BIOCHEMICAL VALUES IN CLINICAL MEDICINE

The Results following Pathological or Physiological Change

BY

R. D. EASTHAM

SIXTH EDITION

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PREFACE
TO THE SIXTH EDITION

In this new edition a dozen new sections or subsections have been added, existing sections have been revised or rewritten and references have been updated. In spite of these additions, the book has been kept to pocket size. A few outdated tests have been demoted, with the titles left in the text, but with a note of their obsolescence. Radioimmunoassay methods have made estimations of the smaller polypeptide hormones more readily available to the clinician, and more information on the significance of test results of these substances is included.

The SI units are not yet used generally throughout the world. To help readers, factors to facilitate simple conversion from the previously used units to the new SI units, and vice-versa, have been inserted where relevant.

Once again, I am grateful to readers who let me have relevant information, notes of errors, and helpful suggestions.

Bristol,
July, 1978

R. D. E.

PREFACE TO THE FIRST EDITION

In this book I have tried to provide an accurate summary of the ways in which various conditions affect many biochemical tests. The attempt has been made because I have found in clinical laboratory practice that junior medical staff tend to read too much or too little into the results returning to them from the laboratory. Inevitably, I have missed out many tests either because I consider them dangerous or useless, or because they have been superseded by better tests, which are included.

A static reading of a result reflects only poorly the dynamic changes occurring in the body. In particular, some of the tests which are included cannot be dealt with adequately in the form used in this book. This applies especially to routine electrolyte examinations. For example, the plasma sodium level can be within the normal range, but the total body sodium may be either depleted, normal, or in gross excess. The patient's clinical state must be considered with every result from the laboratory. Nothing could be more dangerous to the patient's welfare, or more damaging to clinical chemistry, than attempts at either 'blunderbuss' diagnosis using multitudes of tests, or attempts to 'make a firm diagnosis' from a single result.

I have also included tests which are not normally performed by many routine laboratories, either because they demonstrate interesting applied physiology, or because of the exciting possibilities of future advances implicit in these tests.

In fact, if this book serves only to irritate more people into a state of greater interest in clinical chemistry, then it will have performed a useful function.

Finally, I would recommend the following subjects for discussion between the clinician and the clinical biochemist: (1) Clinical cases; (2) The methods of estimation used; (3) The ranges of normal values recognized by the particular laboratory.

I am grateful to *Dr. G. K. McGowan*, Consultant Chemical Pathologist, United Bristol Hospitals, for helpful advice and criticisms, and also for information on various subjects; to *Dr. J. M. Naish*, Consultant Physician, Bristol Clinical Area, for advice and encouragement; and to *Mr. W. B. Yeoman*, Biochemist, Frenchay Hospital, for helpful advice, criticisms, and information on various subjects.

Bristol,
December, 1959

R. D. E.

DEFINITIONS

The Equivalent Weight of a substance is that weight of it which will combine with or displace 1 g atom of hydrogen or 8 g atoms of oxygen. A milliequivalent of the substance is therefore 1/1000 of this weight, e.g.:

	Equivalent Weight	1 *mEq*
Sodium	23 g	23 mg
Potassium	39 g	39 mg
Chloride	35·5 g	35·5 mg
Bicarbonate	2·24 l	2·24 ml CO_2 at NTP
Calcium	20 g	20 mg

Mole: Amount of a substance which contains as many elementary entities as there are atoms in 0·012 kg of $^{12}C \triangleq 6{\cdot}02 \times 10^{23}$ (Avogadro's Number).

Body Surface Area approximation when area > 1 sq m

$$= 1 + \left(\frac{(\text{weight in kg}) + (\text{deviation in height from 160 cm in cm})}{100}\right)$$

= sq m

ACIDITY OF URINE

ACIDIFICATION TEST. After oral ammonium chloride, 0·1 g/kg body weight, in water, urine specimens are collected and stored under liquid paraffin until they can be examined in the laboratory. Delay should be minimal.

Normally the urine pH falls below 5·3 within 3 h, and the urine ammonium excretion increases. The rate of urine ammonium excretion is inversely proportional to the urine pH. Normally under these conditions more than 1·5 mEq of ammonium is excreted per hour; less than 0·5 mEq/hour suggests renal tubular damage.

