

a diagnostic suppression test in order to exclude the possibility of an adrenocortical tumour. If steroid therapy is undertaken it would appear from our results that short intermittent courses of steroid therapy would be as effective as prolonged treatment and much safer, at any rate in cases of simple hirsutism and mild degrees of virilism. Continuous treatment is usually necessary in cases of female pseudohermaphroditism, and prolonged suppression of the degree shown in our patient does not appear to have been reported previously. Prednisone and prednisolone were given orally in doses of 20 mg. daily in this series of hirsute patients in order to ensure adequate suppression, but it is likely that this could be achieved with smaller doses.

Investigations are now in progress to determine the minimal effective dose for this purpose.

Summary

Eight female patients with adrenal virilism, all adults except one pseudohermaphrodite and all with a raised 17-ketosteroid excretion, were treated with a crystalline suspension of prednisolone trimethylacetate injected intramuscularly, with oral prednisone or prednisolone, or with intramuscular injection of hydrocortisone acetate.

As much as 400 mg. of prednisolone trimethylacetate at weekly intervals was required to effect suppression of corticotrophin, judged by depression of the 17-ketosteroid excretion, due no doubt to its very slow absorption, whereas daily doses of 20 mg. of prednisone or prednisolone by mouth caused an immediate and profound suppression, and two injections of 250 mg. of hydrocortisone acetate at an interval of a week were also effective. With all three methods suppression persisted for many weeks or months after withdrawal of therapy. For this reason short intermittent courses are advocated except in female pseudohermaphroditism.

No significant improvement in hirsutism was obtained and therefore steroid therapy is not justifiable on the grounds of hirsutism alone. In two patients with oligomenorrhoea normal menstruation was restored, in one patient amenorrhoea persisted, and in the remainder menstruation was normal before treatment.

We are indebted to Ciba Laboratories Ltd. for generous supplies of prednisolone trimethylacetate.

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In spite of the rise in the prison population, from 20,900 at the end of 1956 to 25,798 at the end of 1958, health has been well maintained, reports the director of medical services. Although the number of those remanded in custody for medical reports has greatly increased, the numbers found insane and mentally defective are the lowest recorded for many years. The director says that the figures taken together suggest not only that cases of mental illness which would otherwise have appeared in court and have been remanded to prison may have been saved from the committal of offences by mental treatment but also that courts are increasingly interested in the mental disabilities or maladjustments of those who appear before them even when this falls short of certifiable disease or defect. (*Report of the Commissioner of Prisons, for the Year 1958*. H.M.S.O., 9s. 6d. net.)

MULTIPLE SERIAL ENZYME STUDIES IN ACUTE MYOCARDIAL INFARCTION

BY

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Elevation of the level of serum glutamic oxalacetic transaminase (S.G.O.T.) follows necrosis of cardiac muscle, and we have recently published our experiences in the use of this enzyme in the diagnosis of acute myocardial infarction (Dewar *et al.*, 1958). The serum levels of other enzymes are also transiently raised after myocardial infarction, and in this communication we report the results of serial estimations of serum glutamic pyruvic transaminase (S.G.P.T.), serum aldolase, and serum oxidase, and the relation to similar estimations of S.G.O.T.

S.G.O.T. catalyses the reversible transfer of the α -amino nitrogen of aspartic acid to α -oxo-glutaric acid, with the production of glutamic and oxalacetic acids. Elevated levels are found in about 92% of cases of myocardial infarction. The level rises within three hours after infarction, usually reaches a maximum on the second day, and falls to normal in three to five days. The peak level is roughly related to the extent of the myocardial infarction in the absence of centrilobular necrosis of the liver due to cardiac failure.

S.G.P.T. reversibly catalyses the conversion of alanine and α -oxo-glutaric acid to pyruvic and glutamic acids. Wróblewski and LaDue (1956) found the mean level to be 16 ± 9 units per ml. in 260 normal subjects. S.G.P.T. failed to rise significantly in eight out of nine of their cases of acute myocardial infarction. They considered that only when the infarct was sizable was the amount of S.G.P.T. liberated great enough to raise transiently the serum level. They concluded that the S.G.P.T. appeared to be elevated above normal only when necrosis is great enough to raise the level of the S.G.O.T. above 150–200 units. Chinsky *et al.* (1957) found the S.G.P.T. elevated in 9 out of 24 cases of acute myocardial infarction, but in only one of these was the rise greater than the rise in the S.G.O.T.

