SERUM ENZYMES IN THE DIAGNOSIS OF DISEASE

BY

W. H. TAYLOR

The enzymes which are detectable in serum are derived from the cells of tissues and are essentially of two sorts: those whose primary physiological function and site of action is in the serum or plasma, and those whose presence in serum under normal, or even abnormal, circumstances would appear not to be of physiological importance.

PRIMARY SERUM ENZYMES

The enzymes of the first sort may suitably be called the primary serum enzymes. They are usually present as precursors and require to be activated to exert their physiological effect. Examples are:

(a) Lipoprotein lipase, which is activated by heparin and heparin-like substances, and which catalyzes the conversion of the triglycerides of plasma lipoproteins to free fatty acids and to di- and mono-glycerides. The enzyme thus assists in the removal of chylomicrons from plasma after a fatty meal. It has been isolated from heart and from adipose tissue. The serum lipoprotein lipase level is reduced in a rare sub-group of patients with essential familial hyperlipaemia.

(b) Caeruloplasmin, which is an \( \alpha_2 \)-globulin to which 98 per cent of the circulating serum copper in man is bound. The protein is an oxidase containing eight copper atoms per molecule with a molecular weight of about 150,000. Its precise in vivo oxidative function is unknown, although it will oxidize, in vitro, substances such as epinephrine and serotonin.

The normal serum caeruloplasmin, as assayed by its oxidase activity, is 20 to 40 mg/100 ml (Cumings, 1968). The level is greatly reduced in Wilson's disease to values from 0 to 8 mg/100 ml and determinations of caeruloplasmin are thus much used in the differential diagnosis of this disease. Normal values have been reported in about 7 per cent of cases, and decreased values are occasionally found in clinically normal heterozygotes.

Other primary enzymes are plasmin (fibrinolytic) and the several enzymes concerned in blood coagulation, i.e. in the formation of fibrin. The serum levels of these physiologically important enzymes are not usually determined directly in the diagnosis of coagulation defects.

SECONDARY SERUM ENZYMES

Enzymes of the second sort, the secondary serum enzymes, are of much greater importance diagnostically than are the primary serum enzymes, because in diseases affecting individual tissues, enzymes from the tissue cells may be released into the serum in increased or reduced amounts. Usually, in normal health, small quantities of these enzymes find their way, by diffusion or otherwise, across the cell and capillary membranes and into the plasma.

CAUSES OF AN INCREASED SERUM ENZYME CONCENTRATION

An increased serum enzyme concentration may arise by one or more of the following mechanisms:

(1) Increased synthesis of enzymes in a tissue, the cell membranes remaining normal.

Examples are the serum alkaline phosphatase and the serum pepsinogen. The former is raised in normally growing children and in conditions such as osteomalacia, associated with increased osteoblastic activity of bone. The serum pepsinogen is often raised in duodenal ulcer. In these instances there is probably an increased number of cells in the bone and stomach respectively, rather than an increased production of enzymes within individual cells. The rate of passage of enzymes from cell to plasma is normal, but since more cells are involved the serum values are raised.

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(2) Increased release of enzymes into the serum.  
This may arise for several reasons.  
(a) Increased permeability of cell membranes and of capillary membranes to intracellular enzymes, as in inflammation. Thus in acute pancreatitis the serum α-amylase rises rapidly.  
(b) Increased release of enzymes may also occur when there is tissue necrosis from trauma or vascular occlusion, so that cell membranes are ruptured. Thus the serum aspartate amino-transferase (SGOT) may rise rapidly in coronary thrombosis (vide infra).  
(c) A third cause of increased release occurs when a malignant neoplasm metastasizes via the blood stream, releasing enzymes into the plasma. For example, a metastasizing carcinoma of prostate is responsible for a raised serum acid phosphatase.

(3) Decreased or diverted excretion of enzymes.  
In obstructive jaundice, for example, alkaline phosphatase, normally excreted in bile, is retained in the circulation and the serum alkaline phosphatase rises. The serum amylase may also increase slightly when there is impaired renal function, as this enzyme, arising in the pancreas (and salivary glands), is excreted in the urine.