After 6 g of oral ammonium chloride, a normal adult would excrete 70–160 mEq of ammonium in the urine per 24 h.

Pathological

1. Generalized renal disease. The urine pH falls normally, but ammonium excretion is scanty. In renal tubular acidosis the urine pH does not decrease, and the rate of ammonium excretion is low, but normal in relation to the urine pH.
2. Sickle-cell anaemia.
3. Hepatolenticular degeneration.

   After treatment with penicillamine for 1 year, the ability to acidify the urine down to pH 5·2 has been described.

N.B. **It is very dangerous to give ammonium chloride to patients suffering from liver failure or hepatic cirrhosis.**

REFERENCES. – Davies H. E. F. and Wrong O. (1957) *Lancet* 2, 625; Kong H. H. P. and Alleyne G. A. O. (1968) *Ibid.* 2, 954.

TITRATABLE ACIDITY. The titratable acidity represents the sum of the organic acids and sodium dihydrogen phosphate excreted in the urine. Added to the ammonium excreted in the urine, it gives a measure of the extent to which the body is able to conserve sodium and potassium while excreting excess anions and hydrogen ions.

N.B. **This is not a useful clinical test.**

CYCLIC ADENOSINE MONOPHOSPHATE IN PLASMA

Normal Value. 15·8 ± 2·8 nmol/l (11·8–20·4).

REFERENCE. – Latner A. L. and Prudhoe K. (1973) *Clin. Chim. Acta* 48, 353.

In adults, there is a circadian rhythm with peak values at 9–12 noon and the nadir at 6–9 p.m.

Pathological

Plasma cAMP rises to peak values by 20 min after parathyroid hormone injection in hypoparathyroidism. No such rise occurs in pseudohypoparathyroidism.

REFERENCE. – Tomlinson S., Hendy G. N. and O'Riordan J. L. H. (1976) *Lancet* 1, 62.

CYCLIC ADENOSINE MONOPHOSPHATE IN URINE

Cyclic adenosine-3', 5'-monophosphate (AMP) is formed from adenosine triphosphate (ATP) by the enzyme adenylate cyclase, and is inactivated by conversion to 5'-AMP by the reaction catalysed by phosphodiesterase. Adenyl cyclase in the cell membrane with a specific receptor associated with part of the enzyme, combines with circulating hormone for which it is specific, and cyclic AMP is released into the cell to modify cell function. Thus circulating hormone or related substance (which includes catecholamine, glucagon, vasopressin, ACTH, LH, TSH, TRF, parathyroid hormone and gastrin) is the 'Primary Messenger', and cyclic AMP inside the cell is the 'Second Messenger'. Urine cAMP output is not correlated with either the urinary calcium output or the estimated intake of calcium.

REFERENCE. – Israelsson B., Lindgärde F. and Malmquist J. (1977) *Acta Med. Scand.* **202**, 43.

Decreased Output

1. Depression.
2. Hypoparathyroidism.

Increased Output

1. Mania.
2. Hyperparathyroidism.

Although estimation of this substance is still experimental, results are encouraging.

In hypoparathyroidism and diabetes insipidus, there is an initial lack of 'Primary Messenger' hormone, with subsequent lack of cyclic AMP generation.

In pseudohypoparathyroidism (and in nephrogenic diabetes insipidus) the particular 'Primary Messenger' hormone is unable to activate the adenylate cyclase system, and there is no subsequent rise in urine cyclic AMP output, with no hormonal metabolic effect. In this form of pseudohypoparathyroidism, infused cyclic AMP results in a normal metabolic response to parathyroid hormone. In Type I pseudohypoparathyroidism the urine cAMP response is subnormal, and in Type II pseudohypoparathyroidism the urine cAMP response is normal.

A further variety of pseudohypoparathyroidism has been described in which there appears to be failure of intracellular reception of cyclic AMP messenger.

REFERENCE. – Drezner M., Neelon F. A. and Lebovitz H. E. (1973) *New Engl. J. Med.* **298**, 1056.

In children there is no correlation between urine cyclic AMP output and age, but when expressed in nmoles per mg creatinine an age relationship is apparent.

