

Interpretation of Biochemical Tests

Introduction

Biochemical tests are now an important part of investigation and management of patients. Understanding the factors which influence laboratory results and how laboratory results could be used for the diagnosis and treatment, is important for the rational and effective use of laboratory tests. As with other investigations, biochemical results should be taken in the context of patients' clinical features (signs and symptoms) and other relevant findings.

Biochemical tests are performed for four main reasons — diagnosis, management, prognosis and screening. When used appropriately, biochemical tests can contribute substantially to the overall care of the patient. However, when used inappropriately, it can lead to unnecessary further investigations, pain and suffering to the patient and increased costs to the health service.

Diagnosis

Clinical diagnosis is usually based on history, physical examination and results of investigations. History and examination are the important elements in arriving at a diagnosis and studies show that up to 80% of cases can be diagnosed from history and clinical findings alone. Biochemical tests very often help to confirm the diagnosis or identify a metabolic syndrome. Seldom are they diagnostic except in a few instances, such as inherited disorders of metabolism.

Management

Biochemical tests are most often used in the management of patients. Approximately 60–70% of all biochemical tests are used for monitoring treatment or to follow the progress of the disease. Serial measurements are valuable in management, e.g. in patients with diabetic ketoacidosis, frequent measurements of blood glucose help to assess the response to insulin and to adjust dosage; in hypothyroid patients on thyroxine replacement therapy, regular measurements of thyroid function tests guide the adequacy of thyroxine replacement.

Biochemical tests are also useful in assessing the severity of the disease. The degree of abnormality in biochemical tests is (usually but not always) related to the severity of the disease. For example, in renal failure, the greater the plasma urea and creatinine, the more severe the reduction in renal function.

Prognosis

Biochemical tests, either individually or in combination, can give an indication of the prognosis, e.g. in patients with malignant tumours, serial measurements of tumour markers are of value in assessing the response to treatment and the possibility of recurrence.

Screening

When tests are done to detect the presence of a disease before clinical features are evident, it is described as screening. Screening may be applied to a population (population screening), to a selected subgroup of a population (selective screening), individuals (individual screening) or it could be opportunistic.

Population screening

These tests are done in an apparently healthy population to identify those who may have subclinical disease or those who are at risk of

developing a disease. Population screening programmes should satisfy the following criteria:

1. The disease should have a significant effect on the quality of life or life expectancy, e.g. screening for Gilbert's syndrome, an inherited disorder of bilirubin metabolism, is of no value as it has no long-term effect on the health of the patient.
2. The screening test can detect the disease before irreversible damage has occurred.
3. Effective treatment is available and is acceptable for asymptomatic patients.
4. The screening test should be effective (specific and sensitive) and acceptable to the population to be screened.
5. The prevalence of the disease and the benefits of treatment should justify the cost of screening.
6. The population at risk can be defined.

Unequivocal benefits of screening have only been established for a few conditions. These include screening for phenylketonuria and hypothyroidism in the newborn and cervical screening for the detection of cervical carcinoma.

Selective screening

Screening can also be applied to a subgroup of the population known to be at risk of developing that disease, e.g. family members of a patient with hypercholesterolaemia or premature coronary heart disease could be screened for high cholesterol.

Individual screening

Here an individual is screened for a particular disease or diseases based on the individual's history. An example is antenatal screening of a foetus for inherited disease when a previous child of the parents has been found to have that disease or when there is a strong family history of that disease.

Opportunistic screening

Opportunistic screening is when a patient is screened for certain diseases when he presents to the doctor with an unrelated condition, e.g. detection of hypertension.

Other Uses of Laboratory Tests

Biochemical profiling

With the availability of multichannel analysers, it is now possible to analyse a small blood sample for a large number of biochemical tests. When a group of tests is applied to otherwise healthy individuals or to all admitted to hospitals, it is termed biochemical 'profiling'. In general, this type of approach has caused more harm than good as the efficiency of detection of a disease is low. Unnecessary investigations may follow when non-specific abnormalities in test results are found. It has been argued that admission profiling can detect potentially treatable diseases at an early stage. Diseases that can be detected by screening hospital patients include hyperparathyroidism, hypothyroidism, diabetes mellitus, renal disease and liver disease (alcoholism). However, the value of such admission screening is yet to be established as this approach can detect diseases, which may not manifest in the lifetime of the patient.