Diagnostic Significance of a raised Serum Enzyme Concentration.  
Generally speaking, the higher the serum concentration of an enzyme, the more severe are the events producing it, and the more likely it is that estimation of the enzyme will yield information of diagnostic value. Conversely, the smaller the lesion, the less likely it is that the serum concentration of appropriate enzymes will rise significantly. Thus the procedure of muscle biopsy does not significantly affect the serum concentrations of aldolase or creatine kinase (Buxton and Taylor, 1968), so that it is perhaps not surprising that quite small cardiac infarcts do not always cause a rise in serum creatine kinase or in the serum amino-transferases (SGOT and SGPT).

CAUSES OF A DECREASED SERUM ENZYME CONCENTRATION  
Decreased concentrations of enzymes in serum always arise from decreased synthesis in the cells of the tissue of origin. Decreased synthesis may arise for several reasons.

(1) Atrophy of a tissue. A good example of this is the fall of serum pepsinogen which occurs in pernicious anaemia, a disease in which the fundic glands of the stomach are atrophic.  
(2) Surgical ablation of a tissue. Again the stomach may be taken as an example. After total gastrectomy, the serum pepsinogen is zero.  
(3) Congenital defects. Many inherited diseases result from defective synthesis of one or more enzymes. Usually their diagnosis does not, at present, involve analyses of serum enzymes. One good example, however, of a hereditary disease which is diagnosed by determination of a serum enzyme, and which indeed is named enzymically, is hypophosphatasia, in which the serum alkaline phosphatase is unduly low. For further examples of importance to anaesthetists, the reader is referred to the paper by Lehmann and Liddell (1969) in this issue.  
(4) Diminished synthesis. Little is known about the acquired, as distinct from the congenital, failure of synthesis of specific intracellular enzymes, but an example may be the low serum cholinesterase values reported in acute hepatitis and in hepatic cirrhosis.

TIME COURSE OF A RAISED SERUM ENZYME CONCENTRATION  
Two general patterns emerge. The serum levels of some enzymes remain elevated over long periods, fluctuating only with progression or retrogression of the relevant disease or in response to treatment. Thus the elevated serum pepsinogen changes very little throughout the day or from day to day in patients with duodenal ulcer; but after partial gastrectomy the level falls. In Paget's disease the serum alkaline phosphatase rises as the disease progresses, although the correlation is not always close. In osteomalacia the raised alkaline phosphatase falls if therapy is successful, and may be used to guide treatment. In each disease, the enzyme determination, whenever carried out, has a diagnostic or therapeutic significance.

In contrast to the above pattern, the serum levels of some enzymes run a course which is a characteristic of the morbid event which has caused the level to rise. Examples are the rise and fall of the serum amylase in acute pancreatitis and of the serum aspartate amino-transferase (SGOT) in coronary thrombosis. In both in-
stances the enzyme levels mirror only poorly the cellular processes of tissue damage and repair and are relatively little influenced by therapy. The enzyme levels must be interpreted in relation to the characteristic time course if they are to be used diagnostically. Thus the serum aspartate amino-transferase cannot be expected to rise after transmural cardiac infarction until 3 hours after the initial occlusion and estimations carried out on blood taken during this interval will be of little value. The fact that the raised level may return to normal after 4 to 7 days is part of a characteristic pattern but does not indicate that the diseased tissue has been repaired, and the falling value is, therefore, no guide to the progress of the disease.

Broadly speaking, the first sort of time course is associated with enzymes whose serum levels are raised because of increased synthesis (group 1 under "Causes") and the second sort with enzymes whose levels are raised because of increased release (group 2).

ISO-ENZYMES
When serum is subjected to electrophoresis, on media such as agar or starch gel, it can be shown that certain enzymes, notably lactate dehydrogenase, are present in more than one site. These different forms of the same enzyme are called iso-enzymes. Iso-enzymes thus have different physical and chemical properties from each other but catalyze the same reaction. In the case of lactate dehydrogenase, five serum iso-enzymes can be demonstrated. Although all five occur in most tissues, some are particularly characteristic of individual tissues. Thus the slowest-moving, numbered 5, is characteristic of liver, and the two fastest (1 and 2) of heart muscle. The two latter are thus proportionately more prominent after myocardial infarction. These multiple enzymes are of great interest, but their determination in serum is not, as yet, of great diagnostic value.

