

Table Identification of patients with overt and borderline hypothyroidism

Case No	Age	Sex	T4 (nmol/l)	TSH (mU/l)	AST (IU/l)	LDH (IU/l)		
Hypothyroidism (n = 2):								
1	81	F	64	35.5	29	337		
2	67	F	34	50+	33	428		
Borderline hypothyroidism (n = 3): (T4 80 - 110 nmol/l; TSH greater than 6.5 mU/l)								
			(a)	(b)	(a)	(a)		
1	69	F	81	83	7.1	2.3	22	337
2	68	M	103	103	8.3	4.6	26	300
3	83	M	82	103	7.5	5.6	25	347

(a) = initial blood test results; (b) = repeat blood test result taken three to nine months later.

increased in 92 cases, AST activities alone were raised in 18, and in 16 both enzymes were high. Thyroid function testing consisted of initial duplicate analyses of serum T4 concentrations by radioimmunoassay using donkey anti-sheep antibodies (RAST Allergy Unit, Benenden Chest Hospital) and ¹²⁵I (Amersham International) as a tracer. Eighty one of 125 samples with T4 concentrations of less than 110 nmol/l

(normal range 50-160) were then assayed for TSH (Serono Kit). Five of 125 patients (table) were found to have abnormal thyroid function tests. The two cases of frank primary hypothyroidism identified had been diagnosed by the admitting physicians and received treatment before the study results were available. All three borderline cases were asymptomatic for thyroid disease and on follow up showed no progression.

The likelihood that unexpected increases in serum enzymes can be explained by undiagnosed hypothyroidism is minimal and hypothyroidism should therefore be low on the list of differential diagnoses.

EA CLARKE
P YATES
DJ GOLDIE

Department of Pathology,
Southmead Hospital,
Bristol BS10 5NB

References

- O'Malley GR, Davies TJ, Rosenthal FD. Effects of rest exercise and warming on serum creatine kinase levels in primary hypothyroidism. *Clin Sci* 1981;60:595-7.
- Doran GR, Wilkinson JH. The origin of the elevated activities of creatine kinase and other enzymes in the sera of patients with myxoedema. *Clin Chim Acta* 1975;62:203-11.
- White GH, Walmsley RN. Plasma enzyme activities in primary hypothyroidism. *Clin Chem* 1984;30:323-5.
- Huisman JW. Enzyme activities and hypothyroidism. *Clin Chem* 1984;30:1422.

Matters arising

Bolton General Hospital,
Minerva Road, Farnworth,
Bolton BLA 0JR

Use of necropsy in clinical audit

The views of Hunt on the necropsy in audit are somewhat surprising.¹ Discrepancies between clinical and necropsy diagnoses have been found in several studies,^{2,4} and the discrepancies have been regarded as important by clinicians. These findings must not be ignored on the basis of an unjustified comparison with surgical operations. The rather confusing sentence, "It has never been claimed that in hospital medicine more than a few erroneous diagnoses could have been made correctly except by luck" is simply not true. This sentence seems to mean that hospital diagnosis is as good as it possibly can be and cannot be improved. There is a considerable body of evidence to suggest that this is not the case.⁵

No comments are made about quality of necropsy and the need for audit of necropsies. There is considerable disquiet about the quality of some coroners' necropsies on cot deaths, and the number done in a single morning by some pathologists suggests that the quality may not be high. Furthermore, not all coroners' necropsies are performed by properly trained histopathologists. The views expressed by Dr Hunt seem remarkably complacent.

D L BISSETT

Department of Histopathology,

References

- Hunt AC. The necropsy in audit in clinical medicine and other medical specialties. *J Clin Pathol* 1989;42:564-5.
- McGoogan E. The autopsy and clinical diagnosis. *J Roy Coll Phys* 1984;240-3.
- Goldman L, Sayson R, Robbins S, Mettman M, Weisberg M. The value of the autopsy in three medical eras. *N Engl J Med* 1983;308:1000-5.
- Karwinski B, Hartveit F. Death certification: increased clinical confidence in diagnosis and lack of confirmation by necropsy is not justified. *J Clin Pathol* 1989;42:13-17.
- Dowie J, Elstein A. *Professional judgement*. Cambridge: Cambridge University Press, 1988.

