



Plasma disappearance of Hypaque on a semilogarithmic scale.

Effect of Aspirin on Glomerular Filtration Rate

Case No.	G.F.R. (ml/min)		% Change in G.F.R.
	Before Aspirin	After Aspirin	
1	168	139	-17.3
2	87	77	-11.5
3	100	88	-12
4	90	78	-13.3
5	96	78	-18.8
6	151	132	-11.3
7	84	69	-17.8
8	124	102	-17.8
9	98	96	-2.0
10	126	129	+2.4
11	146	131	-10.3
12	163	153	-6
13	148	148	0
Mean			-10.5

The results for the remaining 13 patients are shown in the Table.

Plasma salicylate levels were measured at three hours in 10 of the 13 patients and they ranged from 5 to 19 mg/100 ml, with a mean of 12 mg. There was no correlation between

percentage change in clearance and the plasma salicylate level.

Discussion

Aspirin produces a significant reduction in glomerular filtration rate as measured by this method. Though there are many theoretical objections to a single-injection technique (Smith, 1951) it has been shown to correlate well with standard clearance procedures. Under normal conditions Hypaque is excreted rapidly and completely by the kidney, is not taken up by other organs, and is not significantly protein bound. There is good evidence that Hypaque clearance bears a constant relation to inulin clearance (Denneberg, 1965; Donaldson, 1968). Furthermore, in preliminary studies we found that Hypaque clearance by a single injection technique gave highly reproducible results, consecutive measurements of filtration rate varying by less than 5%. We believe that it is accurate and reproducible enough to detect acute changes in filtration rate and that it therefore lends itself to studies of this kind.

The way in which aspirin produces its effect on the plasma clearance of Hypaque is unknown, nevertheless our results have important implications. In a technique which is becoming increasingly popular for following changes in glomerular filtration rate it is obviously vital to know that this measurement can be altered by a single therapeutic dose of a drug as common as aspirin. It would be of interest to know if other commonly used drugs had similar actions. The possibility that aspirin may acutely affect renal function is also of interest in view of its possible role in the long-term nephrotoxicity of analgesic substances.

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MEDICAL MEMORANDA

Gall Stones after Peptic Ulcer Surgery

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The case of a man developing gall stones after two peptic ulcer operations and a review of 406 other cases of gallstones are presented.

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Case Report

In 1961 a 60-year-old man presented with indigestion for 30 years; barium-meal examination showed duodenal ulceration. At operation anterior and posterior ulcers were found and a Polya-type gastrectomy was performed. The gall bladder was normal. In 1966 further digestive symptoms were investigated, and a stomal ulcer was found. Cholecystography showed nothing abnormal. At operation the normal gall bladder was confirmed and truncal vagotomy was performed for the ulcer. In 1967 still further indigestion occurred, and in 1968, after a cholecystogram showed a non-functioning gall bladder, cholecystectomy was performed for gall stones.

Review of Previous Cases

Altogether 406 patients found to have gall stones in the two-year period from 1 January 1965 to 31 December 1966 were reviewed. Of these 26 had undergone previous ulcer surgery, when the gall bladder had been noted to be normal. (Table I). The predominance of the Billroth I procedure among the

TABLE I—Gall Stones and Ulcer Surgery

	Male	Female	Total
No. of patients with gall stones	127	279	406
No. of gall-stone patients with previous ulcer surgery	16	10	26
Percentage of gall-stone patients with previous ulcer surgery	12.6	3.6	6.4

TABLE II—Summary of 27* Ulcer Operations on 26 Patients Developing Gall Stones Subsequently

Ulcer Operation	No. of Patients	Sex	Years between Ulcer Surgery and Confirmed Gall Stones	
			Mean	Range
Polya†	13	M.	11	2—29
Polya	3	F.	14.5	14—15
Billroth I	3	M.	7	2—11
Billroth I	7	F.	7	1—18
Truncal vagotomy	1	M.	2	

*One patient underwent truncal vagotomy for anastomotic ulcer subsequent to Polya gastrectomy but before gall-stone formation.