THE AMINO-TRANSFERASES (TRANSAMINASES)
Two amino-transferases, aspartate amino-transferase (GOT) and alanine amino-transferase (GPT) may be found in increased amounts in serum, the former when there is damage to the liver, heart, skeletal muscle, kidney or pancreas, and the latter when there is liver damage, and to a lesser extent when there is damage to skeletal or cardiac muscle and to the kidneys.

Aspartate Amino-transferase.
Reaction catalyzed:
\[
\text{L-Aspartate + 2-Oxoglutarate} \rightarrow \text{L-Glutamate + Oxaloacetate.}
\]

The normal serum concentration of this enzyme is 5 to 18 mU/ml. In the newborn the normal range extends up to 60 mU/ml, falling to the adult values at about 6 months of life. The principal diagnostic use of the serum aspartate amino-transferase is in detecting acute myocardial infarction. The level rises at 3 to 9 hours after coronary occlusion and reaches a peak at 24 to 48 hours with values ranging up to 150 mU/ml. The higher the peak value, the graver the prognosis. Normal levels return after 4 to 7 days. If the serum level of this enzyme is not raised at the correct time, acute myocardial infarction is unlikely to have occurred, for only 3 per cent of patients with postmortem confirmation of infarction fail to show such a rise. The value is not raised in angina pectoris or when there is pericarditis, but there is a moderate increase in myocarditis (e.g. rheumatic). In dissecting aneurysm of the aorta normal or only slightly raised values are found. About 50 per cent of patients with pulmonary embolism exhibit a slight rise, which at the fourth to sixth day may be as much as twice the upper normal limit. Raised values also occur in liver diseases generally, in acute pancreatitis (50 per cent of patients), in muscular dystrophy (50 per cent of cases), in acute dermatomyositis, and polymyositis, in paroxysmal myoglobinuria, after muscle injury or crushing, and after surgical damage to muscle. Red blood cells also contain the enzyme and it is important, therefore, that the determination is not carried out on haemolyzed sera. Normal values have been recorded in progressive muscular atrophy, myasthenia gravis, acute cholecystitis, and rheumatoid arthritis.

Alanine Amino-transferase (GPT).
Reaction catalyzed:
\[
\text{L-Alanine + 2-Oxoglutarate} \rightarrow \text{L-Glutamate + Pyruvate.}
\]

The normal serum concentration of alanine amino-transferase is 4 to 15 mU/ml, extending
in the newborn up to 45 mU/ml. The principal
diagnostic use of serum levels of this enzyme is
in detecting liver damage. The level of aspartate
amino-transferase also rises when there is liver
damage but usually less so than that of alanine
amino-transferase, so that in liver disease the ratio
of the former to the latter (GOT : GPT) is usually
below 1. The level of alanine amino-transferase
does not increase in acute myocardial infarction
or increases only slightly. When it does increase,
some authorities claim that this is only because
congestive cardiac failure is causing secondary
liver damage. The ratio (GOT : GPT) is therefore
almost always greater than 1 in acute myocardial
infarction. Occasionally, consideration of these
ratios may be diagnostically helpful, but they
must be interpreted with care. For example, if
the enzymic levels are not determined until the
fourth day or later after coronary occlusion, and
there is increasing cardiac failure with congestion
of the liver, the aspartate amino-transferase value
will be falling but the alanine amino-transferase
value increasing, and the ratio may be less than 1.

Almost any sort of liver damage, varying from
passive venous congestion, as noted above, to
acute toxic necrosis will cause the concentrations
of both serum amino-transferases to rise. The
raised levels are therefore not of great value in
distinguishing between different sorts of liver
disease. A raised serum alanine-transferase level is, however, the most sensitive index we have
of liver damage. It has been calculated that dam-
age to only 1 out of every 750 liver cells would
cause the level to rise, so that the determination
is of the greatest value in detecting liver disease
that would otherwise be undetectable.

