JULY, 1980

ISSN 0028-8349

THE NEW ZEALAND JOURNAL OF

medical laboratory technology

An Official Publication of the New Zealand Institute of Medical Laboratory Technology Incorporated

VOLUME 34, No. 2

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The New Zealand Journal of Medical Laboratory Technology

Volume 34, No. 2 JULY, 1980

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Subscription to the JOURNAL for non-members is SIX DOLLARS per year or TWO DOLLARS FIFTY CENTS per single issue, postage paid. Overseas subscription rates on application.

Intending contributors should submit their material to the Editor, Diagnostic Laboratories, Dunedin Hospital. Acceptance is at the discretion of the Editor, and no undertaking is given that any article will be published in a particular issue. The copy deadline for each issue is the first of the month prior to the month of publication.

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An Unusual Case of Hb-H Disease

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Received for Publication, October 1979

Summary

A brief resume of the thalassaemias is presented followed by a case report of an unusual case of Hb-H disease caused by the combination of a 2-α-thalassaemia with a heterozygous 1-α-thalassaemia/β-thalassaemia. The latter combination being unsuspected and originally diagnosed as a β-thalassaemia minor.

Introduction

The thalassaemias are a group of haemoglobinopathies resulting from a genetic defect causing a decreased production of normal α, β or δ polypeptide chains which comprise normal adult haemoglobin. Hb-H disease was the first type of α-thalassaemia to be recognised, Rigas *et al* (1955)[3] and the highest incidence of this disease occurs in South East Asia, Wasi *et al* (1969).[4]

The α-thalassaemias can be divided into two basic types depending on the number of α genes deleted. 1-α-thalassaemia is caused by the deletion of a single gene resulting in only a mild reduction in the total number of α-chains produced and is usually haematologically silent. 2-α-thalassaemia is the result of two genes being deleted causing a moderate reduction in the number of α-chains produced. This leads to the typical blood picture of an α-thalassaemia trait with an erythrocytosis; reduced Mean Cell Volume (MCV) and Mean Cell Haemoglobin (MCH). These two types can combine genetically to form two further clinical entities.

Firstly, if 1-α-thalassaemia combines with another, a total of four genes are deleted which allows no α-chains to be produced. As α-chains are utilised in all normal haemoglobins this state is not compatible with life. This is classical "Hydrops fetalis" in which the child is stillborn and whose haemoglobin consists almost entirely of Hb-Barts. Hb-Barts is the tetramer of α chains and is useless as a transporter of oxygen.

Secondly by combining a 1-α-thalassaemia with a 2-α-thalassaemia only three genes are deleted, allowing sufficient α chain production to maintain life. This is the main cause of Hb-H disease. It may also be caused by the combination of a 2-α-thalassaemia with a Hb-Constant-Spring (which is an elongated chain and behaves in the manner of a 1-α-thalassaemia gene) and in some cases of erythroleukaemia and other myeloproliferative diseases.

The β-thalassaemias are an equally complex group and the most commonly encountered form is β-thalassaemia minor with the typical blood picture of an erythrocytosis, low MCV, MCH and targetting.

The haemoglobinopathies can interact with each other with varying effects. Those involving the same globin chain interact to increase the clinical severity of the disease. However, defects involving the combination of different globin chains often produce a less severe effect than would be anticipated. In the thalassaemias the main pathophysiology of the disease is the deposition of the excess polypeptide chains on the membrane of the red cell, leading to cell rigidity, damage and consequent shortening of the cell life. Zaino *et al* (1974).[5]

Methods

Routine haematological studies were performed with the Coulter Model S. Haemoglobin electrophoresis was performed on cellulose acetate at pH 9.2. Hb-A2 levels were determined by the method of Marengo-Rowe.[2]

Case Report

The mother of the propositus (Indonesian Asiatic) presented for a routine antenatal blood check. Because of the results obtained (Table I) blood film appearances (including microcytosis, target cells and anisochromia) and racial origin, the possibility of a haemoglobinopathy was raised. Haemoglobin electrophoresis was carried out and the Hb-A2 level was found to be raised to 4.1% (normal 1.8%-3.2%). Serum Fe and TIBC were normal. These tests were repeated at six weeks interval and the results remained unchanged. A diagnosis of β-thalassaemia minor was made and it was arranged to obtain a cord blood sample at delivery.