Serum aldolase catalyses the splitting of fructose 1,6-diphosphate to D-glyceraldehyde-3-phosphate and dihydroxyacetone phosphate. It can be estimated by the method of Sibley and Lehninger (1949), and the normal average is 5 units per ml. of serum, with a range of 2.5–8.5 units per ml. (White, 1956). Experimentally, it has been shown that coronary artery ligation in dogs results in a considerable and rapid rise in serum aldolase and that there is a semi-quantitative relationship between the area of myocardial necrosis and serum aldolase (Volk *et al.*, 1956). The rise starts within three hours after infarction, reaches a maximum in about 24 hours, and then falls rapidly by 48 hours (Siegel and Bing, 1956), becoming normal in five days (Losner *et al.*, 1957). When pathological changes are correlated with plasma enzyme activity it is found that coagulation necrosis coincides with the peak of enzyme activity, and as reparative processes in cardiac muscle take place enzyme activity declines (Bing *et al.*, 1956).

Similar elevations of serum aldolase occur after human myocardial infarction. Volk *et al.* (1956) found peak levels of 29–112 units within 24 to 48 hours in eight patients. The levels rapidly fell to normal within five days. Two patients died with peak levels of 112 and 78.6 units, and it was concluded that patients with a moderate elevation fared better than those with large elevations. Siegel and Bing (1956) considered that aldolase rises less than other enzymes. White (1956) found a rise in 11 out of 17 cases of infarction, but many samples were first taken several days after infarction. Losner *et al.* (1957) found peak values of 19–53 units in 15 cases of infarction, whereas in 24 cases of subendocardial infarction or coronary insufficiency the level never rose above 13.5 units. In five cases of coronary insufficiency Volk *et al.* (1956) found no rise in serum aldolase.

Caeruloplasmin, the blue copper-containing protein of serum, exhibits oxidase activity with a variety of substrates. The enzyme is most active with *p*-phenylenediamine. There is a high degree of correlation between the total plasma copper level, the concentration of caeruloplasmin, and the serum oxidase activity in normal subjects, in pregnant women, and after myocardial infarction (Adelstein *et al.*, 1956). Total plasma copper, caeruloplasmin, and serum oxidase are raised in pregnancy and in chronic infections and are low in hepatolenticular degeneration; total plasma copper and caeruloplasmin may be low in the nephrotic syndrome (Markowitz *et al.*, 1955). Hypercupraemia, found in pregnancy, recedes within 10 to 20 days after parturition. Vallee (1952) found that the serum copper level in a normal individual is remarkably constant and does not significantly vary with periods of the day or month, food intake, or sex. Consecutive daily estimations in three normal subjects studied for 25, 29, and 6 days, respectively gave standard deviations which were closely comparable, and these were narrower than the standard deviation obtained from 120 analyses of 40 normal subjects and fell within one standard deviation around the mean of the normal group.

In 12 cases of definite acute myocardial infarction Vallee (1952) found a statistically significant rise in serum copper in all cases. The serum copper tended to rise in the first five days after infarction, reaching a maximum, or plateau, in 5 to 11 days and then progressively fell to just above normal or within the upper third of the normal range within 19 to 30 days.

The serum oxidase level is a much simpler test to use routinely, and probably gives the same information.

Materials and Methods

Observations were made upon 28 episodes of uncomplicated acute myocardial infarction. Specimens of blood were collected daily for at least 10 days. In all cases estimations of S.G.O.T. and S.G.P.T. were carried out. Serum aldolase was estimated in 14 cases, serum oxidase in 13, and all four enzymes in 10 cases. The erythrocyte sedimentation rate (E.S.R.) was estimated daily by the Westergren method. Twelve-lead electrocardiograms were taken daily in seven cases, and on admission, and not less than twice weekly thereafter in the remainder.

Similar daily observations were made on four fatal cases of acute myocardial infarction, three cases of

coronary insufficiency, and one case of cardiac failure due to cor pulmonale.