REFERENCE. – August G. P. and Hung W. (1973) *J. Clin. Endocrinol. Lab.* **37**, 476.

ADENYLATE KINASE IN CEREBROSPINAL FLUID

Normal: Absent from the cerebrospinal fluid.

Pathological

Increase: Brain tumours (probably from tumour cells).

REFERENCE. – Ronquist G., Frithz G., Ericcson P. and Hugosson R. (1977) *Lancet* 1, 1284.

TOTAL FIXED BASE OF URINE

This consists of the total urine excretion of sodium, potassium, magnesium, and calcium per day. It is not a useful estimation.

ADRENAL INHIBITION TESTS

In a normal person cortisone inhibits adrenal cortical activity, probably by inhibiting the formation of ACTH.

Pathological

1. *Virilizing States:* Daily administration of 200 mg cortisone acetate (orally or i.m.) for 2–5 days to those cases with abnormally raised 17-oxosteroid excretion gives the following results:
   a. Adrenal hyperplasia. The daily urine output of 17-oxosteroids is reduced.
   b. Adrenal adenoma } The daily urine output of
   c. Adrenal carcinoma } 17-oxosteroids is unaffected.
2. *Cushing's Syndrome:* Following daily administration orally of 10 mg of 9-alpha-fluorohydrocortisone, the daily urine output of 17-oxogenic steroids is greatly reduced.

Recently it has been found that 9-alpha-fluoro-16-alpha-methyl-prednisolone (dexamethasone) can be used. 0·5 mg 6-hourly for 8 doses suppresses normal adrenals, but no hyperplastic adrenals (whatever cause). 2·0 mg 6-hourly for 8 doses suppresses benign adrenal hyperplasia but not malignant hyperactivity.

REFERENCE. – Sprague R. G., Weeks R. E., Priestley J. T. and Salassa R. M. (1961) In: Gardiner-Hill (ed.), *Modern Trends in Endocrinology* London, Butterworth, p.87.

ALCOHOL IN BLOOD, BREATH, AND URINE

$$\left(\frac{\text{mg/l}}{46} = \text{mmol/l}\right)$$

Subclinical intoxication, 0–100 mg/100 ml.
Critical level of obvious intoxication, probably 150 mg/100 ml.
Gross intoxication, 200 mg/100 ml.
Stupor, more than 300 mg/100 ml.

Urine concentration is usually about one-third higher than the blood concentration. Peak urine output of alcohol is reached 2 h after ingestion. Recently estimation of the breath alcohol has been used as a measure of the blood alcohol concentration.

There is direct correlation between alveolar air alcohol concentration and arterial blood alcohol concentration.

The blood : breath coefficient of alcohol is not constant and therefore breath alcohol measurements are not suitable for legal convictions.

REFERENCES. – Mellor C. S. (1970) *Br. Med. J.* 3, 703. (Nomogram for calculating mass of alcohol in different beverages.) Alobaidi T. A. A., Hill D. W. and Payne J. P. (1976) *Ibid.* 2, 1479.

Before it can be considered the cause of death, blood alcohol must be 5 g/l (methyl alcohol total at a blood level of 1 g/l). After death the blood level falls at 100–200 mg/l per hour. If death takes 10–12 h, the blood alcohol may have fallen to 2 g/l.

The normal elimination rate of alcohol from the blood is 12–21 mg/100 ml per hour, which can be increased by intravenous fructose or large oral doses of fructose.

REFERENCES. – Walls H. J. (1958) *Br. Med. J.* **1**, 1442; Editorial (1966) *Ibid.* **1**, 184.

N.B. There are usually legal implications involved.

ALDOLASE IN SERUM

The enzyme catalyses the reaction:

1 molecule of fructose diphosphate→2 molecules of triose phosphate.

The highest tissue concentrations of the enzyme are found in heart muscle and skeletal muscle.

Normal Range. 2–9·6 unit/ml serum (1·5/7·2 μmol/min/l). Red blood cells contain aldolase in concentrations 150 times higher than the normal serum level.

Physiological

Increase: Normal newborn serum and red-cell levels are higher than the equivalent maternal levels for the first 48 h after birth. Normal adult levels are reached by puberty.