Acute hepatitis.
The behaviour of the serum alanine amino-
transferase in acute hepatitis illustrates the clinical
usefulness of so sensitive a diagnostic test. During
the incubation period of the infection the serum
enzyme levels are normal. In the prodromal phase
when there are symptoms of fever and malaise,
but no jaundice, the amino-transferase levels are
raised. With the onset of jaundice the serum con-
centrations of both amino-transferases continue to
rise and reach a peak at about the end of the
second week. Peak values for alanine amino-
transferase average 500 mU/ml and for aspartate
amino-transferase 400 mU/ml. Values of either
enzyme below 150 mU/ml at this time make the
diagnosis of acute hepatitis unlikely in the
jaundiced patient. Values above 500 mU/ml sup-
port a diagnosis of acute hepatitis or of severe
acute poisoning. Values between 150 and 500
mU/ml require differentiation from acute-upon-
chronic hepatitis as well as from less severe acute
poisoning. After 2 weeks the raised levels fall and
revert gradually to normal at 6 weeks or later.
Persistence of high serum values suggests that
hepatic necrosis, leading to scarring, is occurring.

When acute hepatitis occurs without jaundice,
the serum amino-transferase levels are raised and
enable such a diagnosis to be made with more
confidence than was formerly possible. Similarly,
these determinations may be used during
epidemics to detect cases early. In such non-icteric
patients the peak values are usually below 400
mU/ml.

Chronic hepatitis and hepatic cirrhosis.
The serum levels of both enzymes are usually
raised (in over 90 per cent of patients) in chronic
hepatitis and in hepatic cirrhosis. Values of up to
200 mU/ml may be observed but more usually
the increase is moderate, up to 25 mU/ml.
Generally speaking, the more active the disease
the higher the amino-transferase levels. The ratio
(GOT : GPT) is nearer to 1 in chronic liver
disease and often in cirrhosis exceeds 1.

Hepatic poisons.
When very high serum amino-transferase levels
are recorded, over 1000 mU/ml, poisoning
should always be suspected, as for example by
organic solvents such as carbon tetrachloride.
Minor degrees of poisoning cause smaller in-
creases in amino-transferase levels. In the severe
cases the ratio (GOT : GPT) is usually greater
than 1.

Obstructive jaundice.
The serum levels of both amino-transferases
are initially normal and gradually rise to about
150 mU/ml. The alanine amino-transferase value
usually exceeds that of the aspartate enzyme
(GOT : GPT < 1). If observations are continued
over 2 weeks, therefore, the differentiation of
acute hepatitis from uncomplicated obstructive
jaundice is frequently easily made.
The serum alkaline phosphatase levels are often raised in obstructive jaundice to a greater extent than in acute hepatitis, whereas the reverse is true for the amino-transferases. Use has thus been made of the ratio of alanine amino-transferase to alkaline phosphatase in the differential diagnosis of jaundice.

Cholangitis and biliary cirrhosis.

In cholangitis moderately raised levels of serum amino-transferases occur, varying with the degree of liver damage. In biliary cirrhosis the values do not differ substantially from those in hepatic cirrhosis, but comparatively high values for serum alkaline phosphatase may occur, reflecting persistent cholestasis in biliary cirrhosis as compared with hepatic cirrhosis.

ALKALINE PHOSPHATASE

Reaction catalyzed:

\[ \text{an orthophosphate} \quad \text{an alcohol} + \quad \text{H}_2\text{O} \quad \leftrightarrow \quad \text{orthophosphate} \]
\[ \text{e.g.} \quad \text{phenylphosphate} \quad \leftrightarrow \quad \text{phenol} + \text{orthophosphate}. \]

Alkaline phosphatases are present in almost all human tissues but the activity normally found in serum is derived from two sources, liver and the osteoblasts of bone. It is essentially only in diseases of these two tissues that raised serum levels are found. There is evidence that the enzymes are excreted in bile and are thus retained in obstructive jaundice.