S.G.O.T. and S.G.P.T. were estimated simultaneously by the methods of Reitman and Frankel (1957), using the standardized reagents produced by the Sigma Chemical Company (Agents: G. T. Gurr, London).

Serum aldolase was estimated by the method of Bruns (1954), the reagents being supplied by C. F. Boehringer and Soehne (Agents: Courtin and Warner Ltd., Lewes, Sussex).

Serum oxidase was estimated by the method of Ravin (1956). As an extra precaution the *p*-phenylenediamine was prepared afresh for each batch to avoid the variable colour changes which occur after storage at 4° C.

Normal Values.—Estimations of the level of all four enzymes were carried out on 50 healthy adults. The results are shown in Table I. We consider that enzyme

TABLE I.—Values of S.G.O.T., S.G.P.T., Serum Aldolase, and Serum Oxidase in 50 Healthy Adults

	Method	Range (Units)	Mean (Units)	Standard Deviation	Mean + 2S.D.
S.G.O.T. ..	Reitman and Frankel (1957)	12–36	19	±4.5	28
S.G.P.T. ...	" "	4–24	12	±4.2	21
Serum aldolase ..	Bruns (1954)	2.3–8.8	5.7	±1.74	9.2
Serum oxidase ..	Ravin (1956)	206–365	294	±39	372

levels twice the standard deviation above the mean of the normal values are abnormal. By this standard the upper limit of normal of S.G.O.T. in our series was 28 units, S.G.P.T. 21 units, serum aldolase 9.2 units, and serum oxidase 372 units. In the past the upper limit of normal S.G.O.T. has been accepted as 40 units, but this is undoubtedly too high and probably accounts for many of the false-negative results in acute myocardial infarction which have been reported. Our normal values for S.G.O.T. agree with those reported by Baron *et al.* (1958) and Goble and O'Brien (1958). Our normal values for serum oxidase are slightly higher than those of other workers. Ravin (1956) gives a range of 100 to 300 units; and Ch'en P'ei-En (1957), using the same method, gives a range of 146 to 316 units, with a mean of 234 and standard deviation of 47.

Results

Acute Uncomplicated Myocardial Infarction

The level of S.G.O.T. was raised in all cases. The level of S.G.P.T. was raised in 23 episodes out of 28 (82%), serum aldolase in 13 out of 14 episodes (93%), and serum oxidase in 10 out of 13 episodes (77%). Table II shows the maximum peak level, mean peak

TABLE II.—Maximum Peak Level, Mean Peak Level, Day of Peak, and Duration of Abnormal Levels in Cases of Acute Uncomplicated Myocardial Infarction with Elevated Enzyme Levels

	S.G.O.T.	S.G.P.T.	Serum Aldolase	Serum Oxidase
Maximum peak level (units)	620	90	88.5	755
Mean	157	41	17.5	494
" day of peak (days) ..	2.75	3.6	3.7	9.1
" duration of abnormal levels (days)	2.6	3.3	1.7	5.4

level, the day of the peak, and the duration of abnormal levels. In 10 cases all four enzymes were estimated, using the same samples of blood, and the results are shown graphically in Fig. 1.

Fatal Cases of Acute Uncomplicated Myocardial Infarction

Case 1.—The maximum S.G.O.T. was 70 units on the third day and the S.G.P.T. 56 units on the fifth day.

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Case 2.—The maximum S.G.O.T. was 73 on the fourth day, the S.G.P.T. 25 units on the ninth day, serum aldolase 17 units on the fourth day, and serum oxidase 755 units on the fifth day.

In both cases the peak S.G.O.T. level may have been missed.

Fatal Cases of Acute Myocardial Infarction with Cardiac Failure and Centrilobular Necrosis of the Liver

Case 3.—The maximum S.G.O.T. was 950 units on the third day, S.G.P.T. 810 units on the third day, serum aldolase 88.5 units on the second day, and the serum oxidase 702 units on the fourth day. The patient died on the fifth day.

Case 4.—The patient died on the day of infarction, the S.G.O.T. level being 8,400 units and S.G.P.T. 7,700 units.

In both cases there was extensive centrilobular necrosis of the liver at necropsy.

Coronary Insufficiency.—In three cases serial estimations of S.G.O.T. and S.G.P.T. were normal.