Pathological

Increase

1. *Myocardial Infarction:* Serum level rises after 3 h to a peak by 24 h (2–15 × normal), falling to normal by 4–7 days. There is a semiquantitative relationship between the amount of myocardial necrosis and the peak level in the serum.
2. *Skeletal Muscle Damage*
   - *a.* Progressive muscle dystrophy. (Affected muscles showing true hypertrophy, pseudohypertrophy, or atrophy.) Serum level increases in the early stages to 10–15 × normal in 90 per cent of cases. In pseudohypertrophic muscular dystrophy the serum levels are increased before there are obvious clinical signs of the disease. Levels in serum are higher in affected children than in adults in whom muscular dystrophy is developing for the first time. In the later and terminal stages serum aldolase levels are normal. Dystrophic muscle has an abnormally low aldolase content.
   - *b.* Gangrene affecting muscle.
   - *c.* Erb–Duchenne brachial plexus paralysis, i.e. C.5 nerve torn at birth. Serum level rises in the early stages, falling to normal later. This occurs in any primary neurogenic muscular atrophy.
   - *d.* Dermatomyositis. Normal or moderately increased serum levels are found. Where the serum level is increased, treatment with steroids will reduce the level to normal.
   - *e.* Paroxysmal myoglobinuria. Raised serum levels related to muscle destruction.

     Whenever there is rapid destruction of skeletal muscle

there is an increase in serum aldolase accompanied by parallel rises in serum lactic dehydrogenase, transaminases, and phosphohexoseisomerase, since these enzymes are also released from muscle cells.

Any destruction or wasting of muscle results in increased urine creatine output. In poliomyelitis, myotonic dystrophy, and other muscle disorders of nervous origin the serum aldolase is normal. In muscle wasting following severance of a nerve the serum aldolase shows a transient rise.

f. Carbenoxolone therapy.

3. *Liver Damage*
   a. Acute hepatitis.
   b. Acute alcoholic psychosis (? due to associated liver damage).
   c. Poisoning with carbon tetrachloride and other liver poisons.
   d. Secondary carcinoma invading the liver.
   e. Glycogen storage disease.
4. *Acute Pancreatitis.*
5. *Megaloblastic Anaemia* (serum levels up to 17 × normal may occur).
6. *Haemolytic Anaemia:* Serum levels increased if severe.
7. *Pulmonary Embolism:* Moderate increase with no sharp peak, cf. myocardial infarction.
8. *Carcinomatosis:* Variable rises in serum levels may be found. Successful remission in carcinoma of prostate produced by oestrogens is reflected by a fall in the serum level towards normal. In carcinomatosis the serum levels of aldolase and phosphohexoseisomerase are roughly parallel.
9. Cortisone and ACTH both cause the serum aldolase level to rise in experimental animals. ? similar effect in man.
10. *Tetanus:* Very high serum levels found in severe cases.

N.B. The serum aldolase changes in so many different conditions that it is really only useful either in the detection of cases of muscular dystrophy in the early stages of the disease or to measure response to treatment in carcinomatosis. (Probably serum phosphohexoseisomerase is a better parameter in these latter cases.)

REFERENCES. – Sibley J. A. and Lehninger A. L. (1949) *J. Biol. Chem.* **177**, 859; Volk B. W., Losner S., Aronson S. M. and Lew H. (1956) *Am. J. Med. Sci.* **232**, 38; Thompson R. A. and Vignos P. J. (1959) *Arch. Intern. Med.* **103**, 551; Patel A. A. and Rao S. S. (1966) *Am. J. Med. Sci.* **251**, 290.

ALDOLASE IN CEREBROSPINAL FLUID

Pathological

Increase

1. Niemann–Pick disease.
2. Infantile amaurotic familial idiocy.

ALDOSTERONE IN PLASMA

Pathological

Increase

1. Renin-secreting juxtaglomerular renal tumour.
2. Secondary hyperaldosteronism.

N.B. Assay of 24-h urine output of aldosterone is preferred.

ALDOSTERONE IN URINE

The hormone aldosterone is formed in the glomerulosa cells of the adrenal cortex. Normal excretion in the urine – up to 15 μg/24 h as aldosterone and its 18-glucuronide (equivalent to about 10 per cent of the adrenal secretion rate).