This was duly received after a normal full-term birth. All parameters were reduced (Table I) and the blood film was extremely bizarre (Figure 1) with marked poikilocytosis, targetting and erythroblasts present. Electrophoresis on cellulose acetate was performed and two fast-moving com-

Figure 1

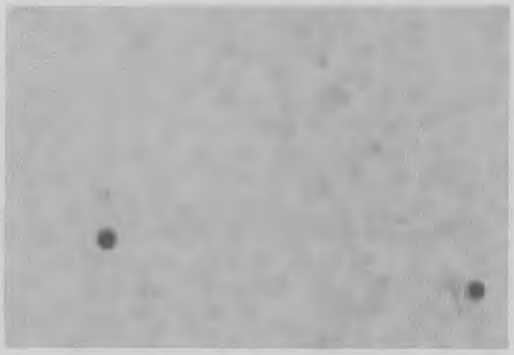

Figure 2

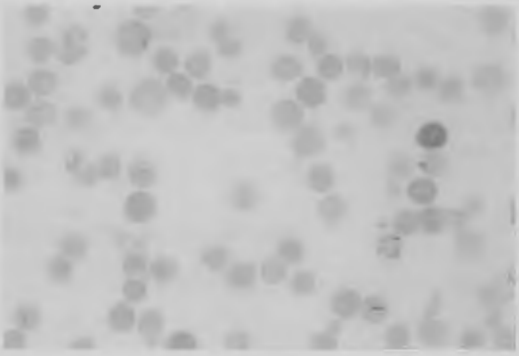

Table I

Patient	HAEMOGLOBIN Gm/litre	ERYTHROCYTES x 10^{-12}	MCV fl	MCH $\mu\mu$gm	MCHC gm/litre	Hb-A2	Hb-F	Comments
Mother 24.5.78	125	4.8	75	26	346	4.1%	1.0%	
Mother 16.10.78	140	5.3	81	27	332	3.9%	0.9%	
Father 18.10.78	130	6.5	64	20	322	1.0%	0.5%	
Baby Cord Blood	120	5.0	84	24	289	18% Hb-Barts		Extremely bizarre red cell morphology
Baby Age-6 days	84	4.0	70	21	299			
Baby Age-6 months	91	5.3	59	17	290			80% cells contain Hb-H inclusions

ponents were seen. These proved to be Hb-Barts and a lesser amount of Hb-H. The amount of Hb-Barts present was 18%. Incubated reticulocyte preparations showed the classical Hb-H inclusions (golf-ball cells). In a large series, Wasi *et al*[4] found that patients with more than 20% Hb-Barts at birth had three α genes deleted and developed Hb-H disease later. On these findings a tentative diagnosis of Hb-H disease was made.

A sample of blood was obtained from the father and the results (Table I) indicated that he was a 2-α-thalassaemia. The blood film confirmed this with microcytosis, and targetting of the red cells.

Mother and child were discharged six days after delivery and the child was considered to be quite healthy although the haemoglobin was only 84 g/litre (Table I). When they returned one month later for follow-up a further sample was obtained from the mother. The parameters had become normal (Table I) and the blood picture was unremarkable except for some targetting. The Hb-A2 level however remained increased. It was therefore proposed that she was a double heterozygote 1-α-thal/β-thal.

The child's haemoglobin remained stable but now exhibited far more Hb-H inclusions and approximately 80% of the erythrocytes now contained inclusions (Figure 2). No splenomegaly (a feature of ± 80% of Hb-H disease patients) is present at this stage and the child is progressing well.

Discussion

Hb-H disease is frequently caused by the genetic combination of a 1-α-thalassaemia with a 2-α-thalassaemia resulting in a deletion of three α genes. This case is complicated by the fact that the mother is a heterozygote 1-α-thalassaemia/β-thalassaemia with a raised Hb-A2 level but with a normal blood film and blood parameters. This illustrates the combination of two haemoglobinopathies ameliorating each other's ill-effects. If the mother was a 2-α-thalassaemia than a total of four α genes would be deleted resulting in Hydrops fetalis.