Baseline

Biochemical tests are often also used as a baseline before starting treatment to detect any harmful effects of treatment or to monitor the treatment.

Collection of Specimens

Biochemical investigations are done in body fluids, most often in plasma or serum. It is essential that blood samples are collected appropriately to prevent artefacts. In patients receiving intravenous

therapy, blood should be collected from a different site to avoid contamination of the blood sample with the infusion fluid. Tourniquet is often used to obstruct venous blood flow in order to make the venepuncture easy. However, if the tourniquet is applied too long, the increased pressure will cause transfer of water and small molecular weight constituents into the interstitial compartment. This will often result in an increase in the concentration of large molecular weight substances such as proteins and in protein-bound substances such as calcium in the serum sample.

While transferring the blood from the syringe into the bottle, care should be taken to avoid haemolysis.

Once the blood is taken, it should be put into appropriate bottles containing the appropriate preservatives. Most investigations are now done in serum. However, there are some investigations for which plasma is required, e.g. measurement of fibrinogen requires plasma. Inappropriate use of anticoagulants has often led to spurious results, e.g. taking blood sample for electrolytes into an EDTA tube will cause very high potassium and low calcium concentrations. Blood for the measurement of glucose concentration should be taken into a fluoride tube; otherwise the blood glucose will artificially decrease due to continued glycolysis by red cells. Once the blood is collected, it should be transported to the laboratory within a specified time to prevent artificial results, e.g. if the blood sample is left at room temperature for several hours, it will lead to high potassium concentration. Storing samples below room temperature has similar effects.

Some investigations are done in urine — a random or a 24-hour urine collection. Appropriate preservatives should be used to avoid artefactual results, e.g. urine for calcium should be collected in a container with acid preservative to prevent precipitation of calcium phosphate. When 24-hour samples are required, patients should be given appropriate instructions on how to collect the urine samples. In investigations done on 24-hour samples, the most important source of error is incomplete urine collection. Measurement of urine creatinine concentration is sometimes used to check whether urine collection is complete.

Identification of Patient Specimens

It is essential that the sample is collected from the correct patient. Many errors have occurred due to improper identification of the patient. Once collected, the sample should be correctly labelled and accompanied by a properly completed request form.

Interpretation of Laboratory Results

In interpreting laboratory results, one of two questions is usually asked:

- (i) Is the result normal or abnormal?
- (ii) Has the result changed significantly from a previous result?

In answering the first question, the result is compared to a range (reference range).

Reference Ranges

Reference ranges can be either population-based or risk-based.

Population-based reference ranges

To determine the population-based reference range, blood samples are taken from a defined population — usually healthy individuals, but it can be from any defined population. If the analyte concerned is known to be affected by sex and age, the population should be divided according to these two factors. Once the blood is analysed, the results are examined to see whether it follows a Gaussian (symmetrical) distribution. If the result fails to follow a Gaussian distribution, transformations such as a log transformation can be done. The reference range is calculated as mean \pm 2 standard deviation (SD), but often the range is taken as the value that represents 95% of the population (2.5–97.5%) when the values are ranked. This type of reference range excludes 5% of the population who are apparently healthy. It is also possible that some subjects with an undiagnosed ‘disease’ may be included

in the population used to establish the reference range (for example, undiagnosed diabetes mellitus).

The probability of finding abnormal results in a healthy population increases if multiple tests are done at the same time, especially if the tests are not dependent on each other. If 20 independent tests are done, the probability of finding at least one result outside the reference value is 64%.

Risk-based reference range

Reference range is sometimes based on disease risk. The reference values for cholesterol are based on the risk of developing coronary heart disease. Epidemiological studies have shown that a cholesterol value of 4.0 mmol/L or lower carries a low risk of coronary heart disease.