Discussion

In our experience elevation of S.G.O.T. is a reliable index of myocardial necrosis if other factors, especially centrilobular necrosis of the liver, can be excluded. In all the cases in this report there was elevation of S.G.O.T., and we have evaluated the other enzymes by this yardstick. The level of S.G.P.T. is raised in over 80% of cases of myocardial infarction, but the elevation is of less degree than that of S.G.O.T. In only one uncomplicated case was the peak S.G.P.T. higher than the peak S.G.O.T. We do not agree with Wróblewski and LaDue (1956) that a S.G.O.T. level of 150 to 200 units is required before there is a rise in S.G.P.T. There

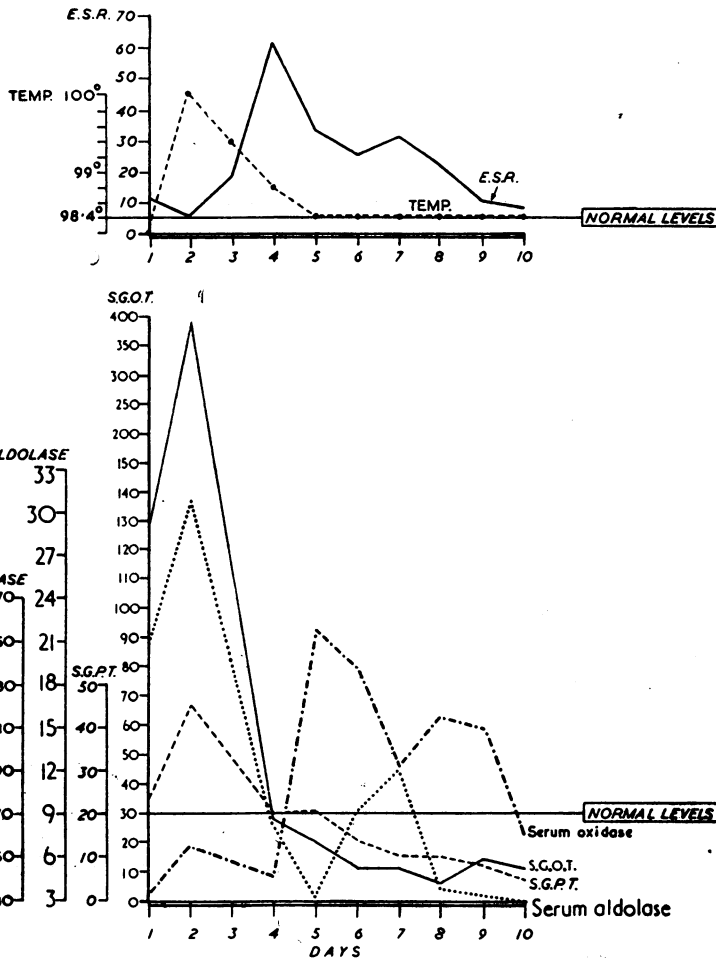


FIG. 2.—Curves of S.G.O.T., S.G.P.T., serum aldolase, serum oxidase, E.S.R., and temperature in a patient with acute uncomplicated myocardial infarction. Note the early elevation of S.G.O.T., S.G.P.T., and serum aldolase, the secondary elevation of serum oxidase, and the delayed rise in serum oxidase.

was a significant rise in S.G.P.T. in 14 episodes in our series when the S.G.O.T. remained below 150 units. If serial estimations are carried out, minor changes in S.G.O.T. can be mirrored by similar changes in S.G.P.T. In one of our cases a peak level of S.G.O.T. of 47 units was associated with a peak level of S.G.P.T. of 26 units. These findings are in agreement with the concentration of the two enzymes in the myocardium.

The peak S.G.P.T. level occurs a day later and lasts a day longer than the S.G.O.T. elevation. Although it has been said that the S.G.P.T. is elevated to a greater extent in liver disease, our evidence is insufficient to postulate that the slightly later rise in S.G.P.T. is associated with changes in the liver.

In the diagnosis of acute myocardial infarction S.G.O.T. is a much more valuable routine index of myocardial necrosis than S.G.P.T.