†Polya refers to partial gastrectomy with gastrojejunal anastomosis.

women indicates the relatively greater incidence of gastric ulcer (Table II). Conversely, the predominance of Polya operations in men reflects the incidence of duodenal ulcer. It is of interest that only one patient had undergone vagotomy. Wastell (1969) reviewed 192 vagotomies performed at this hospital with a minimum follow-up of 10 years. In only one out of all these cases were gall stones confirmed.

The results indicate that though gall stones are much more common in women than in men very few have had previous ulcer surgery. Male patients predominate in the gastric clinic, and the close follow-up of these patients leads to the detection of gall stones which might escape undiagnosed in a non-attending population, hence the high incidence, 1 : 8, of previous ulcer surgery.

Comment

The development of gall stones in a patient only two years after vagotomy was in keeping with the theory that the altera-

tion of biliary tract dynamics by vagotomy might predispose to gall stones. The object of this review was to see whether, in fact, ulcer surgery might be a significant aetiological factor in cholelithiasis. Johnson and Boyden (1952), Cox *et al.* (1958), and Tinker and Cox (1969) noted alterations of gall-bladder physiology after vagotomy, and Wyatt (1969) noted changes after partial gastrectomy. After vagotomy there is an increased gall-bladder volume with increased emptying rate, the gall bladder becoming supersensitive to cholecystokinin.

Nielsen (1964) quoted four cases of gall stones within one year of vagotomy. Nobles (1966) found that 18% of patients undergoing vagotomy later required cholecystectomy. Major and Suren (1947), however, found only 6 cases out of 394 in which ulcer surgery preceded gall stones. Chapa and Engel (1959) found that 7 out of 135 cholecystectomies followed within seven years of gastric resection. Griffiths and Holmes (1964) found 17 out of 238 patients with gall stones who had had Polya gastrectomy.

Peptic ulcer surgery preceded one in eight cholecystectomies in male patients but only 1 in 30 in females. Vagotomy is not apparently of significance. Cholecystography should be performed in all patients presenting with new indigestion some years after ulcer surgery.

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Acute Hypercalcaemia and Renal Failure after Antacid Therapy

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Intensive therapy with antacids, especially with calcium carbonate, is recognized as a cause of hypercalcaemia and also of the milk alkali syndrome. Attention has been drawn by Kirsner (1964) to the occasional occurrence of a hypercalcaemic syndrome after the use of antacids. McMillan and Freeman (1965) pointed out the dangers of oral treatment with any calcium salt, and particularly the possibility of renal damage.

Case Report

In 1965 a 59-year-old retired farmer had a radiologically proved duodenal ulcer causing only minor symptoms of dyspepsia, which he controlled by self-medication with antacids. In August 1969 he developed severe dyspepsia after drinking a large amount of alcohol. The severity of the symptoms was such that he took large daily doses of antacid. Within three days of the initial attack he developed excessive thirst, polyuria, and anorexia; these symptoms persisted over the next four weeks, during which he continued with the high intake of antacid. He was referred for a urological opinion and further investigations. Clinical examination was negative. Intravenous pyelography showed no dye excretion on either side but cystoscopy and retrograde pyelography showed nothing abnormal. A catheter urine specimen showed red blood cells and 100 mg of albumin per 100 ml, but organisms were not cultured. The blood urea was 93 mg/100 ml, the serum creatinine 7.6 mg/100 ml, and the creatinine clearance 9 ml/minute. The fasting serum calcium on two occasions was 7.1 mEq/litre and the 24-hour urinary calcium excretion was 15.6 mEq. No other serum abnormality was detected.

In view of the history of peptic ulcer, thirst, polyuria, hypercalcaemia, and hypercalciuria a confident clinical diagnosis of hyperparathyroidism was made and the patient was transferred from the surgical to the medical unit. Apart from bilateral Dupuytren's contractures no other positive findings were present on clinical examination. The blood pressure was 130/80 mm Hg and the results of further relevant investigations were as follows: serum

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