patients. In 146 patients the channel curved, making a wall visible which was superior in 19, posterosuperior in 23, posterior in 10, posteroinferior in 12, inferior in 20, anteroinferior in 37, anterior in 16, and anterosuperior in nine. Duodenal ulcers or scars were identified in 34 patients; they occupied the centre of the visible field in nine and lay superiorly in one, posteriorly in 12, and anteriorly in 12.

Discussion

By centring the pylorus in the field of view the tip of the endoscope was kept close to the axis of the distal stomach. The duodenal wall visible through the pylorus should therefore lie directly in the path of a jet of food and acid leaving the stomach.

The results show that no portion of the duodenal wall was uniquely exposed to, or protected from, emerging gastric contents. Also, the position of duodenal ulcers or scars did not seem to be determined by exposure to a localized jet. The peristaltic mobility of the gastric antrum, pylorus, and duodenal bulb, make it unlikely that a discrete area should be subjected to localized attack. It would also be necessary to invoke two discrete jets to explain the occasional finding of active anterior and posterior bulbar ulcers.

No local anatomical feature has been described that would explain the site of bulbar duodenal ulcers, apart from variation in vascularity[4] and the presence of localized pallor on the anterior duodenal bulbar wall when the gastric antrum is drawn to the left.[5] An emerging jet cannot be indicted for localized peptic ulceration after the formation of a side-to-side gastroenterostomy; neither can a local anatomical feature be invoked, since the segment of jejunum is selected fortuitously by the surgeon. The site of peptic ulcer, however, may be determined stochastically as the first area at which the balance of defence breaks down. But the frequency with which the ulcer remains solitary is at present inexplicable. Chronic peptic ulceration seems to have the intrinsic characteristics of singularity and discreteness.

[1] Ivy, A. C., Grossman, M. I., and Bachrach, W. H., *Peptic Ulcer*, p. 765. Philadelphia, Blakiston, 1950.
[2] Portis, S. A., and Jaffe, R. H., *Journal of the American Medical Association*, 1938, **110**, 6.
[3] Oi, M., *et al.*, in *Peptic Ulcer*, ed. C. J. Pfeiffer, p. 252. Copenhagen, Munksgaard, 1971.
[4] Piasecki, C., *British Journal of Surgery*, 1971, **58**, 660.
[5] Kirk, R. M., *Gut*, 1968, **9**, 414.

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Hyperthyroidism After Cholecystography

The Jod-Basedow phenomenon—hyperthyroidism induced by iodide—has been recognized for many years in iodine-deficient areas when iodide prophylaxis for goitre has been introduced. In other circumstances iodide has been shown to induce hyperthyroidism. Single exposure to high iodide dose, as in intravenous pyelography, has been followed by hyperthyroidism.[1] We report here two cases of hyperthyroidism after cholecystography.

Case Reports

A 56-year-old woman developed attacks of abdominal colic suspicious of biliary tract disease. She had a multinodular goitre but no symptoms or signs of thyroid overactivity. A cholecystogram with 3 g of sodium ipodate (1800 mg iodine) was performed and showed a non-functioning gall bladder. Within a week she developed palpitations, nervousness, irritability, trembling of her hands, and heat intolerance. When seen four weeks later she had lost 12 kg, despite a good appetite. She was agitated, had lid retraction, warm peripheries with digital tremor, and a tachycardia of 110/min. Her nodular goitre was unchanged. Her serum T-4 was over 300 nmols/l (23 µg/100 ml) (normal 58-167 nmol/l (4·5-13 µg/100 ml)). Serum T-3 uptake was 66 (normal range 92-117). ^{131}I uptake was 52% at two hours. Treatment was started with carbimazole, 10 mg thrice daily, and she became clinically euthyroid after four weeks. She continues on this therapy and is awaiting partial thyroidectomy.

A 47-year-old college lecturer consulted his doctor complaining of dyspepsia. A cholecystogram was carried out with 6 g sodium ipodate (3600 mg iodine). Four days after this he developed trembling of his limbs, increased sweating and heat intolerance, nervousness, and irritability. When seen four weeks later he had lost 4 kg, despite a good appetite. He had a small diffuse midline goitre, warm peripheries with digital tremor, a sinus tachycardia of 110/min, but no eye signs. Serum T-4 was 350 nmols/l (27 µg/100 ml) and serum T-3 uptake was 61. Therapy with carbimazole, 10 mg thrice daily, was started, and after four weeks this was reduced to 5 mg thrice daily when the patient appeared euthyroid. Further reduction of the dose was attempted after three months' therapy, but the signs of hyperthyroidism recurred necessitating return to the previous dose of carbimazole.