Dr Hunt comments:

It is difficult to reduce a half hour presentation to 500 words, and it is a shame that Dr Bissett did not come to the meeting. I stick by my opinion that most misdiagnoses in modern hospitals follow careful consideration by a medical team and are seldom the result of negligence or lack of individual skill. I dread a return to my early days in pathology when we often were regarded as busybody corpse-cutters trying to teach clinicians their job and were not part of clinical pathology. It is up to clinicians to

regulate their own specialty; it is up to us to provide a high quality necropsy service, which with present staffing levels would be impossible if there were to be a dramatic increase in necropsy numbers, the necessity for which I question. Professor Scheuer recently quoted to me Professor Hamperl's autobiographical account (not available to us monoglots) of the old tradition, "We tried to stop the surgeons sending specimens to us—it was interfering with the real work of the department". And that was in my own lifetime.

The standard of necropsy was not mentioned in my presentation because it was not part of my brief. I share Dr Bissett's disquiet, especially in view of my belief that coroners' necropsies are a particularly important form of audit.

Clinical importance of squamous metaplasia in invasive transitional cell carcinoma of the bladder

Merely to set the record straight, Martin and colleagues state that with respect to squamous metaplasia an invasive transitional cell carcinoma of the bladder, "Its importance for prognosis is not known," and, "It is only relatively recently that histopathologists have recognised that transitional cell carcinoma with squamous areas is an entity distinct from squamous cell

carcinoma."¹ Older pathologists may remember a report by Dukes and Masina entitled, "Classification of Epithelial Tumours of the Bladder" in which they not only had a category of transitional cell carcinoma with metaplasia, separate from transitional cell carcinoma and pure squamous cell carcinoma, but they drew attention to its common association with rapidly growing tumours of a relatively high grade of malignancy.² Nevertheless, I do think that periodic reiteration is worthwhile, and it has been 40 years.

V F COULSON

Department of Pathology,
UCLA School of Medicine,
Center for the Health Sciences,
10833 Le Conte Avenue,
Los Angeles, California 90024-1732, USA

References

- 1 Martin J. Clinical importance of squamous metaplasia in invasive transitional cell carcinoma of the bladder. *J Clin Pathol* 1989;42:250-3.
- 2 Dukes CE, Masina F. Classification of epithelial tumours of the bladder. *Br J Urol* 1949;21:273-95.

Hodgkin's disease presenting with hypercalcaemia

Mayne and Bunch reported a case of Hodgkin's disease presenting with hypercalcaemia.¹ We also report a patient in this relatively rare category of hypercalcaemia in lymphoma.

A 67 year old retired miner presented as an emergency admission with shortness of breath and chest pain radiating to the shoulders. He also complained of backache, difficulty in walking, and weight loss. He had chronic faecal fistulae following diverticulitis and peritonitis five months earlier.

Haemoglobin concentration was 11.2 g/dl and erythrocyte sedimentation rate 102 mm in the first hour. Chest x-ray picture and lung scan showed no focal abnormality. Cardiac enzymes, plasma amylase, and electrolytes were all normal. The chest pain, thought to be of musculoskeletal origin, quickly resolved and he was discharged after a few days on codeine phosphate.

Three weeks later he was readmitted with similar symptoms. Examination showed bronchopneumonia and dehydration. The plasma electrolyte concentrations were as follows: sodium 138 mmol/l, potassium 2.3 mmol/l, chloride 92 mmol/l, and bicarbonate 34 mmol/l. Creatinine concentration was 142

μmol/l and urea 13.1 mmol/l. Haemoglobin concentration was now 10.9 g/dl, red blood cell count $4.1 \times 10^{12}/l$, alkaline phosphatase activity 409 IU/l and gamma glutamyl transferase (GGT) 183 IU/l. He was treated with rehydration and calcitonin (320 U/12 hours). Two days later he became very breathless and his general condition continued to deteriorate. The following day he died.