In 1972 Knox-Macauley *et al*[1] reviewed a Cypriot family with the same genetic pattern. In this family with four children, one had Hb-H disease, one had β-thalassaemia minor, one was a double heterozygous 2-α-thalassaemia/β-thalassaemia and one child was unaffected.

In conclusion the family presented here illustrates the complex combinations that can be obtained not only in the thalassaemias but in all the haemoglobinopathies.

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The Thalassaemias

Vicki Grant
Hamilton Medical Laboratory
Student Award, Essay Section, 1978

Introduction

The thalassaemias are a heterogeneous collection of inherited anaemias thought to have originated from the populations of the Mediterranean. It is now known that this condition is spread all over the world.

The anaemia is due to a combination of defective rate of haemoglobin synthesis and shortened red cell survival. Normal haemoglobin is not replaced by abnormal haemoglobin but its formation is suppressed due to a disturbance of one of the polypeptide chains. The degree of anaemia is relative to the type and nature of the inherited trait.

The Haemoglobin Molecule

Each haem group of the haemoglobin molecule is enfolded in one of four chains of amino acid units that collectively form the protein part of the molecule called globin. Four chains of globin consist of two identical pairs of peptide chains (see Figure 1).

Human haemoglobin consists of several structurally distinct fractions at all stages of development. The main haemoglobin component in intrauterine life is Haemoglobin F ($\alpha_2\gamma_2$). Foetal haemoglobin contains a chain known as Gamma. Synthesis of Hb F ceases at about term but small amounts 2.3% are detectable in normal infants and after the first year of life, only less than 1% is detectable.

In adult life two forms of haemoglobin exist. The major component Haemoglobin A_1, (α_2 β_2) contains a beta chain, very similar to the gamma chain found in foetal Hb. The minor component, Haemoglobin A_2 (α_2 δ_2) contains delta chains and totals only 2.5% of the total haemoglobin in circulation.

NB. All fractions contain α chains.

Control of Haemoglobin Synthesis

A mechanism must exist whereby gamma chain synthesis is turned off shortly after birth and beta

Figure 1.—Haemoglobin chains in the infant and adult.

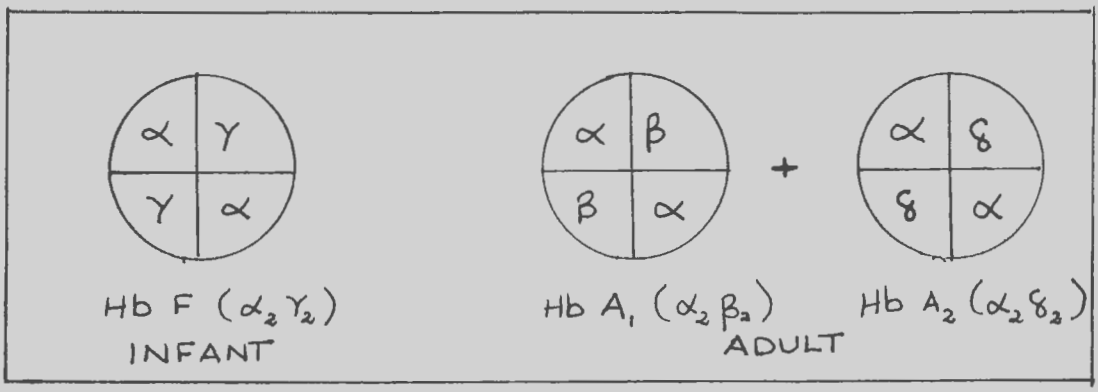
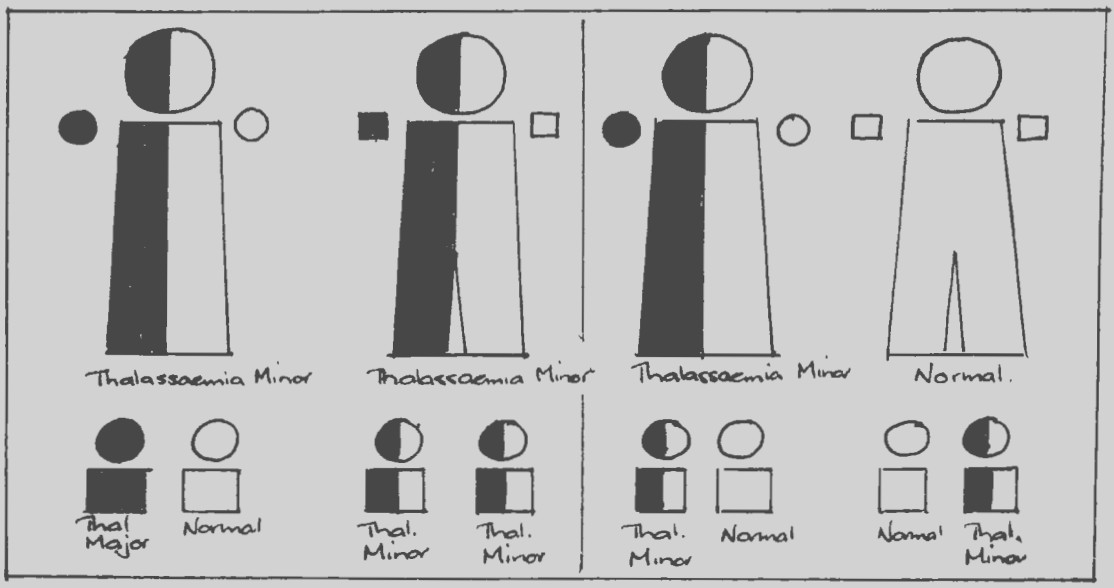


