated omission of radiation injury. Similarly, developmental and genetic disease is explicitly excluded. The virtual absence of shock, DIC and pathological fibrosis are regretted by the reviewer. Was it necessary to classify the viruses to the extent attempted, while leaving malaria and other parasitic diseases largely untouched? On the other hand, is it fair, in reviewing a short text for beginners, to criticise gaps in the coverage of a subject as broad and as diverse as medicine itself?

This is a nicely produced and economical book, in the printing of which a single added colour is used effectively for contrast. A brief reading list is provided. There are some half-tone illustrations, a few of which are disappointing, and some useful diagrams. The value of the schematic mice on page 449 remains unclear! Professor Woolf has taken on one of Pathology's most difficult tasks and deserves credit for his success, as reflected in the publication of this second edition. He mostly manages to explain 'how diseases happen' at a level which is scientifically valid and which still remains comprehensible to a junior medical student.

PGT

Basic surgery. By John A McCreadie, Gerard P Burns and Carol Donner. 2nd ed. (pp 656. Illustrated. £24.75). New York: Macmillan Publishing Co, 1986.

This 1986 book appears nine years after the first edition, but there have been few changes in format, length and content. Although the editors and several contributors have Belfast connections, the authors are mainly North American and the book is designed as a textbook and text supplement for medical students and surgical residents. The 35 chapters are grouped into four units — 'Basic considerations', 'Total care of the surgical patient', 'Principles of general surgery', 'Principles of specialty surgery'. The editors emphasise the importance of understanding basic science principles and their application to surgical management. Unfortunately the major fault with this type of book is that the spectrum of material covered allows space for only superficial coverage of physiological concepts and therapeutic applications. Medical students will find the reviews of the metabolic response to injury, immune response, cancer spread and pain management particularly useful, but may have difficulty integrating these basic principles into the management of specific surgical conditions. Surgical trainees will be frustrated by the superficial discussion of most topics and the paucity of up-to-date references but may find it a useful 'aide-memoire' prior to examinations. Many of the illustrations are excellent, presenting abundant information which is easily assimilated, but the colour plates of surgical anatomy add nothing to the book, apart from expense. Indeed, at the recommended price, this book is poor value for money on this side of the Atlantic. Its greatest appeal will be to students who have only limited access to clinical material and who require an easily digested overview of surgical science.

BJR

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This 1986 book appears nine years after the first edition, but there have been few changes in format, length and content. Although the editors and several contributors have Belfast connections, the authors are mainly North American and the book is designed as a textbook and text supplement for medical students and surgical residents. The 35 chapters are grouped into four units — 'Basic considerations', 'Total care of the surgical patient', 'Principles of general surgery', 'Principles of specialty surgery'. The editors emphasise the importance of understanding basic science principles and their application to surgical management. Unfortunately the major fault with this type of book is that the spectrum of material covered allows space for only superficial coverage of physiological concepts and therapeutic applications. Medical students will find the reviews of the metabolic response to injury, immune response, cancer spread and pain management particularly useful, but may have difficulty integrating these basic principles into the management of specific surgical conditions. Surgical trainees will be frustrated by the superficial discussion of most topics and the paucity of up-to-date references but may find it a useful 'aide-memoire' prior to examinations. Many of the illustrations are excellent, presenting abundant information which is easily assimilated, but the colour plates of surgical anatomy add nothing to the book, apart from expense. Indeed, at the recommended price, this book is poor value for money on this side of the Atlantic. Its greatest appeal will be to students who have only limited access to clinical material and who require an easily digested overview of surgical science.

BJR

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BOOK REVIEWS

Cell, tissue and disease: the basis of pathology. By Neville Woolf. 2nd ed. (pp 503. Illustrated. Paperback £8.50). London: Baillière Tindall, 1986.

It seems almost by accident that Professor Woolf provides, in his preface, a useful definition of the term 'General Pathology'. This book, he claims, is primarily about how diseases happen. Generations of pathologists have struggled with this remit in the attempt to produce an intelligible and reasonably comprehensive text. The first problem is that most medical students are thrown into this subject with little or no background knowledge of the terminology or of the clinical features of disease. The second problem is the weight of tradition and precedent which largely indicates what topics will and will not appear on the Contents page of such a book. Professor Woolf has resolved these problems as well as anyone is likely to do within the format of a pocket-book of 500 pages.

