

A study of total serum alkaline phosphatase activity in men following partial gastrectomy

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SUMMARY Total serum alkaline phosphatase (SAP) activity has been measured in 463 men with partial gastrectomy (Polya type), and in a control group of 271 men with vagotomy with pyloroplasty or gastroenterostomy.

An analysis of variance of the values in the range of 3.0 to 11.5 KA units/100 ml showed that the enzyme serum activity is influenced by three independent factors: age, ABO blood group, and the type of operation. Marginally raised levels (12.0-17.0 KA units/100 ml) were found to be affected by the same factors, and it was concluded that these levels do not, usually, indicate either bone or liver disease. In 18 men the total serum alkaline phosphatase was over 17.0 KA units: 16 had Paget's disease of bone, and two had liver disease.

There have been a number of reports of raised SAP activity in patients who have been treated by Polya gastrectomy, but both the frequency and the cause have been disputed. Earlier workers (Jones, Williams, Cox, Meynell, Cook, and Stammers, 1962; Deller, Edwards, and Addison, 1963; and Clark, 1964) attributed the change to a subclinical osteomalaciatic syndrome, but unequivocal evidence of bone disease was often lacking. In a large survey carried out by Morgan, Paterson, Woods, Pulvertaft, and Fourman (1965) it was shown that an SAP level of more than 17.0 KA units following Polya gastrectomy could usually be explained either by the presence of Paget's disease of the bone or liver disease, but a cause for the marginally raised SAP levels was often lacking. They suggested the source of this fraction might be the gut. Although Yong (1966) found some evidence to support this suggestion, Pulvertaft, Luffman, Robson, Harris, and Langman (1967) were unable to confirm this hypothesis.

The problem has been reinvestigated using the same source of patients used by Morgan *et al* (1965).

Patients and Methods

The patients attended the gastric follow-up clinic at the York County Hospital, at yearly intervals, after having had their operation within the York group of hospitals. The survey was conducted over the years 1966 to 1968 inclusive so that each patient would be expected to attend the clinic at least twice during this period. All blood samples were collected at the weekly afternoon clinic under comparable conditions, whilst the patients were taking their normal diet. The sera were immediately separated and stored at 4°C until the following morning when the SAP was estimated. It was established that this storage did not influence the estimation.

The SAP activity was measured by the automated method of Morgenstern, Kessler, Auerbach, Flor, and Klein (1965). The sera were incubated with p-nitrophenyl phosphate substrate in 1-amino 2-methyl 1-propanol buffer of pH 10.25. P-Nitrophenol, liberated by the action of the enzyme, was dialysed into a fresh stream of the buffer, and the optical density of the product of

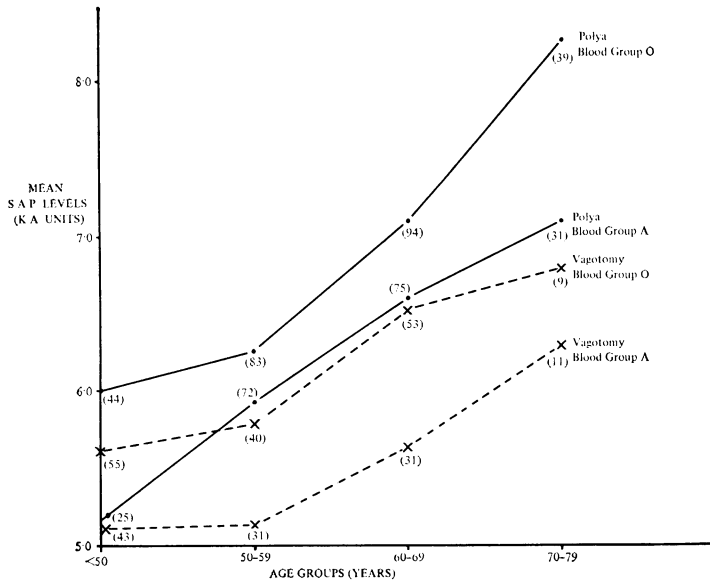


Fig. 1 The mean SAP (range 3.0-11.5 KA units/100 ml) in relation to operation, age, and blood group. The figures in parentheses indicate the numbers of men in each group.

this reaction was measured directly at 410 m μ at the pH of the reaction mixture. The method was simple and quick to operate and no colour reagent, series of serum blank estimations was necessary.

The method was calibrated in KA units using calf intestinal enzyme standards (Ambler and Brittain, 1967). The use of enzyme standards allowed for the compensation of any small daily changes in the automated method. The estimation in 30 male volunteers, under the age of 55, from the laboratory staff indicated the normal range to be 3.0-11.5 KA units/100 millilitres.

The ABO blood group of the patients was determined by a standard agglutination method.

Results

The mean values for SAP for range 3.0-11.5 KA units are summarized in relation to age, type of operation, and blood group in Figure 1. The factors of age, operation, and blood group would appear to exert some effect on the mean serum alkaline phosphatase value.