The level of serum aldolase rises rapidly after myocardial infarction, reaching a peak by the second to third day, and rapidly falls to normal. Secondary elevation occurs about five days after the initial peak, or about eight days after infarction, and is not accompanied by any rise in S.G.O.T. Fig. 2 shows the changes in a typical case. Secondary elevations were seen in 10 out of 11 cases of apparently uncomplicated myocardial infarction. In only one case did the S.G.O.T. rise similarly, suggesting a fresh infarction. The cause of the secondary rise in aldolase is not apparent, and further work is required to elucidate this point. It may

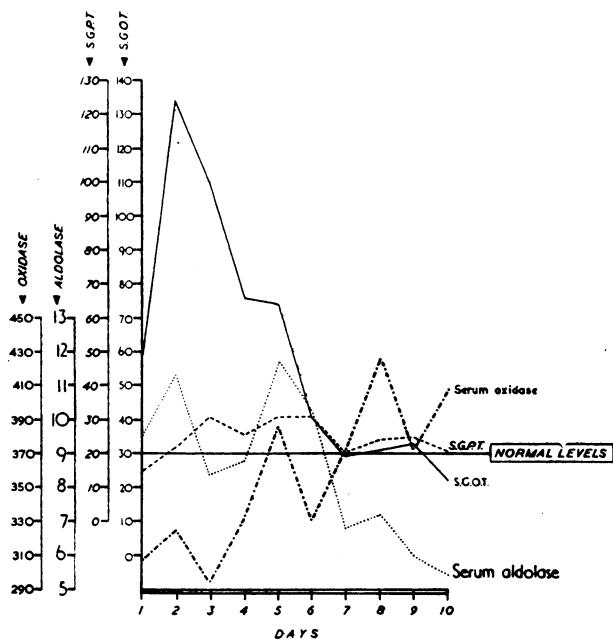


FIG. 1.—Mean levels of S.G.O.T., S.G.P.T., serum aldolase, and serum oxidase in 10 patients with acute myocardial infarction.

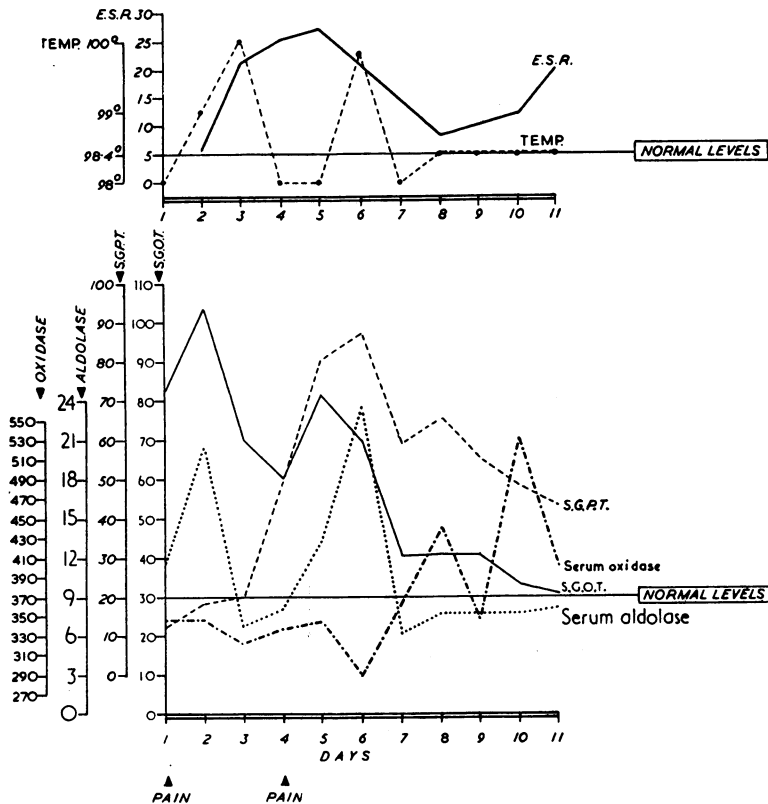


FIG. 3.—Curves of S.G.O.T., S.G.P.T., serum aldolase, and serum oxidase in a patient with further myocardial infarction during the course of treatment.