This is a readable book. The subject order is partly dictated by tradition and partly by logic, from cell injury and inflammation through to oncogenesis. After Chernobyl, the author may regret the calculated omission of radiation injury. Similarly, developmental and genetic disease is explicitly excluded. The virtual absence of shock, DIC and pathological fibrosis are regretted by the reviewer. Was it necessary to classify the viruses to the extent attempted, while leaving malaria and other parasitic diseases largely untouched? On the other hand, is it fair, in reviewing a short text for beginners, to criticise gaps in the coverage of a subject as broad and as diverse as medicine itself?

This is a nicely produced and economical book, in the printing of which a single added colour is used effectively for contrast. A brief reading list is provided. There are some half-tone illustrations, a few of which are disappointing, and some useful diagrams. The value of the schematic mice on page 449 remains unclear! Professor Woolf has taken on one of Pathology's most difficult tasks and deserves credit for his success, as reflected in the publication of this second edition. He mostly manages to explain 'how diseases happen' at a level which is scientifically valid and which still remains comprehensible to a junior medical student.

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The Ulster Medical Journal, Volume 55, No. 2, pp. 187 – 189, October 1986.

Case report

Primary malignant lymphoma of the appendix

R J Stewart, M Mirakhur

Accepted 1 August 1986.

Primary malignant lymphoma of the appendix is a rare tumour. We report a case and review the literature discussing the management and prognosis.

CASE HISTORY

A 33-year-old female presented with an acute onset of lower abdominal pain of sixteen hours' duration. She gave a three-month history of general malaise but was otherwise asymptomatic. On examination she was pyrexial, temperature 37.5°C with lower abdominal tenderness and rebound. The haemoglobin was 12.9 g/dl and the white cell count 16 × 10^3 µl with a normal differential. A gynaecological opinion was requested, vaginal examination revealing a fullness in the right side of the pelvis, which on ultrasound scan was compatible with an ovarian cyst. Laparotomy through a Pfannensteil incision revealed a 7 × 4 cm tumour in the body of the appendix which was perforated. The caecum was normal. In view of limited access, appendicectomy plus resection of adjacent caecum was performed, following which the patient made an uneventful recovery. Postoperatively her leucocytosis resolved and her white cell count to date remains within normal limits.

Macroscopically the resected specimen showed the appendix to be distended by greyish-white tumour which was infiltrating along the wall into the caecum. Histologically the lesion was a diffusely infiltrating lymphoma replacing the normal lymphoid tissue of the appendix, the limits of resection being free of tumour. On immunoperoxidase staining, the lesion was confirmed to be a B-cell lymphoma of the centrocytic/centroblastic type.

Subsequent screening, with a small bowel series, bone marrow examination and CT scan, did not reveal the presence of further tumour. A chemotherapy regimen consisting of vincristine, cyclophosphamide and prednisolone was commenced three weeks after surgery, and eighteen months later the patient remains free from relapse.

DISCUSSION

Malignant lymphomas comprise one to four per cent of malignant neoplasms of the gastrointestinal tract.[1] Primary involvement of the bowel occurs in five per cent of all lymphomas[2] of which 33 – 63 per cent affect the stomach, 25 – 60

Departments of Surgery and Pathology, The Queen's University of Belfast.
R J Stewart, FRCS, Surgical Registrar.
M Mirakhur, MD, MRCPath, Senior Medical Officer.

Correspondence to: Mr R J Stewart, Department of Surgery, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.

per cent the small intestine and 3 – 30 per cent the large intestine.[1-4] Sole involvement of the appendix is rare, Collins reporting 11 cases in 71,000 appendix specimens, an incidence of 0.015 per cent.[5] A review of the literature shows all tumours reported to be of the non-Hodgkins variety, presenting from 4 – 55 years (mean 18 years) and with a male predominance of 1.5:1.[1, 6-12]

The commonest presenting symptom was right iliac fossa pain recurring over a period of months, frequently associated with a palpable mass. A lesser number presented acutely with systemic features or 'appendicitis', our patient developing peritonitis secondary to tumour perforation. This complication explains her leucocytosis which rapidly resolved postoperatively.