The normal serum alkaline phosphatase activity ranges in the adult from 3 to 13 King-Armstrong units/100 ml, or from 2 to 5 Bodansky units/100 ml, or from 25 to 92 mU/ml, using phenyl phosphate as substrate. The upper normal limit may be approximately doubled in children who are still growing.

In hepatic disorders, the serum alkaline phosphatase level is mainly of use in differentiating acute obstructive jaundice from acute hepatitis. Values above 30 K-A units/100 ml support the former diagnosis and values below this level support the latter. Clearly if obstruction is incomplete the level may not rise above 30 units/100 ml, and for this reason, in the author's experience, the determination is diagnostically unreliable. As already explained, its value may be enhanced when taken in conjunction with the alanine amino-transferase level.

In bone disease, it is generally accepted that the serum alkaline phosphatase level is raised whenever there is osteoblastic overactivity. The estimation is therefore of great value in distinguishing osteoporosis (in which there is no osteoblastic overactivity and therefore a normal serum enzyme level) from osteomalacia. It is also of value in the diagnosis of osteitis deformans (Paget's disease); indeed a persistent and otherwise unexplained raised serum level of alkaline phosphatase should always make one suspect the presence of an undiscovered zone of Paget’s disease. When primary hyperparathyroidism affects bone, the serum alkaline phosphatase is also raised, and very high values may occur in primary malignant bone tumour (osteosarcoma) and in secondary neoplasia of bone, e.g. metastasizing carcinoma of the prostate. A raised serum alkaline phosphatase is one of the earliest features of childhood rickets and may be present for as much as a month before the disease is clinically obvious. During the treatment of rickets, osteomalacia and primary hyperparathyroidism, the alkaline phosphatase values fall to normal; treatment cannot be considered satisfactory until a normal level has been restored.

Lower than normal serum levels of alkaline phosphatase occur in hypophosphatasia and in childhood diseases in which growth is arrested, such as achondroplasia, cretinism and scurvy.

Normal values of serum alkaline phosphatase are usually found during the uniting of simple fractures and in benign bone tumours such as osteoma, chondroma and adamantinoma.

ACID PHOSPHATASE

Reaction catalyzed: as for alkaline phosphatase, but at an acid pH.

Acid phosphatases occur in erythrocytes, bone, kidney, spleen, liver and pancreas, but of more importance in diagnosis is the acid phosphatase from the prostate gland.

The normal serum level, in both sexes, is 1 to 4 King-Armstrong units/100 ml (2 to 7 mU/ml) and little, if any, of this is of prostatic origin, not more than 1 K-A unit/100 ml. Slightly higher values, up to 6 K-A units/100 ml, are found in growing children and adolescents. The prostatic enzyme is inhibited by incubation with 40 per
cent ethanol and by tartrate, but not by formaldehyde or by cupric ions, which destroy the acid phosphatase of erythrocytes. Prostatic acid phosphatase is thus determined as, "formaldehyde-stable", "copper-resistant" or "tartrate-labile" phosphatase. The upper normal limits for formaldehyde-stable acid phosphatase and tartrate-labile acid phosphatase are 2.5 and 1 K-A units/100 ml respectively (4 and 1.5 mU/ml).

Acid phosphatases are inactivated in serum at room temperature, so that the estimation should be carried out quickly or the serum should be stored immediately in the refrigerator. The enzymes are also inhibited by fluoride, which must not, therefore, be used as an anticoagulant.

Raised values occur in only about 5 per cent of patients with a non-metastatic prostatic carcinoma and in about 85 per cent of patients with metastases. Raised values are also found after prostatic palpation or massage. A raised acid phosphatase level, which is not tartrate-labile, occurs in the serum of some female patients with mammary carcinoma and in Gaucher's disease.