It is important to remember that results within the reference range do not exclude disease and results outside the reference range do not always indicate the presence of a pathological disease. However, the more abnormal the result, the greater the chance that there is a disease process. The diagnosis is seldom based solely on biochemical results. Test results should be taken in conjunction with clinical findings and usually there is no absolute demarcation or cut-off values between disease and normal.

Detection of a Significant Change

The second question asked about a test result is whether there is a significant change from a previous result. In deciding whether a significant change has occurred, several factors need to be taken into account. These include analytical variation, biological variation related to the time of sampling and the procedure used. Ideally biological variation should be minimised by taking the sample under identical conditions of time, posture, etc. Other preanalytical factors should be minimised by using exactly the same techniques. When these factors are minimised, the variation between two results depends on the imprecision of the assay. If the difference between two results is equal to or more than 2.8 times the standard deviation (SD)

Table 1.1 Calculation of total variation

Serum free thyroxine concentration measured in a subject 2 months apart were 12 and 18 pmol/L. Is this difference significant?

The analytical variation for free thyroxine measurement is 1 pmol/L and the biological variation 1.2 pmol/L.

$$\begin{aligned}\text{Total variation} &= \sqrt{(\text{SD}_A^2 + \text{SD}_I^2)} = \sqrt{(1^2 + 1.2^2)}, \\ &= \sqrt{(1 + 1.44)} = \sqrt{2.44} = 1.6.\end{aligned}$$

For a difference between two values to be significant at 5% level, the two results should be greater than $2.8 \times$ the total variation.

In this case, $2.8 \times 1.6 = 4.48$.

The difference observed is 6 pmol/L and therefore this change is clinically significant.

of the method, the difference is significant at 5% confidence limit. For example, if the analytical SD for serum sodium is 2 mmol/L, a change less than 5.6 mmol/L is within the limit of the analytical variation.

In order to decide whether the change is clinically significant, biological variation should be taken into account. Total variation (biological and analytical) is calculated from the analytical and biological variations using the formula:

$$\text{SD}_{\text{Total}}^2 = \text{SD}_A^2 + \text{SD}_I^2$$

where SD_{Total} is the total variation, SD_A is the SD of analytical variation and SD_I is the SD of biological variation (Table 1.1).

Factors Affecting Test Results

Test results can be affected by preanalytical, analytical and postanalytical factors. Preanalytical factors may be biological factors or factors related to the collection of specimen. The latter has already been discussed.

Biological Factors (Table 1.2)*Age*

Many biochemical variables vary with age, and an appropriate age-related reference range should be used to interpret results of these tests. Examples of tests which vary with age include alkaline phosphatase, phosphate and gonadotrophins.

Sex

Tests such as sex hormones, serum creatinine, urate and GGT show differences between sexes.

Body composition

Body fat and lean body mass can influence some results. Creatinine and creatine kinase, which are derived from muscle, are said to be related to muscle mass. Triglycerides tend to be higher in obese individuals.

Table 1.2 Biological factors affecting biochemical results

Factors	Biochemical tests
Age	Alkaline phosphatase, uric acid, creatinine
Sex	Gonadotrophins, gonadal steroids, creatinine
Body composition	Creatinine, creatine kinase, triglycerides
Race/Ethnicity	Creatine kinase, prostate specific antigen
Time	Cortisol
Posture	Protein, renin, aldosterone
Stress	Prolactin, cortisol
Food intake	Glucose, triglycerides
Alcohol	Triglycerides
Exercise	Creatine kinase
Drugs — <i>in vivo</i> effects	Phenytoin — gamma-glutamyl transferase Thiazides — potassium Oestrogens — sex hormone-binding globulin

Ethnicity/race

The range found in healthy individuals from different ethnic groups vary for some analytes. Prostate specific antigen (PSA) is higher in African Americans and lower in Japanese compared to Caucasians. Serum creatine kinase (CK) values in African Americans are higher than in Caucasians.