Operative treatment may be by appendicectomy with or without resection of caecum or a right hemicolectomy. In the event of resection not being possible tumour limits should be outlined by metal clips to facilitate subsequent radiotherapy. At operation the abdomen should be thoroughly explored for involvement of regional and distant lymph nodes, hepatosplenomegaly and multicentric lesions within the gut.

Postoperative management may comprise radiotherapy, systemic chemotherapy or a combination depending on the histopathological features and stage of disease. Irradiation is a potent agent for achieving local control and is curative in over 50 per cent of patients with stage I and II non-Hodgkin's lymphoma.[13] With the identification of effective combination chemotherapy for advanced lymphoma, it is not surprising that these drugs have also been utilised for patients with stage I and II disease, with results as good and probably better than radiotherapy alone.[14] Combined modality therapy reports excellent results for stage I and II disease but shows no improvement in advanced disease to date.[15]

Details regarding survival of patients with a primary lymphoma of the appendix are scanty, with reports varying from one month to 28 years. In the absence of adequate staging and postoperative treatment, few conclusions may be drawn, but an early presentation, as with this patient, and adequate treatment should result in a prolonged survival.

We are grateful to Mr S T D McKelvey and Dr P Abram for permission to report this case.

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BOOK REVIEW

Aids to the examination of the peripheral nervous system. (New ed.). (pp 61. Illustrated. £2.95). London: Baillière Tindall on behalf of the Guarantors of Brain, 1986.

This slim volume details the wiring diagram of the limbs and the methods of testing individual muscles with beautiful black and white illustrations. I have examined this new edition with interest. The previous edition has taken its place in my bag beside my ophthalmoscope and tendon hammer as an essential tool of the trade of a practising clinical neurologist. The new edition has retained the style of the old, being commendably brief and clear. It has made good one significant lack in previous editions, with the addition of a coloured diagram of the lumbosacral plexus.

There is something in this book for every student of neurology, no matter how old. At any price it is a bargain, but at its present price every student should have one. I hope the new publishers make it their business to ensure that there is a steady supply in the bookshops. Previous editions have gone out of print rapidly.

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The Ulster Medical Journal, Volume 55, No. 2, pp. 190 – 192, October 1986.

Case report

Biliary peritonitis due to choledochal cyst presenting in late pregnancy

T Diamond, K J S Panesar

Accepted 1 August 1986.

CASE HISTORY

A previously healthy 23-year-old primigravida at 35 weeks' gestation presented with ante-partum haemorrhage and evidence of placental abruptio on ultrasound scanning. Emergency Caesarean section was performed via a Pfannenstiel incision, and a healthy baby was delivered in good condition. The obstetrician noticed that the peritoneal cavity contained some free reactive fluid, and surgical assistance was requested. It was difficult to carry out a full investigative laparotomy through the Pfannenstiel incision, but the appendix appeared normal and the stomach, duodenum, gallbladder, and pancreas were all normal on palpation. The colon was dilated from the caecum to the splenic flexure. The appendix was removed and a caecostomy tube was inserted via the appendix stump, to deflate the colon. A peritoneal drain was inserted and the incision closed. Following this, her condition did not improve and she remained ill, with abnormal liver function tests, elevated temperature and signs of generalised peritonitis.

Four days after the Caesarean section a further laparotomy was carried out, through a right paramedian incision. On this occasion, the peritoneal cavity contained a lot of bile and the gallbladder was oedematous and inflamed, with a gangrenous and perforated cystic duct. Emergency cholecystectomy was performed and the common bile duct was explored via a supraduodenal incision. An intra-operative T-tube cholangiogram revealed a large choledochal cyst, extending from the origin of the cystic duct to the lower end of the common bile duct, with absence of flow from the common bile duct into the duodenum (Fig 1). The choledochal

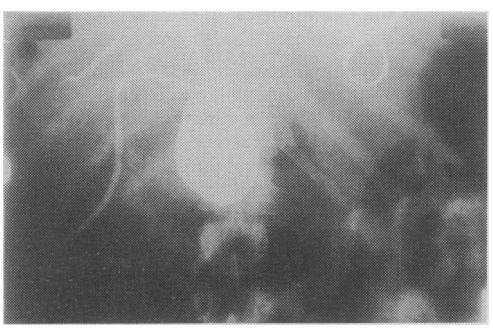

Fig 1. Intra-operative T-tube cholangiogram showing the choledochal cyst and absence of flow of contrast into the duodenum.