**α-Amylase**

Reaction catalyzed:

\[ \text{Starch or glycogen} + \text{H}_2\text{O} \rightarrow \text{Maltose + other polysaccharides (dextrins).} \]

α-Amylases are secreted in saliva and in pancreatic juice and occur also in the liver and in skeletal muscle. The normal range in serum is 80 to 180 Somogyi units/100 ml (30 to 120 Henry-Chiamori units/100 ml or 1.6 to 3.7 U/ml). The normal value is attained at 1 year and is thereafter independent of age and sex. The enzyme normally present in serum is probably of hepatic origin. Pancreatic α-amylase has a molecular weight of 45,000 and the enzyme thus finds its way into urine relatively readily.

In acute pancreatitis, the serum α-amylase rises after 3 to 6 hours, reaching a peak around 24 hours and returning to normal after 2 to 3 days. Very high values, up to 20 times normal, may be obtained and values above 550 Somogyi units/100 ml make the diagnosis virtually certain in the absence of mumps and of salivary duct obstruction. In the latter two diseases, equally high α-amylase levels (from the salivary glands) occur in serum. Increased levels, up to 500 Somogyi units/100 ml, may occur in perforated peptic ulcer, intestinal obstruction, acute peritonitis, acute cholecystitis and following morphine administration, when the latter causes contraction of the sphincter of Oddi. Values up to 400 Somogyi units/100 ml may also occur in patients with oliguric renal disease, when α-amylase excretion is diminished.

In chronic pancreatitis, in carcinoma of the pancreas and in acute pancreatitis after the third day, serum levels of α-amylase are essentially normal, although in the latter disease the enzyme may still be detected in excessive amounts in the urine for a further 12 hours (>35 Wohlgemuth units/ml). If high serum levels in acute pancreatitis continue for a longer period, pancreatic necrosis is indicated and the prognosis is less favourable.

**ENZYMES CONCERNED WITH DISORDERS OF SKELETAL MUSCLE**

Muscle contains many enzymes which may be found in serum, of which the following have at different times been used in the diagnosis of muscle disease: the two amino-transferases, lactate dehydrogenase, (ketose-1-phosphate) aldolase, creatine kinase and iditol (sorbitol) dehydrogenase. It is now generally agreed that creatine kinase is, singly, the most useful diagnostically. There are three principal reasons for this: it is the most abundant of the above enzymes in muscle and therefore the most sensitive indicator of muscle damage; although found in heart and in liver it is present in much smaller quantities than in muscles: unlike lactate dehydrogenase and ketose-1-phosphate aldolase, it is not present in erythrocytes, so that the determination is not affected by small amounts of haemolysis into serum.

**Creatine Kinase.**

Reaction catalyzed:

\[ \text{ATP + creatine} \rightarrow \text{ADP + phosphocreatine.} \]

The normal range for creatine kinase is 3.5 to 65 mU/ml (Griffiths, 1964). Severe muscular work may cause the serum level to rise, so that blood samples should be taken from the resting patient. Most anticoagulants inhibit the enzyme, so that the assay should always be carried out on serum. Severe muscle trauma also causes raised values, but a simple muscle biopsy usually does not.
Muscular dystrophy.

The serum creatine kinase is raised in muscular dystrophy. This is invariably so in the Duchenne type when values of 5 or more times the upper normal range are not uncommon. The frequency of raised values is less in the limb girdle and facio-scapulo-humerals types, and when raised values are recorded they are not often more than twice the upper normal limit. The highest values in the Duchenne type occur at the onset of the illness, and the levels fall, sometimes into the normal range, as the disease progresses over the years with increasing loss of muscle fibres.

The disease may be suspected and to some extent predicted in the brothers of affected patients by finding a moderately raised serum creatine kinase value. Known female carriers (mothers) may have moderately raised serum creatine kinase values, the incidence varying in different series from 25 to 85 per cent, depending on factors such as the precise level of the upper normal range. In the unmarried female siblings of affected males, raised values are also seen, but the incidence is less than in mothers. A female sibling may wish to know if she is likely to be a carrier. If the serum creatine kinase is persistently raised it seems likely in our present state of knowledge that she will be; if it is not raised the chances are probably less, but the possibility is by no means excluded.

Polymyositis; dermatomyositis.