An analysis of variance was carried out on the findings for men aged between 40 and 65 seen in 1966 and 1967. Normal equivalent deviate plots showed that the incidence in each age group approximated to normal distributions. In order to simplify the statistics, it was necessary to limit the number of patients to 25 who were randomly selected in each age group. From the results of the study (shown in Table I) it was concluded that the mean SAP was affected by age, operation, and blood group, which caused a highly significant difference in the mean values, and that there was no interaction between the three factors; they acted separately and were not modified one by another.

During the period 1966 to 1967, 35 men with partial gastrectomy and three with vagotomy and drainage had values of 12.0-17.0 KA units/100 ml (Table II). The difference in the distribution of such values between partial gastrectomy and vagotomy and drainage was highly significant ($P < 0.005$).

In the partial gastrectomy group, the frequency of the marginally raised values increased with age ($P < 0.001$); furthermore these values were found to be more common in blood group O than in A, the difference being just significant ($P \leq 0.05$). Fourteen of these men, all well and free of symptoms, were studied in 1966, 1967, and 1968, the mean values being very similar, 13.5, 13.0, and 13.0 KA units/100 ml. The individual values were also similar (Table III).

In 18 men, the SAP level was over 17.0 KA units and this group differs from the previous group in that, although the frequency increases with age ($P < 0.05$) there was no relationship with either operation ($P > 0.05$), or blood group

Source	Estimate of Variance	Variance Ratio	Significance (P)
Between operations (M)	23.280625	9.19	<0.01
Between blood groups (F)	20.475625	9.08	<0.01
Between age groups (C)	36.327292	14.34	<0.005
M \times F interaction	0.950625	0.38	>0.05
M \times C interaction	1.570625	0.62	>0.05
F \times C interaction	1.402292	0.55	>0.05
M \times F \times C interaction	2.210625	0.87	>0.05
Residual	2.534010		

Table I Analysis of variance in men aged 40 to 65 years

Age	Polya				Vagotomy and Drainage			
	Blood Group				Blood Group			
	O		A		O		A	
	Total in Group	Raised SAP	Total in Group	Raised SAP	Total in Group	Raised SAP	Total in Group	Raised SAP
35-49	44	1	25	1	55	0	43	0
50-59	83	6	72	2	40	0	31	0
60-69	94	7	75	3	53	0	31	0
70+	39	11	31	4	9	2	11	1

Table II The frequency of marginally raised SAP levels (12.0-17.0 KA units/100 ml) in relation to age, blood group, and type of operation

Patient	SAP Level of Patient (KA units)		
	1966	1967	1968
1	13.0	12.0	15.0
2	15.0	12.5	12.5
3	12.5	13.0	12.5
4	15.5	13.0	15.0
5	13.0	12.0	12.0
6	15.5	12.5	11.5
7	13.0	14.0	12.0
8	14.0	12.0	16.0
9	13.0	14.5	13.5
10	12.5	12.5	11.0
11	12.0	14.5	12.5
12	15.0	12.0	12.0
13	14.5	15.5	15.5
14	12.0	12.0	11.0
Mean SAP level \pm SE ¹	13.5 \pm 0.31	13.0 \pm 0.36	13.0 \pm 0.50

Table III The results from 14 patients with marginally raised SAP levels who were reinvestigated during the three years of the survey

¹Standard error of the mean.

($P > 0.05$). Sixteen men had Paget's disease of the bone and two had liver disease.

Discussion

Metabolic bone disease following gastrectomy has stimulated interest in serum alkaline phosphatase, and several investigators (Jones *et al*, 1962; Deller *et al*, 1963; Clark, 1964) have measured the enzyme as a screening test for osteomalacia in patients with gastrectomy.

The basically accepted normal upper limit is 13.0 KA units/100 ml (Wooton, King, and Smith, 1951), but Clark, Beck, and Shock (1951), Hobson and Jordan (1959), and Klaassen and Sierstema (1964) have shown that the average SAP increases with age after the age of 50, and values of 16.0 KA units are not uncommon in patients over 60 years.

In a survey of patients submitted to gastric surgery in York, Morgan *et al* (1965) found that a cause for values over 17.0 KA units could usually be demonstrated, but values in the range 12.0-17.0 KA units were largely unexplained. They suggested, on the basis of the findings of Bamford, Harris, Luffman, Robson, and Cleghorn (1965), that such marginally raised levels might be due to the intestinal fraction; however, Pulvertaft *et al* (1967) were unable to confirm this hypothesis.

The present study shows that, in the range 3.01-2.0 KA units, the average value increases with age in men over the age of 50 who have undergone surgery for peptic ulceration; this increase was

observed following Polya type gastrectomy and vagotomy and drainage. Following either type of operation the average was higher for men with blood group O than for those with blood group A. Presumably this is due to the intestinal fraction. For both blood groups, however, the average was higher following gastrectomy than after vagotomy and drainage; this difference is being investigated.

Values in the range 12.0-17.0 KA units followed the same pattern as the lower values and were influenced by the same three factors, and it is suggested that these values represent, in general, the extreme additive effect of these factors.

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