Department of Surgery, Altnagelvin Hospital, Londonderry, BT47 1SB.
T Diamond, BSc, FRCSEd, FRCSI, Registrar in Surgery.
K J S Panesar, MB, FRCS, FRCSEd, Consultant Surgeon.
Correspondence to: Mr Panesar.

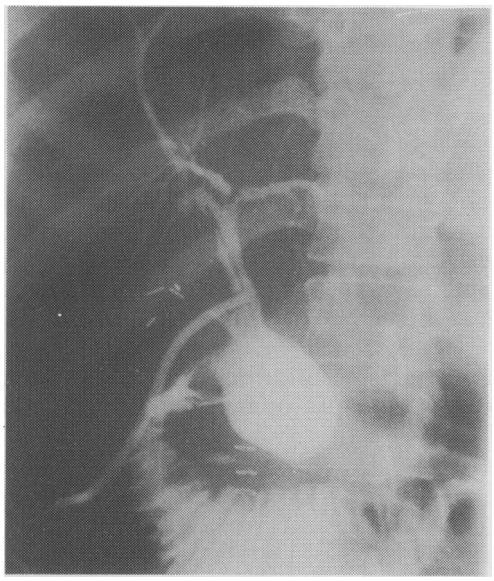

Fig 2. T-tube cholangiogram, seven days post-operatively, showing free flow through the choledochocysto-duodenostomy.

cyst was not apparent prior to the cholangiogram. In the first instance an inflamed and distended gall-bladder was found and, after its removal, an operative cholangio-gram revealed a cystic dilatation. There was no evidence of cyst formation in the liver, kidneys or pancreas. Biopsy of the choledochal cyst was not attempted. A chole-dochocysto-duodenostomy was performed and the common bile duct was drained via a T-tube.

Her post-operative recovery was uncomplicated, liver function tests returned to normal and a T-tube cholangiogram, seven days post-operatively, showed free flow through the choledochocysto-duodenostomy (Fig 2). Six months post-operatively she remained well, with normal liver function tests.

COMMENT

Choledochal cyst is a rare anomaly of the biliary tract. A male-to-female ratio of 1:4 is generally recognised[1,2] and the majority of cases occur in childhood. Twenty-five per cent of patients are diagnosed within the first year of life and a further 30 per cent before the age of 10 years.[3]

The classical triad consisting of intermittent abdominal pain, a mass in the right upper quadrant of the abdomen and jaundice, is present only in approximately 38 per cent of cases, but the majority of patients present with at least one of these clinical features. Rarely, the patient may present with biliary peritonitis due to rupture of the cyst. In most instances this apparently occurs spontaneously, but traumatic rupture has been documented, and rupture has also been reported during pregnancy or labour, in approximately 50 patients.[3] The association of this complication of rupture during pregnancy is quite significant in this condition and is presumably due to compression of the cyst as a result of increased intra-abdominal pressure in late pregnancy and labour.

The occurrence of acute cholecystitis, gangrene of the cystic duct and biliary peritonitis in this patient is unusual. The most likely explanation was obstruction of the biliary system due to increased pressure on the choledochal cyst in late pregnancy, or perhaps a result of direct compression of the cystic duct and artery by the cyst.

The pre-operative investigations in an elective patient suspected of having a choledochal cyst and not presenting as an emergency would be an ultrasound of the upper abdomen, percutaneous transhepatic cholangiography and possibly ERCP (endoscopic retrograde cholangiopancreatography). The only acceptable method of treatment of choledochal cyst is surgical. However, the choice of operation between an internal drainage on the one hand and complete excision

and reconstruction on the other remains controversial. Internal drainage is performed either into the duodenum as a choledochocysto-duodenostomy, or into the jejunum as a Roux-en-Y choledochocysto-jejunostomy, the latter being preferable.