Physiological

Increase

1. Low sodium in the diet, with adequate potassium, especially if ACTH is given also.
2. Excessive sodium loss, with adequate potassium intake, e.g. after sweating.
3. After administration of potassium salts.
4. Normal pregnancy in third trimester.

Decrease

1. Excessive water intake.
2. Excess hypertonic saline infusion.
3. Low potassium intake.

Pathological

Increase

A. Without hypertension

Haemorrhage.
Abnormal sodium loss.
Congestive cardiac failure.
Nephrotic syndrome.
Hepatic cirrhosis.
Idiopathic oedema.
Postural hypertension.
Barrter's syndrome.
Desmit's syndrome.
21-hydroxylase deficiency.
Drug-induced secondary hyperaldosteronism due to the nephrotoxic effects of gentamicin, viomycin, capreomycin, for example during the treatment of pulmonary tuberculosis.

B. With hypertension

1. Primary hyperaldosteronism
   Low renin output – 65 per cent with adrenal tumour; 20–33 per cent adrenal hyperplasia, adrenal nodules.
2. Thiazide diuretics
   Some oral contraceptives, due to presence of oestrogen.
   Pregnancy – pre-eclampsia, eclampsia.
   Renal hypertension during the malignant phase.
   Renin-secreting renal tumours.
   'Congenital aldosteronism'.
   Renal tubular acidosis.

Decrease

A. Without hypertension

Addison's disease.
Isolated aldosterone deficiency.

B. With hypertension
Excess secretion of deoxycorticosterone
Cushing's syndrome.
17-alpha-hydroxylase deficiency.
11-beta-hydroxylase deficiency.
Apparent isolated excess of deoxycorticosterone.
Corticosterone excess.
18-hydroxydeoxycorticosterone excess.
Liddle's disease.
Proximal renal tubule sodium avidity.
Turner's syndrome (in 25 per cent of cases).
Carbenoxolone therapy.
Liquorice ingestion.

N.B. **The production of aldosterone, in cases other than adrenal tumour cases, appears to be related to the effective plasma volume. It is not apparently directly controlled by the pituitary gland.**

The estimation of urine (or plasma) aldosterone is clinically only indicated in the detection of primary hyperaldosteronism (Conn's syndrome). Combined with plasma renin estimation, primary and secondary hyperaldosteronism can be distinguished. It is essential that diuretics, purgatives, oral contraceptives, etc., should be discontinued for at least 3 weeks before samples for estimation are collected. Aldosterone secretion is not depressed by corticosteroid therapy.

REFERENCE. – Thorn G. W., Ross E. J., Crabbe J. and Van 'T Hoff W. (1957) *Br. Med. J.* **2**, 955.

ALKAPTONURIA

This is a rare condition inherited via a recessive Mendelian character. Excessive amounts of homogentisic acid are excreted in the urine. The urine darkens on standing, especially if it is alkaline. Homogentisic acid is an intermediate substance formed during conversion of phenylalanine to tyrosine; its output in the urine is proportional to the amount of protein in the diet.

Theories

1. Homogentisic acid is manufactured by the renal tubular cells.
2. Renal tubular cells extract traces of homogentisic acid present in the blood in these cases, and actively secrete it.

Both these theories are compatible with the finding that the renal threshold for this substance is extremely low.

AMINO ACIDS

AMINO ACIDS IN BLOOD

mmol/l × 1·4 = mg/100 ml.
mg/100 ml × 0·714 = mmol/l.

Normal Range. In plasma 3·1–5·7 mmol/l (as nitrogen). Higher readings are obtained with serum since amino acids are liberated during clotting. The red blood cells normally contain twice as much as the plasma.

Physiological

Increase: After a protein-containing meal the plasma level rises. The plasma level returns to the preprandial concentration within 4 h.

Decrease: The plasma level falls after glucose ingestion or insulin administration.

The plasma level also falls after growth-hormone or androgen ingestion. Presumably protein synthesis is stimulated.

N.B. In starvation the blood level does not usually fall below the normal fasting level (i.e. the level is maintained at the expense of body protein).