Time of day

Cortisol, osteocalcin, parathyroid hormone, etc. show a circadian rhythm. Some analytes show seasonal changes, e.g. plasma 25-hydroxycholecalciferol.

Stress

Stress causes the release of cortisol, ACTH, prolactin, growth hormone, catecholamines, etc. Thus, it is very important to avoid stress when taking samples for these measurements.

Posture

Posture increases aldosterone and renin activity. Plasma proteins and protein-bound compounds tend to be higher on attaining a standing posture. This is due to the movement of fluid from the vascular compartment to the interstitial compartment.

Food intake

Glucose, triglycerides and insulin are examples of substances affected by food.

Drugs

Drugs can influence results by either interfering with the analysis or by physiological mechanisms. For example, in patients taking phenytoin, serum gamma-glutamyl transpeptidase (GGT) is higher due to enzyme induction.

Exercise

Exercise and trauma release CK and myoglobin.

Intrinsic biological variation

Although many biochemical variables are tightly controlled, there is variation within an individual. This individual variation is small for some analytes and large for others. For example, serum iron concentration fluctuates rapidly within the same individual whereas serum sodium, creatinine and calcium concentrations show less variation (Figure 1.1). For analytes which have a low intraindividual variation, the serum concentration may change within the reference range and

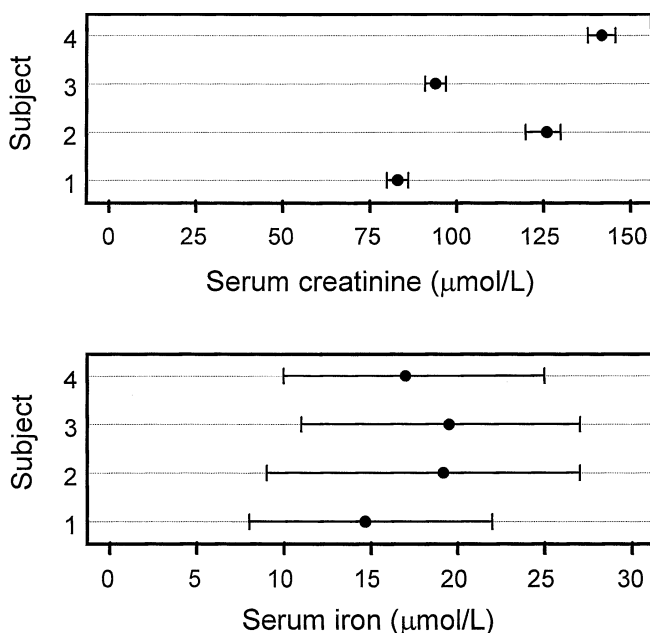


Figure 1.1 Within individual variation for (a) serum creatinine and (b) serum iron in four individuals. The circle represents the mean for the individuals and the lines indicate the range found in that individual (adapted from Fraser and Stevenson, 1998 with permission).

become abnormal for that individual. For analytes with low intraindividual variation, population reference ranges are less useful.

Analytical Factors

All analytical methods have errors — inaccuracy and imprecision (Figure 1.2). Inaccuracy refers to how close the result is to the true value. Imprecision refers to the reproducibility of the result and is usually expressed as coefficient of variation. To estimate imprecision, a sample is analysed several times and the mean and standard deviation (SD) are calculated. Coefficient of variation (CV) is derived using the formula:

$$CV = \frac{SD}{Mean} \times 100.$$

The Diagnostic Value of an Investigation

The diagnostic value of a test is described in terms of sensitivity, specificity and predictive value. The sensitivity of a test is the frequency with which a positive result is found in patients known to have the disease i.e. true positive (TP) rate. The specificity of a test is a measure of the frequency of negative results in patients (or persons) known to be free of the disease, i.e. true negative (TN) rate. A sensitivity of 90% implies that 90% of patients with the disease will have a positive result and 10% of people with disease will not show a positive result; a false negative (FN) result. A specificity of 95% means 95% of people without the disease will show a true negative result and 5% of the