Necropsy showed that he had an enlarged spleen (200 g) and liver (1700 g), both with numerous small deposits of tumour (about 0.5 and 1.0 cm, respectively). Sections of these organs showed nodules of large cell non-Hodgkin's malignant lymphoma. The cause of death was recorded as bronchopneumonia secondary to non-Hodgkin's malignant lymphoma in addition to chronic diverticular disease with fistulae.

Like the case of Mayne and Bunch¹ our patient with Hodgkin's disease presented with hypercalcaemia but without clinically apparent bone disease. Skeletal metastases were not apparent and none was found at necropsy. Raised plasma alkaline phosphatase activity probably reflected hepatic disease rather than bone disease as GGT activity was also increased.

The hypercalcaemia in our patient did not respond quickly to treatment. Little could be done as his general condition rapidly deteriorated in association with the bronchopneumonia and diverticular disease.

R D ELLIS

P R BECK

B K MONDAL

Department of Clinical Biochemistry,
Rotherham District General Hospital,
Moorgate Road, Oakwood,
Rotherham S60 2UD

Reference

- 1 Mayne K M, Bunch C. Hodgkin's disease presenting with hypercalcaemia. *J Clin Pathol* 1989;42:219.

Immunohistochemical identification of bacteria in tissue sections

In their paper on the immunohistological demonstration of *Salmonella virchow* Bignardi and Khong state that they are not aware of any reports describing the identification of bacteria in routinely processed human tissue sections using the immunoperoxidase method.¹ We reported the identification of group B streptococci in necropsy material in *The Journal of Clinical Pathology* using the immunoperoxidase technique with both monoclonal and poly-

clonal antibodies.² The latter was serum used for routine serology in microbiology laboratories. The technique has also been used for the identification of *Leptospira*,³ *Mycobacterium leprae*,⁴ and *Chlamydia trachomatis*.⁵

We have also used rabbit antiserum raised against *Listeria monocytogenes* types 1 and 4 to stain this organism in human formalin fixed tissue. A section of meninges from a woman who died with an *L monocytogenes* type 1 meningitis was stained with immunoperoxidase. The paraffin wax embedded section was stained using the peroxidase-antiperoxidase technique; the serum was diluted 1 in 100 and incubated for 30 minutes. The serum was specific for species but did not distinguish between types.

We are concerned that Bignardi and Khong did not test their serum against other organisms as it is quite possible that the antiserum used would also react with other species of *Salmonella* and maybe other Gram negative organisms such as *Escherichia coli* as well. We feel that it is important to show the specificity of sera used for microbial identification by testing it against other organisms as we have reported.² Because of the potential cross reactions between bacteria it is desirable to use monoclonal antibodies when possible.

R G FELDMAN

J R SALISBURY*

Department of Medicine,
University College, London
*Department of Morbid Anatomy,
King's College Hospital
Medical School,
London

References

- 1 Bignardi GE, Khong TY. Immunohistological demonstration of *Salmonella virchow* in a case of infant death. *J Clin Pathol* 1989; 42:329-30.
- 2 Feldman RG, Law SM, Salisbury JR. Detection of group B streptococcal antigen in necropsy specimens using monoclonal antibody and immunoperoxidase staining. *J Clin Pathol* 1986;39:223-6.
- 3 Ferreira Alves VA, Vianna MR, Yasuda PH, De Brito T. Detection of leptospiral antigen in the human liver and kidney using an immunoperoxidase staining procedure. *J Pathol* 1987;151:125-31.
- 4 Narayanan RB, Ramu G, Sinha S, Sengupta U, Malaviya GN, Desikan KV. Demonstration of *Mycobacterium leprae* specific antigens in leprosy lesions using monoclonal antibodies. *Indian J Lepr* 1985;57:258-64.
- 5 Winkler B, Reumann W, Mitoa M, Gallo L, Richart RM, Crum CP. Immunoperoxidase localization of chlamydial antigens in acute salpingitis. *Am J Obstet Gynecol* 1985;152: 275-8.