Pathological

Increase

1. Liver disease
   - *a.* Acute yellow atrophy. The amino acid level in the plasma is roughly proportional to the degree of liver damage. The greatest increase is in methionine and tyrosine.
   - *b.* Fatal liver poisoning with phosphorus, phenylhydrazine, carbon tetrachloride, or chloroform.
   - *c.* Kwashiorkor. There is an increase in beta-amino-isobutyric acid. During recovery with liver regeneration, the predominant amino acid is ethanolamine.
   - *d.* Severe yellow fever.
   - *e.* Eclampsia.
   - *f.* Coeliac disease and idiopathic steatorrhoea (if liver damage is also present).
2. Severe burns. Peptides derived from the burnt tissues appear in the plasma.
3. Severe shock.
4. After haemorrhage (especially gastrointestinal bleeding).
5. Diabetes mellitus in ketosis (probably associated with gluconeogenesis).
6. Slight increases have been reported in acute infections, hyperthyroidism, congestive cardiac failure, some cases of anaemia and after the administration of corticotrophin or cortisone.

Decrease

1. Nephrosis.
2. Kwashiorkor. Reduced to 45 per cent of normal.

The isolated estimation of the amino acid content of the blood is not often useful. Severe liver damage is more easily detectable by other means, but an abnormally raised plasma level could possibly assist in the detection of acute yellow atrophy of the liver.

The protein ingestion test of West has been used in the diagnosis of fibrous cystic disease of the pancreas in children. Its extension for the detection of chronic pancreatitis in adults has been found unsatisfactory by the author.

Probably chromatographic separation and identification of amino acids showing abnormal increase in the plasma is useful occasionally, e.g. in liver disease. Generally the more important changes in the plasma amino acids are reflected in the urinary chromatogram.

REFERENCES. – Folin O. (1922) *J. Biol. Chem.* 51, 377; Smith I. (1958) *Chromatographic Techniques.* London, Heinemann.

AMINO ACIDS IN URINE

The daily urine amino acid output in normal adults is about 1·1 g as free amino acids and about 2 g as conjugated amino acids, with wide variation between individuals. This variation may be caused by diet, genetic differences, pregnancy, etc.

Physiological

1. On a high meat diet, excess histidine and methyl histidine are excreted.
2. In starvation excess beta-amino-isobutyric acid is excreted.
3. During normal pregnancy increased amounts of histidine and threonine are excreted, returning to normal during lactation.
4. In full-term and premature babies increased amounts of glycine, alanine, threonine, serine, asparagine, glutamine, cystine, glutamic acid and proline are excreted in excess in the urine.

N.B. **Patients treated with a mixture of D- and L-amino acids show a gross amino aciduria, since the dextrorotatory forms of the amino acids are only poorly utilized by the body and are rapidly lost in the urine. Patients having intravenous infusions of protein hydrolysates may show amino aciduria, presumably due to incomplete utilization.**

Pathological

1 *Pure 'Overflow' Amino Aciduria*

Liver Disease

i. Massive liver necrosis.

ii. Advanced cirrhosis of the liver.

In both these conditions the amount of amino acids present in the plasma, cerebrospinal fluid and urine is proportional to the degree of liver damage.

The appearance and amounts of cystine, beta-amino-isobutyric acid and ethanolamine are a useful indication of liver damage. Glutamine may appear in the urine if the patient has been treated with flutamic acid.

iii. Postanaesthetic transitory cystinuria.

iv. Liver regeneration. Predominantly an increase in ethanolamine.

v. Kwashiorkor. Increased beta-amino-isobutyric acid and ethanolamine.

Severe Burns: Amino acids and peptides are excreted in the urine.

2. *Renal Damage*

Poisoning by lead, uranium, mercury, cadmium, or thallium.

3. *Unclassified*

a. Untreated Pernicious Anaemia: There is amino aciduria with an excess excretion of taurine, especially if there is associated subacute combined degeneration of the spinal cord. Amino aciduria does not occur in other megaloblastic anaemias.

b. March Haemoglobinuria: Cystine and beta-amino-isobutyric acid may appear.

c. Acute Intermittent Porphyria: Urine contains delta-amino-laevulinic acid.

d. Alactasia: Urine contains lactose plus amino acids after a lactose-containing diet.

e. Cachexia: The predominant amino acid appearing in the urine is beta-amino-isobutyric acid.

f. Glycogen Storage Disease.

g. Severe Diabetic Ketosis: The predominant amino acids in the urine are leucine and lysine.

h. Old deteriorated tetracyclines cause a Fanconi-type syndrome with amino aciduria, glycosuria, hypokalaemia, metabolic acidosis and polyuria.