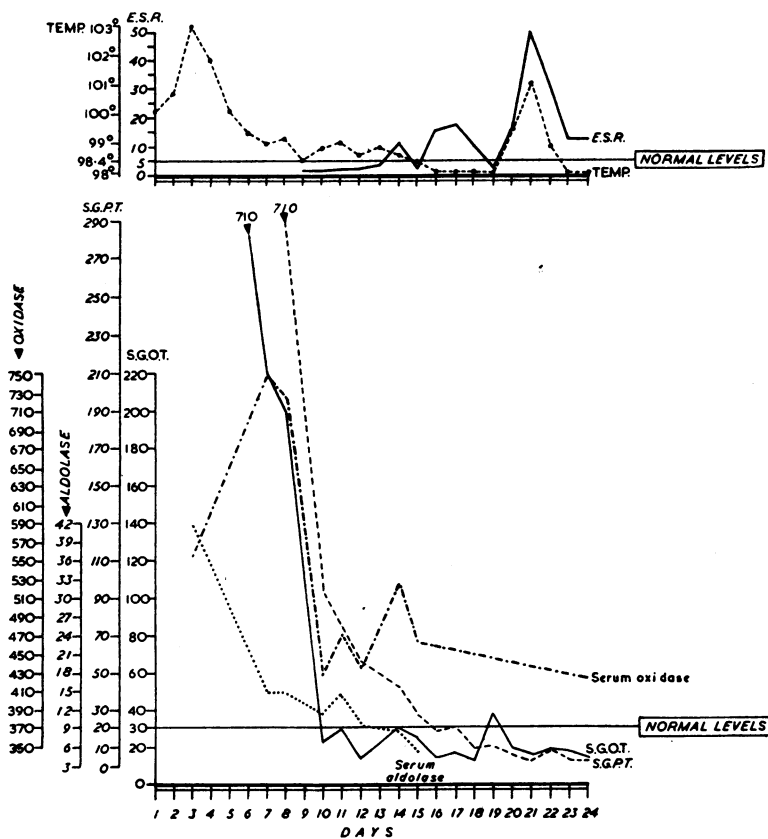


FIG. 4.—Curves of S.G.O.T., S.G.P.T., serum aldolase, and serum oxidase in a 29-year-old woman with cardiac failure due to emphysema and respiratory infection.

be that aldolase is being released from other organs such as the liver.

Serum oxidase activity increases gradually after myocardial infarction, reaching a peak about the ninth day, and thereafter falls slowly to normal. In some cases a normal level is reached between the twelfth and eighteenth days, but in others the level does not return to normal by the end of three weeks. This confirms the observations of Vallee (1952), although he did not carry out estimations daily. In three cases there was no rise in oxidase activity and there was no direct correlation between the degree of elevation of S.G.O.T. and oxidase. In two cases a peak S.G.O.T. activity of 510 and 620 units was accompanied by normal oxidase activity. In two fatal cases peak levels of 755 and 702 units were obtained with peak S.G.O.T. levels of 73 and 950 units, respectively. The peak of S.G.O.T. in the first of the two cases was probably missed.

There was no consistent correlation between the E.S.R., temperature, or electrocardiogram and either the secondary rise in serum aldolase or the rise in serum oxidase.

When extension of infarction occurs S.G.O.T., S.G.P.T., and aldolase usually rise as in the initial episode. This is well shown in Fig. 3, further pain having occurred on the fourth day. The rise in aldolase due to the second infarct may have obscured the secondary rise expected from the first infarct. The usual rise in oxidase activity has not been immediately influenced by the fresh infarction.

That changes in these enzymes may be explained in part by liver damage is shown in Fig. 4. This shows the serial changes in enzyme levels in a woman of 29 in cardiac failure due to emphysema and respiratory infection. There was no evidence of cardiac infarction. The abnormal levels decreased with control of the cardiac failure, although oxidase levels had not returned to normal by the twenty-second day.

In the clinical use of these enzyme estimations, it must be remembered that both transaminases and aldolase are released into the blood in liver disease and in muscle destruction as well as in coronary infarction. The serum oxidase is also elevated in certain non-specific infections and grossly depressed in Wilson's disease. Thus none of these enzymes, considered alone, are organ specific. They are, however, of great aid in the interpretation of the clinical condition in three ways.