In these two diseases increased levels of serum creatine kinase may be found and often the increase is marked. Successful treatment with steroids causes a fall in the serum creatine kinase pari passu with the clinical improvement. Treatment should probably not be discontinued before a normal level is restored. In muscular dystrophy, steroids do not produce a progressive lowering of the serum creatine kinase.

Other muscular and neuromuscular diseases.

Raised serum levels of creatine kinase are recorded with much less frequency in other muscle diseases (table I). In addition to the values given in the table, Buxton and Taylor (1968) have found the serum creatine kinase level to be normal in myotonia congenita, ocular myopathy, cerebellar ataxia, Werdnig-Hoffman syndrome, Jacob-

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Kreutzfeld syndrome, cervical spondylosis and McArdle's syndrome.

Hypothyroidism.

About 70 per cent of patients with hypothyroidism have a moderately raised serum creatine kinase concentration.

MYOCARDIAL INFARCTION

The role of the amino-transferases in the diagnosis of myocardial infarction has already been considered. The serum level of creatine kinase is also greatly increased in this condition. The rise occurs from 2 to 4 hours after coronary occlusion, so that assay of this enzyme may result in earlier diagnosis than may assay of aspartate aminotransferase. The peak value occurs from 24 to 36 hours and normal values are restored in 3 to 6 days. Thus if enzymic assays are delayed until after
the third day, the increased serum level of creatine kinase may be missed. At this stage after coronary occlusion, raised serum levels of lactate dehydrogenase (above 200 mU/ml) will more certainly be found, or of its variant, the so-called "hydroxybutyrate dehydrogenase". The serum lactate dehydrogenase does not return to normal after coronary occlusion for 8 to 9 days, but it must be remembered that raised serum values of this enzyme are also found in liver disease, including liver congestion, in muscle disease, in pernicious anaemia and in sera showing haemolysis.

The serum creatine kinase offers certain other advantages in the diagnosis of myocardial infarction, for normal values are usually found in congestive cardiac failure, after pulmonary embolism, and in acute pancreatitis, in all of which aspartate amino-transferase may be raised.

CONCLUSION

The diagnostic usefulness of serum concentrations of α-amylase, alkaline phosphatase and acid phosphatase have long been accepted, and the manner of interpreting any particular level, in the context of a patient's history and symptomatology, has become incorporated into the general body of medical knowledge. The upsurge in the last decade of new information about many other serum enzymes has caused two problems. One is to know which enzymes should be assayed in a given clinical circumstance in order to give the most useful information, and the second is, having made a wise choice, how to weight that information in relation to other factors that bear upon the diagnosis and management of an individual patient.

The solving of the first of these problems is made difficult by the continuing introduction of new enzyme assays which replace those introduced a few years earlier. Until a new stability is achieved at this phase, the second problem is insoluble. Thus in writing about, and in learning about, serum enzymes in diagnosis at the present time, one must always be conscious of the possibility that another enzyme may shortly replace one to which much attention has been devoted, and that one's interpretation is still relatively unsophisticated—to the patient's great disadvantage.

The number of new enzymes that can be introduced is large, but finite, so that eventually certain enzymes and iso-enzymes will assume diagnostic roles as stable as those now occupied by α-amylase and acid phosphatase. As this phase seems unlikely to be reached for some considerable time, we must, in the meantime, make use of our new knowledge with a proper appreciation of its potential limitations and fallibility.

For further information on diagnostic enzymology the student may refer to the texts by King (1965), Schmidt and Schmidt (1967) and Wilkinson (1962).

REFERENCES AND FURTHER READING


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For the Final F.F.A.R.C.S. Examination

The course, to be held on Saturday mornings, 9.30–12.15, will consist of 30 lectures and tutorials for ten weeks from April 19 to June 28, 1969. Written questions set and marked each week. Fee £10 10s. Course recognized by the South-East Metropolitan Regional Hospital Board.

Details and application forms from Dr. R. M. A. McClelland, Department of Anaesthetics, King's College Hospital, Denmark Hill, London S.E.5.

Closing date for application: April 10, 1969.