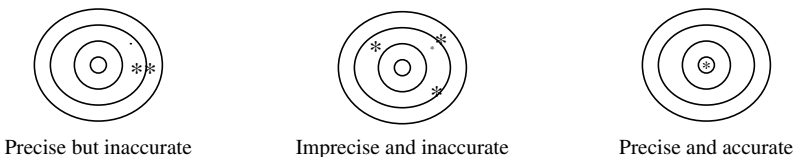


Figure 1.2 Diagram illustrating accuracy and imprecision.

population without the disease will have a positive result, a false positive (FP) result. An ideal test should be 100% sensitive and 100% specific. However, in practice, no such test exists. Specificity and sensitivity can be calculated from the following formulae:

$$\text{Specificity} = \frac{\text{true negative}}{\text{false positive} + \text{true negative}} \times 100.$$

$$\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}} \times 100.$$

The predictive value of a positive test is a measure of the likelihood of having the disease under consideration when the test is positive. The predictive value of a negative result is the likelihood of not having the disease when the test result is negative. In determining the specificity, sensitivity and predictive values, it is important to be able to assign subjects to the right categories, i.e. patients should be allocated to a particular disease based on independent diagnosis. For some diseases, histological confirmation may be the only way of confirming the diagnosis. Calculation of predictive values is illustrated in Table 1.3.

In the preceding discussion, it has been assumed that the prevalence of the disease is 50%. When establishing the diagnostic value of a new test, it is not unusual to apply the test to selected groups of equal sizes — a group with the disease and a control group — a prevalence of 50%. In clinical practice however, the test will be applied to a larger number of people where the prevalence will be lower. The example given in Table 1.4 illustrates the effect of prevalence on the predictive value of a test, which has a sensitivity of 99% and specificity of 99%. When the prevalence is 50%, the predictive value of a positive result is 99%. However, when the prevalence is 1%, the predictive value falls to 50%. The predictive value of a test falls with decreasing prevalence. One way of improving the efficacy of a test would be to use the tests more selectively, i.e. by applying the test only on sound clinical grounds, thus increasing the prevalence of the disease.

Table 1.3 Calculation showing predictive value of a test

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \times 100.$$

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} \times 100.$$

$$\text{Predictive value of a positive result} = \frac{\text{TP}}{\text{TP} + \text{FP}} \times 100.$$

$$\text{Predictive value of a negative result} = \frac{\text{TN}}{\text{TN} + \text{FN}} \times 100.$$

$$\text{Efficiency} = \frac{\text{TP} + \text{TN}}{(\text{TP} + \text{FP} + \text{TN} + \text{FN})} \times 100.$$

Example

	Positive	Negative	Total
Disease	(TP) 90	(FN) 10	100
Health	(FP) 5	(TN) 95	100
	95	105	200

*TP = True positive; TN = True negative;

FD = False positive; FN = False = negative.

$$\text{Predictive value of a positive result} = \frac{90}{(90+5)} \times 100 = 94.7\%.$$

$$\text{Predictive value of a negative result} = \frac{95 \times 100}{(95+10)} = 90.5\% = \frac{95}{(95+10)} \times 100 = 90.5\%.$$

$$\text{Efficiency} = \frac{(90+95)}{200} \times 100 = 92.5\%.$$

Cut-off Value

In the discussion thus far, the test result was designated as positive or negative. As biochemical results are usually quantitative, the cut-off value, the concentration at which the test is considered as positive, can be varied.

Selection of the cut-off value will depend on the purpose of the test. In circumstances where the consequences of not diagnosing the diseases is great, it is important to select a cut-off value so as not to

Table 1.4 Effect of prevalence on the predictive value

Sensitivity of the test = 99%
Specificity of the test = 99%

Population of 1000 with a prevalence of 50%

	+ve results	-ve test	Total
Disease	4950	50	5000
Without the disease	50	4950	5000
Total	5000	5000	10,000

$$\text{Predictive value of a +ve result} = \frac{4950}{4950+50} \times 100 = 99\%$$