REFERENCES. – **Harris H. and Milne M. D. (1964) In: Thompson R. H. S. and King E. J. (ed.) *Biochemical Disorders,* 2nd ed. Ch. 18, p. 743. London, Churchill; Milne M. D. (1964) *Br. Med. J.* 1, 327 (156 references); Eastham R. D. and Jancar J. (1968) *Clinical Pathology in Mental Retardation.* Bristol, Wright.**

HEREDITARY CONDITIONS WITH ASSOCIATED AMINO ACIDURIA

Clinical Condition	*Amino Acidaemia*	*Amino Aciduria*
Carbamyl phosphate synthetase deficiency	Glycine	Glycine
Ornithine transcarbamyiase deficiency	No increase	Moderate amino aciduria with increased glutamine
Citrullinuria	Citrulline	Citrulline
Argininosuccinic aciduria	Argininosuccinic acid + citrulline	Argininosuccinic acid
Arginase deficiency	Arginine	Gross amino aciduria with excess arginine
Congenital lysine* intolerance	Lysine with moderate increase in arginine, glutamine, ornithine	Lysine, with ornithine, ethanolamine, gamma-aminobutyric acid
Phenylketonuria	Phenylalanine	Phenylalanine + keto derivatives
Tyrosinaemia	Tyrosine, with increased methionine in acute attacks	*p*-Hydroxyphenyl derivatives
Hartnup disease	Abnormally low plasma tryptophan	Generalized amino aciduria with specific pattern
Tryptophanuria	Tryptophan	Tryptophan
Indolylacroyl glycinuria	No increase described	Indolylacroyl glycine
Maple-syrup urine disease	Valine, leucine, isoleucine	Valine, leucine, isoleucine
Hypervalinaemia	Valine	Valine
Isovaleric acidaemia	Isovaleric acid (essential amino acids depressed)	Isovaleric acid
Hypermethioninaemia	Methionine + tyrosine	Amino aciduria with specific pattern
Oast-house syndrome	No increase	Phenylalanine, tyrosine, methionine plus various keto acids
Homocystinuria	Methionine + homocystine	Homocystine plus other sulphur-containing substances
Cystathioninuria	Methionine after methionine load	Cystathionine
Cystinosis	Free cystine in leucocytes increased	Amino aciduria with increased cystine
Cystinuria	Normal	Cystine, lysine, arginine, ornithine
Sulphite oxidase deficiency	No report	Cystine derivative
Histidinaemia	Histidine	Histidine plus imidazol derivatives
Hereditary orotic aciduria		Orotic acid
Hyperglycinaemia with hyperglycinuria (ketotic variety)	Glycine, with moderate increases in branched amino acids + methionine	Glycine
Hyperglycinaemia with hyperglycinuria (non-ketotic)	Glycine	Glycine

HEREDITARY CONDITIONS – *continued*

Clinical Condition	*Amino Acidaemia*	*Amino Aciduria*
Monilethrix	Glutamic acid	Variable
Hypersarcosinaemia	Sarcosine	Sarcosine
Oculo-otocerebrorenal syndrome	Alpha aminobutyric acid	Alpha-aminobutyric acid
Hyperbeta-alaninaemia	Alanine+gamma-iso butyric acid	Beta-alanine, beta-amino-isobutyric acid, gamma-aminobutyric acid
Familial hyperprolinaemia, Type I	Proline	Proline, glycine, hydroxy-proline
Familial hyperprolinaemia, Type II	Proline	Proline + delta-pyrroline-5-carboxylic acid
Hydroxyprolinaemia	Hydroxyproline	Hydroxyproline (free)
Oculocerebrorenal syndrome	Normal	Multiple amino aciduria
Methylmalonic aciduria	Normal	Methylmalonic acid
A-beta-lipoproteinaemia	Normal	N n-specific
Amaurotic familial idiocy	Normal	Carnosine and derivatives of histidine may be found
Hereditary fructose intolerance	General increase	General amino aciduria
Galactosaemia		Amino aciduria
Familial lactic acidosis		Moderate amino aciduria
Hepatolenticular degeneration	Normal	Generalized amino aciduria

ALANINE AMINOTRANSFERASE AND ASPARTATE AMINOTRANSFERASE

ASPARTATE AMINOTRANSFERASE IN SERUM

Aspartate aminotransferase IFCC method (no difference between results with serum and heparinized plasma).