Firstly, the pattern of the enzyme change is of help in localization of the disease. Thus the rise of the S.G.P.T. to a lower peak than the S.G.O.T.,

together with the secondary rise of the aldolase at about five days after its primary peak, and the increasing value of the serum oxidase seem to be characteristic of cardiac infarction.

Secondly, in late diagnosis where the patient comes under observation some time after the infarct, the serum transaminases may have returned to normal. Here the diagnosis may be established by finding the secondary peak of the serum aldolase and by the increasing level of the serum oxidase.

Thirdly, in prognosis the quicker return of the serum aldolase level to normal may be of aid in assessing the severity of the infarct whilst the transaminases are still elevated. The peak of the aldolase in second infarcts is also more obvious because of this.

Summary

Serial daily estimations of serum glutamic pyruvic transaminase (S.G.P.T.), serum aldolase, and serum oxidase for at least 10 days have been made in a series of cases of acute myocardial infarction. The results have been compared with similar estimations of serum glutamic oxalacetic transaminase (S.G.O.T.) and with the erythrocyte sedimentation rate (E.S.R.), temperature, and electrocardiogram.

Estimations of these enzymes have been made in 50 healthy adults. The upper limit of normal (mean plus twice the standard deviation) in the present series is S.G.O.T. 28 units, S.G.P.T. 21 units, serum aldolase 9.2 units, and serum oxidase 372 units.

Elevation of S.G.P.T. occurs in 82% of cases of myocardial infarction with a raised S.G.O.T. The rise occurs a day later, lasts a day longer, and is of much smaller degree than the rise in S.G.O.T.

Serum aldolase rises rapidly in almost all cases of acute myocardial infarction. It reaches a peak in two to three days and falls rapidly. A secondary rise occurs about five days after the initial peak.

Serum oxidase rises gradually over the first nine days, may remain steady for a few days, and then falls to normal in most cases by the end of three weeks. There is no direct correlation with S.G.O.T. levels, and serum oxidase may remain normal with markedly elevated S.G.O.T. levels.

There is no consistent correlation between the E.S.R., temperature, or electrocardiogram and the secondary rise in serum aldolase or the rise in serum oxidase.

Coronary insufficiency without infarction does not alter the level of S.G.O.T. or S.G.P.T.

Elevations of S.G.O.T., S.G.P.T., serum aldolase, and serum oxidase may occur in cardiac failure with centrilobular necrosis of the liver.

The clinical use of these enzyme estimations is discussed.

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CASES OF ATTEMPTED SUICIDE ADMITTED TO A GENERAL HOSPITAL

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Perhaps one of the deepest impressions left by a survey of the literature of suicide is the extraordinary range of ways of looking at the problem. The available scientific data on attempted suicide are collectively so very complicated and the relationship between causes so intricate that there are obvious dangers in oversimplifying concepts about it. It is not easy to devise adequate conditions of experimental control so that the various determining causes can be isolated. The main difficulties are, first, to obtain reliable evidence; secondly, to get a representative sample; and, thirdly, to relate an attempt at suicide to significant psychiatric, ecological, cultural, and other factors. This explains why the quite extensive investigations already published have only been partially successful in furthering understanding. Several workers in the field have stressed the need for more comparative studies (Sainsbury, 1955).

The present investigation attempts to analyse certain aspects of cases of attempted suicide admitted to the wards of a large general hospital in Birmingham during 1956, 1957, and 1958. The medical and surgical consultant staff in charge of these wards were specially requested to refer all their cases of attempted suicide for psychiatric assessment. Their co-operation did much to facilitate the investigation. All the cases were personally examined by one of us (J. A. H.); data were recorded on a statistical form which was evolved after a pilot study on about 30 cases not included in the final analysis. Where possible, independent evidence from relatives and other sources was obtained, and cases for which clear-cut information was not obtained were seen for out-patient follow-up or on transfer to psychiatric units.

All studies of attempted suicide are suspect on the grounds that they are not based on a fully representative sample. Certainly the most trivial and some of the more serious cases may avoid admission to hospital or be concealed in other ways. In a few cases, particularly of coal-gas poisoning in the aged and minor barbiturate intoxication, the intent to commit suicide may be missed or difficult to establish with certainty. The hospital concerned in this investigation is under an obligation