The main advantage of internal drainage is the technical ease with which the operation may be performed, and the low operative morbidity and mortality. However, the ineffectual musculature and incomplete endothelial lining of a dilated cyst predisposes to stomal stenosis and resultant ascending cholangitis. The high morbidity and mortality previously associated with primary excision has been reduced by modern techniques, intensive care facilities and antibiotics. Excision also offers the added advantage of the elimination of the small, but real, risk of carcinoma developing in a choledochal cyst.[6] For these reasons, most recent reviews on this subject recommend excision and reconstruction with a Roux-en-Y jejunal loop in elective cases where a pre-operative diagnosis has been made.[1, 3, 7, 8, 9]

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The Ulster Medical Journal, Volume 55, No. 2, pp. 193 – 194, October 1986.

Book reviews

Cecil. Essentials of medicine. Editors T E Andreoli, C C J Carpenter and F Plum. (pp 831. Illustrated. £19.50). Philadelphia. London: Saunders, 1986.

The text of this excellent book is divided into twelve major system components, including a small section on oncology. Each section begins with a review of the relevant anatomical and physiological aspects of the system involved, followed by a review of the cardinal clinical and laboratory manifestations of the main diseases and, where appropriate, descriptions of additional diagnostic procedures such as endoscopic examination. Each section contains a series of chapters describing major clinical disorders in very adequate detail. These are clearly listed at the beginning of the book, under a table of contents format enabling rapid location in the text. All common disease states are comprehensively covered. An additional bonus is the built-in description of physical signs and their variation in different disease processes. This subtle blend of clinical skills and descriptive medicine in a single volume is a unique and highly commendable achievement. The overall presentation of the work is of the highest standard, the style is flowing and pleasant and the authors have undoubtedly achieved their aim of developing a "reader friendly" book.

The few original radiographs included are of a satisfactory standard, adequately conveying their intended message. The book is enhanced by numerous, attractive, concise, well-prepared, two-colour diagrams which highlight main points and relevant summaries. An even more useful feature is the tabular summaries of major disease processes with their relevant physical signs — a most useful means of rapid revision for the undergraduate. Overall, this is a refreshing and unique approach to the presentation of general internal medicine to the student and is much more than a short introductory textbook. It will fulfil the basic intention of the authors to present the fundamental principles and practice of medicine. They promise a regular revisionary update to allow for ongoing advances. Like its famous ancestor *Cecils Textbook of Medicine, Cecils Essentials of Medicine* is highly recommended and has much to commend it as a standard student work.

JIC

Chronic pain: management principles. Edited by Steven F Brena and Stanley L Chapman. (pp 240. £12.50). London: Saunders, 1985. (Clinics in anaesthesiology, vol 3, no 1, January 1985).

The medical profession, and indeed related disciplines, have become increasingly aware in recent years that persistent pain is, in itself, a significant clinical problem. A problem, moreover, which justifies, and occasionally rewards, a serious approach to its symptomatic management. One product of this current interest in chronic pain has been a gradual realisation of its complexity, in turn promoting extensive research and an impressive proliferation of the literature.

The present publication, from the *Clinics in anaesthesiology* series, incorporates the views of fifteen authors, and although Great Britain and Australia have distinguished representatives, depends heavily on North American experience. Dr John Bonica, to many the initiator of the Pain Clinic movement, reviews its history and evolution. It is, perhaps, salutary to note that Paracelsus (AD 1490 – 1540) advocated opium, electrotherapy, massage and exercise. Somewhat updated, such methods form a significant part of our armamentarium today! The following chapter, by Dr Duggan, gives a concise yet very adequate summary of physiological principles.

The remainder of the book, with the exception of a sensible review of basic nerve blocks by Dr Parris is confined to what might be termed non-invasive aspects such as psychological, social and organisational considerations, drug therapy and hyperstimulation analgesia. This book deals well with a limited number of topics, but could certainly not be considered a comprehensive review of the subject. Those already involved in chronic pain work may find that reading it serves to broaden their perspectives, and those contemplating the establishment of a Pain Clinic should find some sections particularly thought-provoking. It may have less to offer the general reader, although it could be a worthwhile addition to a departmental library, in that pain is universal and this quite readable little book might stimulate interest in its more adequate management. At £12.50 it is not, by modern standards, expensive.