Prevalence of 1% — Population 10 000 with a prevalence of 1%

	+ve results	-ve test	Total
Disease	99	1	100
Without the disease	99	9801	9900
Total	198	9802	10,000

$$\text{Predictive value of a +ve result} = \frac{99}{99+99} \times 100 = 50\%$$

miss any individual with the disease, i.e. to keep false negatives as low as possible. Hence, a lower cut-off value to ensure a sensitivity of 100%, should be chosen. An example of this situation is in the screening for phenylketonuria (PKU), when missing the diagnosis of PKU has grave consequences. This approach however, will reduce specificity and will give a larger number of false positive results. In circumstances where it is important not to cause unnecessary anxiety and investigations, a high specificity is required and a high cut-off value should be selected.

To compare the performance of two tests, receiver operating characteristic (ROC) curves can be used. The sensitivity and specificity at

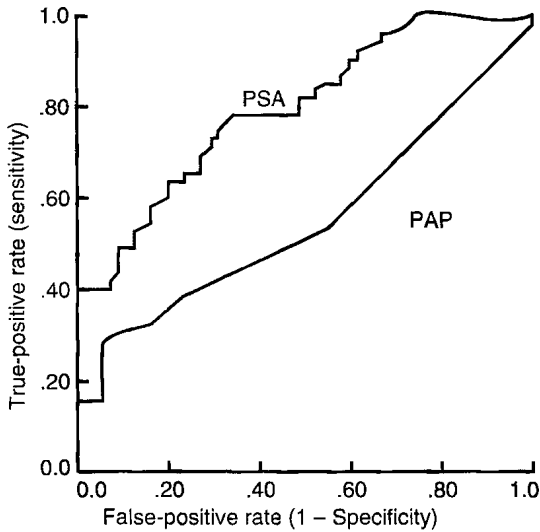


Figure 1.3 Receiver operating characteristic (ROC) curve for prostate-specific antigen (PSA) and prostatic acid phosphatase (PAP) in the diagnosis of prostatic carcinoma. The area under the curve for PSA is greater than PAP showing the PSA is a better test.

different cut-off values for each test are calculated and plotted as shown in Figure 1.3. The area under the curve is a measure of the performance — the greater the area under the curve, the more specific and sensitive the test.

Likelihood Ratios

Likelihood ratios are an alternative way of summarising the usefulness of a diagnostic test. The ratio tells us how many more (or less) times patients with the disease are likely to have that particular result than patients without the disease. Likelihood ratios can be calculated for a positive (LR+) or a negative (LR-) results by the following equations:

The likelihood for a positive result is calculated as

$$LR + = \frac{\text{sensitivity}}{1 - \text{specificity}}$$

The likelihood for a negative result is calculated as

$$LR - = \frac{1 - \text{sensitivity}}{\text{specificity}}.$$

The higher the likelihood ratio of a positive result, the greater the chances of finding the disease. Likelihood ratios above 10 and below 0.1 are considered strong evidence to rule in or rule out diagnoses respectively.

General Principles

Steady State vs. Transient State

In order to understand the pathophysiology of diseases, it is important to explain the difference between steady state and transient state. This principle can be illustrated by the following case example:

In a patient with chronic renal failure, the following blood results are found:

Sodium (mmol/L)	138	135–145
Potassium (mmol/L)	5	3.5–5.0
Bicarbonate (mmol/L)	18	23–32
Chloride (mmol/L)	102	90–108
Urea (mmol/L)	35	3.5–7.2
Creatinine ($\mu\text{mol/L}$)	565	40–60

If students are asked about the urinary excretion of creatinine in this patient, most students will say that the excretion of creatinine will be low due to the low glomerular filtration rate. Similarly, if students were asked about the excretion of carbon dioxide in a patient with chronic obstructive airways disease, most would answer that it would be decreased and the arterial partial pressure of carbon dioxide is increased. However, in both these examples, it is likely the excretion will not be low as these patients are in a steady state. This can be explained using the diagram below (Figure 1.4).