Discussion

The effects of iodide on thyroid function are remarkably diverse. Iodide is essential for thyroid hormone formation. The antithyroid action of iodide is a well-recognized clinical phenomenon in hyperthyroidism, though the normal thyroid gland appears to be insensitive to this antithyroid action of iodide. This may be related to the intracellular concentration of iodide, which is considerably raised in hyperthyroidism, when the iodine trapping mechanism is enhanced. Occasionally prolonged ingestion of iodides has resulted in hypothyroidism and goitre formation.[2] Patients who have previously received radio-iodine therapy or who have chronic thyroiditis appear to be particularly prone to iodide induced hypothyroidism.[3]

In contrast, iodide administration may also induce hyperthyroidism. The Jod-Basedow phenomenon has been clearly confirmed in recent years by workers in Tasmania[4] after iodation of bread in an iodine-deficient area. Hyperthyroidism induced by iodide has also occurred in areas of iodine sufficiency. Vagenakis[5] in Boston described four patients with nodular goitre without evidence of iodine deficiency. Iodide ingestion resulted in prolonged hyperthyroidism.

The mechanism of hyperthyroidism after a large dose of iodine remains unknown, though the normal homoeostatic regulation of thyroid function appears to be ineffective. This could be due to the presence of autonomously functioning nodules, independent of the action of thyroid stimulating hormone, which can increase the hormone synthesis in the presence of excess iodide.

[1] Blum, M., *et al.*, *New England Journal of Medicine*, 1974, **291**, 24.
[2] Harrison, M. T., Alexander, W. D., and Harden, R. McG., *Lancet*, 1963, **2**, 1238.
[3] Braverman, L. E., Woeben, K. A., and Ingbar, S. H., *New England Journal of Medicine*, 1969, **281**, 816.
[4] Stewart, J. C., *et al.*, *Australian and New Zealand Journal of Medicine*, 1971, **3**, 203.
[5] Vagenakis, A. G., *et al.*, *New England Journal of Medicine*, 1969, **287**, 816.

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Serum Lipids and Lipoproteins in Children with Kwashiorkor

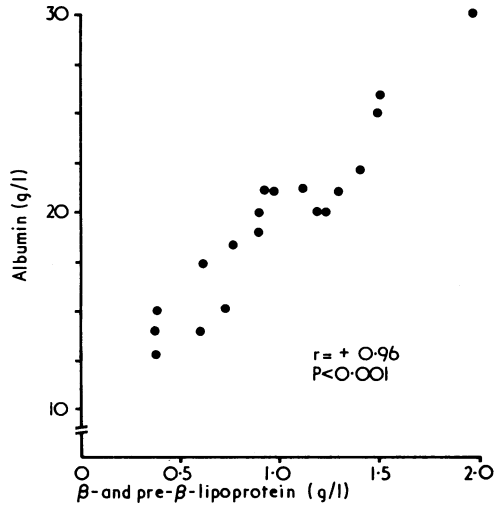
Though disorders of lipid metabolism have been described in kwashiorkor,[1] controversy still exists about their exact nature. Inconsistencies may be due to differences in methodology as well as geographical variations in the patterns of kwashiorkor. They suggest the need for further investigations if only to attempt the clarification of the pathophysiology of some striking aspects of the disease—for example, the extreme cerebral lethargy of kwashiorkor children and the enlarged fatty liver often found at necropsy. We have examined the concentrations of serum lipids, albumin, and total proteins in Nigerian children with florid kwashiorkor when admitted to hospital and before treatment.

Methods and Results

Investigations were carried out on 19 consecutive children, aged from 8 to 30 months, presenting with oedema, hepatomegaly, dermatoses, and cerebral lethargy. They were bled while fasting on the morning after admission. Ten healthy children of similar ages admitted for minor surgical procedures

served as controls. Serum lipids, albumin, and total proteins were determined by standard techniques. Serum β- and pre-β-lipoproteins were measured turbidimetrically.[2]

Serum concentrations of cholesterol, triglyceride, and β- and pre-β-lipoproteins were appreciably lower in the kwashiorkor children than in the control children ($P<0.001$ in all instances). The fig. shows a direct proportion between the concentrations of serum albumin and serum β- and pre-β-lipoproteins in kwashiorkor children.



Relationship between serum albumin concentrations and serum β- and pre-β-lipoprotein concentrations in children with kwashiorkor.