WL

Plastic and reconstructive surgery. Edited by Ian F K Muir. (pp 173. Illustrated. £29.50). London: Baillière Tindall, 1986. (Current operative surgery).

This book, which is well written, is as up-to-date as any text book can be. Some of the recent advances described are quite new and their proven value may require refinement with experience and time. The authors, who are internationally recognised, have dealt with their subjects expertly but it should also be pointed out that the compass of this book is limited and it can only be seen as a supplement to the average bench library. It is not too expensive and good value for those who require an up-to-date appraisal in reconstructive surgery. It would also prove valuable reading for those intending to sit a specialty examination.

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The Ulster Medical Journal, Volume 55, No. 2, pp. 193 – 194, October 1986.

Book reviews

Cecil. Essentials of medicine. Editors T E Andreoli, C C J Carpenter and F Plum. (pp 831. Illustrated. £19.50). Philadelphia. London: Saunders, 1986.

The text of this excellent book is divided into twelve major system components, including a small section on oncology. Each section begins with a review of the relevant anatomical and physiological aspects of the system involved, followed by a review of the cardinal clinical and laboratory manifestations of the main diseases and, where appropriate, descriptions of additional diagnostic procedures such as endoscopic examination. Each section contains a series of chapters describing major clinical disorders in very adequate detail. These are clearly listed at the beginning of the book, under a table of contents format enabling rapid location in the text. All common disease states are comprehensively covered. An additional bonus is the built-in description of physical signs and their variation in different disease processes. This subtle blend of clinical skills and descriptive medicine in a single volume is a unique and highly commendable achievement. The overall presentation of the work is of the highest standard, the style is flowing and pleasant and the authors have undoubtedly achieved their aim of developing a "reader friendly" book.

The few original radiographs included are of a satisfactory standard, adequately conveying their intended message. The book is enhanced by numerous, attractive, concise, well-prepared, two-colour diagrams which highlight main points and relevant summaries. An even more useful feature is the tabular summaries of major disease processes with their relevant physical signs — a most useful means of rapid revision for the undergraduate. Overall, this is a refreshing and unique approach to the presentation of general internal medicine to the student and is much more than a short introductory textbook. It will fulfil the basic intention of the authors to present the fundamental principles and practice of medicine. They promise a regular revisionary update to allow for ongoing advances. Like its famous ancestor *Cecils Textbook of Medicine, Cecils Essentials of Medicine* is highly recommended and has much to commend it as a standard student work.

JIC

Chronic pain: management principles. Edited by Steven F Brena and Stanley L Chapman. (pp 240. £12.50). London: Saunders, 1985. (Clinics in anaesthesiology, vol 3, no 1, January 1985).

The medical profession, and indeed related disciplines, have become increasingly aware in recent years that persistent pain is, in itself, a significant clinical problem. A problem, moreover, which justifies, and occasionally rewards, a serious approach to its symptomatic management. One product of this current interest in chronic pain has been a gradual realisation of its complexity, in turn promoting extensive research and an impressive proliferation of the literature.

The present publication, from the *Clinics in anaesthesiology* series, incorporates the views of fifteen authors, and although Great Britain and Australia have distinguished representatives, depends heavily on North American experience. Dr John Bonica, to many the initiator of the Pain Clinic movement, reviews its history and evolution. It is, perhaps, salutary to note that Paracelsus (AD 1490 – 1540) advocated opium, electrotherapy, massage and exercise. Somewhat updated, such methods form a significant part of our armamentarium today! The following chapter, by Dr Duggan, gives a concise yet very adequate summary of physiological principles.

The remainder of the book, with the exception of a sensible review of basic nerve blocks by Dr Parris is confined to what might be termed non-invasive aspects such as psychological, social and organisational considerations, drug therapy and hyperstimulation analgesia. This book deals well with a limited number of topics, but could certainly not be considered a comprehensive review of the subject. Those already involved in chronic pain work may find that reading it serves to broaden their perspectives, and those contemplating the establishment of a Pain Clinic should find some sections particularly thought-provoking. It may have less to offer the general reader, although it could be a worthwhile addition to a departmental library, in that pain is universal and this quite readable little book might stimulate interest in its more adequate management. At £12.50 it is not, by modern standards, expensive.