REFERENCE. – *Clin. Chim. Acta* 70, F19–42.

Normal Range. 2–20 iu/l.

Physiological

Increase: The ASA is raised in the normal newborn. Normal adult levels are reached by 7 years.

Pathological

Increase: Normally almost all the enzyme is intracellular. Following any injury to, or death of, physiologically active cells, the enzyme is released into the circulation, i.e. it can be used as a measure of cell damage rather than cell function. Equilibration between plasma and interstitial fluid then follows within 6–18 h, i.e. the serum rise is not as great as would be expected from total enzyme released from damaged tissue.

1. *Heart*
   a. Myocardial infarction: The ASA level increases about 4 h after an infarction and persists at an abnormally raised level for about 3 days. ASA also rises in acute congestive failure related to centrilobular liver necrosis and congestion. In uncomplicated cases ASA is not specific enough for satisfactory detection of small infarctions. CPK, HBD, or LDH are better.

REFERENCE. – Auviner S. (1972) *Acta Med. Scand.* Suppl., 539.

   b. Acute rheumatic carditis: Serum level related to severity in the early stages.

c. Cardiac surgery: On the second day after operation the serum level is increased, falling to normal by the tenth day – e.g. after operation for pulmonary stenosis the ASA is 7–8 × normal.
d. After angiocardiography and passage of cardiac catheter.
e. After external cardiac massage.

2. *Liver*
   a. Infective hepatitis: The serum level rises in the prodromal phases of the disease, increasing to a peak when the patient shows the greatest malaise and liver tenderness. The rise in the enzyme is parallel with the rise in serum iron (cf. extrahepatic biliary obstruction). ASA correlates well with the course of chronic hepatitis. The level is raised in non-icteric attacks.
   b. Hepatic damage: Carbon tetrachloride and other liver poisons cause the ASA to rise.
   c. Infiltration of liver:
      i. Carcinoma
      ii. Leukaemia
      iii. Lymphoma
      } Cases may show an increase.
   d. Cholangitis.
   e. Infectious mononucleosis: Maximal results by the second week, falling to normal by the fifth week.
   f. Alcoholic debauch: ASA rises afterwards.
   g. Pulmonary infarction: ASA rises later and slower than after cardiac infarction. Possibly related to associated congestive failure.
   h. Rifampicin and isoniazid therapy, especially in slow acetylator phenotypes.

REFERENCES. – Lal S., Singhal S. L., Burley D. M. and Crossley G. (1972) *Br. Med. J.* **1**, 48; Bailey W. C., Weill H., De Rouen T. A., Ziskiad M. M., Jackson H. A. and Greenburg H. B. (1974) *Ann. Intern. Med.* **8**, 200.

   i. Salicylate therapy or poisoning.
   The rise in aspartate aminotransferase is proportional to plasma salicylate levels, when salicylate concentrations exceed 1·81 mmol/l (25 mg/100 ml).
   j. Following large doses of desferrioxamine.

REFERENCES. – Russell A. S., Sturge R. A. and Smith M. A. (1971) *Br. Med. J.* **2**, 428; Rich R. R. and Johnson J. S. (1973) *Arthritis Rheum.* **16**, 1.

3. *Pancreas:* Acute pancreatitis. No apparent correlation with; (*a*) Damage to pancreas, (*b*) Serum lipase, (*c*) Serum amylase, (*d*) Serum calcium, but there is direct correlation with the serum bilirubin level suggesting increase due to biliary obstruction.
4. *Trauma*
   a. Intestinal infarction.
   b. Intestinal surgery.
   c. Crush injury.
   d. Local irradiation injury.