Discussion

We have shown by a simple quantitative technique using the selective precipitation of β- and pre-β-lipoproteins that the serum concentrations of these lipoproteins were decreased in children with kwashiorkor. The concentrations of serum cholesterol and triglyceride were also decreased. Since cholesterol and triglyceride are the major transport cargo of β- and pre-β-lipoproteins, the accumulation of fat in the liver of children with kwashiorkor may be partly due to the impaired release of these lipids from the liver into the plasma.[1] In addition the concentrations of serum albumin are directly proportional to the concentrations of serum β- and pre-β-lipoproteins in children with kwashiorkor. This is not the case in the fatty liver induced in rats by feeding orotic acid, an inhibitor of protein synthesis. Experimentally, though a total inhibition of the synthesis of β-lipoproteins occurs, the synthesis of albumin remains unchanged. An impaired synthesis of albumin in kwashiorkor, however, has been noted.[4] We suggest that a diminished synthesis of β- and pre-β-lipoproteins may accompany the diminished synthesis of albumin. Thus the impairment of the synthesis and possibly the transport functions of these proteins may result in a generalized poor nutritional state of the cells and tissues. This may render kwashiorkor children more susceptible to infections[5] and probably account for their striking cerebral lethargy.

[1] Truswell, A. S., in *Protein-Calorie Malnutrition*, ed. R. Olson, p. 119. New York, San Francisco, London, Academic Press, Inc., 1975.
[2] Walton, K. W., and Scott, R. J., *Journal of Clinical Pathology*, 1964, 17, 267.
[3] Windmueller, H. G., and Levy, R. I., *Journal of Biological Chemistry*, 1967, 242, 2246.
[4] Dean, R. F. A., and Schwartz, R., *British Journal of Nutrition*, 1953, 7, 131.
[5] Frood, J. D. L., Whitehead, R. G., and Coward, W. A., *Lancet*, 1972, 2, 1047.

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Oral Contraceptives and Myocardial Infarction in Young Women: A Further Report

We have recently reported an increased risk of myocardial infarction among women using oral contraceptives.[1] The conclusions were based on a controlled investigation of 58 women under 45 years of age who had survived myocardial infarction during 1968-72 in two hospital regions of England and Wales. The nature of the findings was such that it was thought desirable to submit them for publication before the collection of data in a third region was complete. The results for a similar group of patients investigated in the Wessex Region are presented in this report.

Patients, Methods, and Results

The methods for the selection of myocardial infarction and control patients and the investigation procedure in the North-West Metropolitan and Oxford Regions were described in detail in our previous publication. In the Wessex Region myocardial infarction patients and controls (three patients matched with each infarction patient in respect of marital status, five-year age group, and year of hospital admission) were identified by the medical information unit of the regional health authority. Altogether 21 myocardial infarction patients (aged 32 to 44 years) were identified in the Wessex Region, but four had died in hospital or before the study was undertaken and three could not be traced. The diagnoses of the control patients, methods of data collection, and statistical analyses were similar to those reported.[1]

The oral contraceptive practice of the Wessex patients and of the consolidated group of 72 infarction patients and their controls is shown in the table.

Oral Contraceptive Practice Among Patients with Myocardial Infarction (M.I.) and Controls

Oral Contraceptive Practice	Wessex Patients		Consolidated Patients	
	No. (%) of Patients with M.I.	No. (%) of Controls	No. (%) of Patients with M.I.	No. (%) of Controls
Never used	9 (64·3)	18 (75·0)	44 (61·1)	150 (78·9)
Used during month before admission	3 (21·4)	2 (8·3)	20 (27·8)	16 (8·4)*
Used only more than one month before admission	2 (14·3)	4 (16·7)	8 (11·1)	24 (12·6)
Total	14 (100·0)	24 (100·0)	72 (100·0)	190 (100·0)

*Comparison between proportions of patients using oral contraceptives during the month before admission: $\chi^2 = 13{\cdot}28$, $P<0.001$.

For the consolidated group the proportion of patients who had used oral contraceptives during the month before admission was significantly higher amongst the patients with infarction than among the controls ($P<0.001$), as was the proportion of those who had used oral contraceptives at any time ($P<0.01$). No appreciable difference was, however, apparent in the proportions who had used oral contraceptives only at some time in the past. The risk of admission for myocardial infarction in women who had been using oral contraceptives in the previous month relative to that in women who were not currently using them is estimated from these figures to be 4·2 to 1. After standardization for possible confounding by other risk factors for myocardial infarction (hypertension, pre-eclamptic toxaemia, cigarette smoking, and hypercholesterolaemia) the risk ratio was 3·1 to 1. This threefold increase in risk attributable to oral contraceptives was significant at the 2% level.

Comment

The difference in oral contraceptive use between the two groups of patients in the Wessex region is very similar to that which might have been expected from the experience in the larger group of subjects but does not reach statistical significance when examined independently. This is hardly surprising because the numbers are so small. The findings are, however, considered to be of particular interest since the method of ascertainment used should have identified all cases of non-fatal myocardial infarction in this region and provide confirmatory evidence of the association between oral contraceptive use and myocardial infarction in young women.

We are grateful to Professor M. Alderson for his help with patient identification and for obtaining permission from the appropriate consultants;