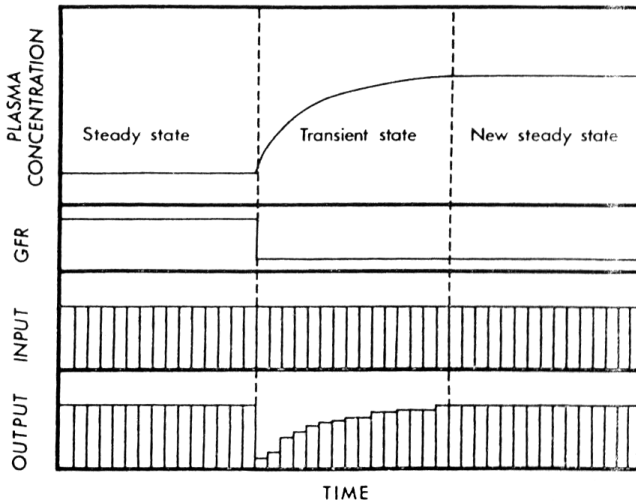


Figure 1.4 Theoretical changes in plasma concentration, GFR, production rate and urinary excretion of creatinine before and after a reduction in GFR. (Reproduced with permission.)

When the patient is healthy, the amount of creatinine excreted is equal to the amount produced (which depends on the person's muscle mass). As creatinine is excreted by filtration without reabsorption or significant secretion, the amount excreted is equal to the amount filtered (Equation 1).

$$\begin{aligned} \text{Amount produced} &= \text{amount excreted} = \text{amount filtered,} \\ &= \text{GFR} \times \text{plasma creatinine.} \end{aligned} \quad (1)$$

If the GFR falls, the amount filtered will fall resulting in less excretion. This will increase the plasma concentration. As the plasma concentration increases, the filtered amount will increase thus excretion will increase. Eventually, the amount excreted will be equal to the amount produced, and the plasma concentration will be steady at a higher value. In this new steady state, input (production of creatinine in this case) will be equal to the output (urinary excretion).

In the steady state if there is a transient increase in input (e.g. sudden increase in potassium intake), the plasma concentration and the

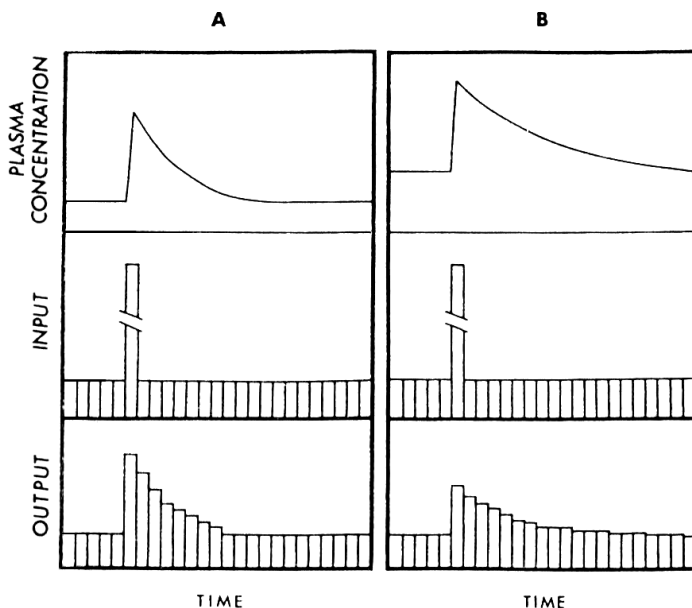


Figure 1.5 Changes in plasma concentration, input and output with time of potassium following a transient increase in input, (a) in the normal steady state and (b) in an abnormal steady state; chronic renal failure with reduced glomerular filtration rate.

excretion will increase until the load is excreted and the plasma concentration will come back to the previous level (Figure 1.5a). If the steady state is an abnormal one (like the patient with chronic renal failure described above), the increase in plasma concentration will be greater and it will take a longer time before the steady state is re-established (Figure 1.5b).

The following general principles will be of help in the understanding of changes in plasma concentration:

1. A change in plasma concentration of a substance is the result of either a change in input rate (production or intake) or due to a change in the output rate (metabolism or excretion).
2. When the steady state is disturbed, plasma concentration and output will change until input and output are equal — a new steady state.