WL

Plastic and reconstructive surgery. Edited by Ian F K Muir. (pp 173. Illustrated. £29.50). London: Baillière Tindall, 1986. (Current operative surgery).

This book, which is well written, is as up-to-date as any text book can be. Some of the recent advances described are quite new and their proven value may require refinement with experience and time. The authors, who are internationally recognised, have dealt with their subjects expertly but it should also be pointed out that the compass of this book is limited and it can only be seen as a supplement to the average bench library. It is not too expensive and good value for those who require an up-to-date appraisal in reconstructive surgery. It would also prove valuable reading for those intending to sit a specialty examination.

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Active management of labour: the Dublin experience. By K O'Driscoll and D Meagher. 2nd ed. (pp 204. Graphs. £9.95). London: Baillière Tindall, 1986.

That a second edition of this book makes its appearance so soon after the first edition (1980) is in itself a recommendation. The authors and their colleagues express views that have evolved from their experiences with some 150,000 deliveries. Many will not necessarily agree that the duration of labour should be defined as "the number of hours a woman spends in the delivery unit from the time of admission until the time the baby is born". However, the point is made that this is the period that is relevant to the management of labour in clinical practice.

The chapters (5 and 26) discussing the importance of having a clear understanding of what is meant by dilatation and effacement of the cervix are excellent and that fact that labour has commenced only when dilatation of the cervix has started is again emphasised because it is so fundamental a concept to labour and its management. The graphical representation of the events in labour are most valuable and for those who are involved in clinical practice their superiority over the written or verbal account of labour is unquestionable. The chapters on the "Care of the Fetus" and "Caesarean Section Rates" are very informative and should provide every obstetrician with much food for thought.

In conclusion, the authors are to be congratulated on what is an important contribution to obstetrics, and it is recommended that all midwives and obstetricians should read this book so that they will have the opportunity to reflect on many of the matters discussed, particularly in relation to their own management of labour.

JMGH

MCQs in psychiatry. By C Grant, G McDonald and P Bell. (pp 123. £7.95). Hemel Hempstead: Pastest, 1986.

In asking me to review this book, the editor suggested that I say what I really thought about multiple choice questions (MCQs). Did he hope for startling revelations about the futility of this form of assessment? My own view is very much in favour of the use of carefully constructed MCQs, which bring a degree of objectivity to the assessment of medical knowledge, provided of course they are combined with some additional tests of clinical competence and basic literacy. Making a true/false decision concentrates thinking wonderfully, and is an excellent training for doctors who above all else must be prepared to make decisions and live with them.

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The management of the acute coronary attack. The J Frank Pantridge Festschrift. Edited by J S Geddes. (pp 128. £15.00). London: Academic Press, 1986.

In the foreword to this book, Professor Julian, President of the British Cardiac Society, pays tribute to the introduction of mobile coronary care in Belfast in 1966, as a milestone in the history of cardiology and indeed of medical practice. In its own way this book is also a milestone on the pathway towards better management of the acute coronary attack. A distinguished international group of cardiologists met in Belfast in March 1986 to pay tribute to Professor Frank Pantridge, and in their presentations and discussions have provided an up-to-date assessment of many aspects of the problem. The impact of mobile coronary care on medical practice in Northern Ireland, Great Britain and the USA is analysed and the views of the Chief Medical Officer of the Department of Health and Social Services at the Elephant and Castle, London, on future UK policy are presented.

Further prospects for prevention of arrythmias and for correction of ventricular fibrillation by pharmacological or by electrical means, and the community problems of making these skills and techniques available where and when they are needed are also discussed.

Milestones should be clearly inscribed, easily visible and placed at appropriate intervals along the way. Dr John Geddes has been successful in the first two of these matters — in the production and editing of this volume. While the exact location of the next milestone still remains uncertain, there is no doubt that this *festschrift* will guide and stimulate those who set out to find it.

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