3. In the steady state, irrespective of weather, this is a normal or abnormal state, input and output are equal.
4. A transient increase in input when the steady state is abnormal will be handled at a different rate than when the steady state is normal.

Concentration vs. Amount

Most clinical biochemistry investigations are done in plasma or serum and what is measured is the concentration. A change in concentration of an analyte can be due to a change in the amount of substance in plasma or due to a change in the volume of fluid. It is a common mistake to assume that when the plasma sodium concentration is low, the amount of sodium in the body is low. However, very often a low plasma sodium concentration is due to an increase in water content.

Concentration vs. Activity

In many circumstances, we measure the total concentration of a substance in serum or plasma. However, the substance may be partly bound to proteins, and very often, it is the unbound or free analyte which is the physiologically important fraction. For example, calcium in serum is bound to proteins (mainly albumin) and the physiologically active form is ionised calcium. The total concentration however, may change due to changes in the binding protein concentration, e.g. in pregnancy, the concentration of binding protein for thyroxine increases due to increased synthesis and this will cause the total thyroxine concentration to be high with normal free thyroxine concentration. Therefore, in interpreting the total concentration of an analyte, it is important to bear in mind that the total concentration may change without a change in the active fraction.

Urinary Excretion

When the excretion or concentration of a substance is measured in the urine, it is important to remember that there is no reference range. This is particularly true for urine electrolytes, urea and

osmolality. The concentration of electrolytes in serum is highly regulated such that, if there is a change in serum concentration, homeostatic mechanism(s) will return the serum concentration back to the original value. Urinary excretion, on the other hand, is a method of regulating plasma concentration. Therefore, one cannot determine a reference value for it. In the steady state, urinary excretion is a reflection of input. In the case of electrolytes, it is a reflection of intake. For example, a urinary excretion of 100 mmol/d of sodium implies that the person is taking 100 mmol per day of sodium. On the other hand, if we know that the person is taking 50 mmol of sodium per day, a urinary excretion of 100 mmol/d of sodium tell us that he is losing sodium through his kidneys. Interpretation of urinary values should be done in relation to the input (intake) and/or in relation to the clinical state. For example, if a person is volume depleted (extracellular volume is low), the body's response is to increase sodium reabsorption and the urinary exertion should be very low (usually < 20 mmol/L or d). Any value higher than this implies that the person is losing sodium through his kidneys.

Further Reading

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Summary/Key Points

1. Biochemical tests are useful in the diagnosis, monitoring, screening and prognosis of disease. Most biochemical tests are done for monitoring treatment or to detect complications of treatment. Biochemical screening of healthy subjects are of little value except in a few well-defined situations.

2. A test result can vary due to biological and analytical variation. Analytical variation or imprecision is assessed by the standard deviation (or coefficient of variation).
3. When interpreting results, they are usually compared to a reference range, which encompasses 95% of values in a healthy population. For analytes such as serum cholesterol and serum 25-hydroxyvitamin D concentration, this approach is not valid and risk-based value is used to compare results.
4. A test result within the reference range does not necessarily imply that there is no disease and a test result outside the reference range does not indicate disease.
5. Tests results can vary due to many physiological factors such as age, gender, ethnicity, time of day, body size, etc.
6. Even when these physiological factors are controlled, there is intrinsic variation within an individual. This intraindividual variation is large for some analytes (e.g. iron, cortisol) and low for others (e.g. sodium, calcium and thyroxine).
7. For an analyte with low within person biological variation, a change within the reference range is potentially clinically significant.
8. The diagnostic value of a test is described by sensitivity (percentage of positive results in a group with the disease) and specificity (percentage of negative results in a group without the disease). The predictive value of a test is influenced by the prevalence of the disease in the population. For a disease with low prevalence, even a test, which is highly specific and sensitive, will give a large number of false positives.
9. The value of two tests can be compared using the receiver operating characteristic curves (ROC) in which specificity is plotted against sensitivity.