Figure 2.—Illustration of the inheritance of Beta Thalassaemia.



and delta chain synthesis fully activated to give rise to the production of adult haemoglobin.

At each stage alpha chain synthesis must be so synchronised with the synthesis of other globin units, such that there is no great excess of these units, for example such a mechanism must maintain gamma chain synthesis for the rate of beta chain synthesis to result in an Hb A_2 level of 2.5% of the total haemoglobin.

In thalassaemia the rate of production of normal globin chains is reduced due to primary defect in the mechanism which controls the rate of globin synthesis. Since the alpha and beta chains of haemoglobin are synthesised independently and are under separate genetic control, inherited abnormalities of haemoglobin synthesis can either involve the alpha or beta chain loci. Hence there are two groups of thalassaemias, one affecting the rate of synthesis of alpha chains, α thalassaemia and the other affecting the rate of synthesis of beta chains, β thalassaemia.

The precise molecular abnormalities of thalassaemias and the mechanisms responsible for the haemoglobin switches have yet to be properly elucidated.

β Thalassaemia

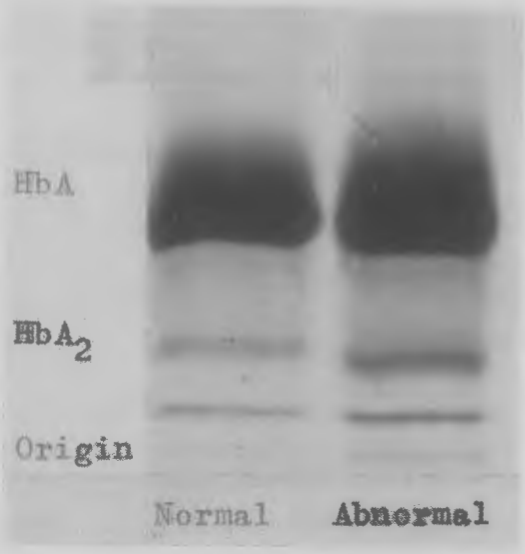
The most common type of thalassaemia is beta thalassaemia which results in an excess of alpha peptide chain formation due to the reduction of beta chain production. The free unstable alpha chains may precipitate out within the red cell and the attachment of this denatured globin to the red cell may cause it considerable damage resulting in a haemolytic anaemia.

This syndrome is characterised by the persistence of foetal haemoglobin beyond the neonatal period accompanied by the shortage of adult haemoglobin-Hb A_1 (α_2 β_2). It is thought that delta and gamma chains are produced in an attempt to compensate for the deficient beta chains, hence the elevation of Hb A_2 and Hb F.

An infant, in its early months is unaffected as most of its haemoglobin is Hb F. It is not until adult haemoglobin synthesis is activated that the anaemia may become apparent due to a combination of reduced haemoglobin production and shortened red cell survival. Faulty production of Hb A_1 component results from the primary deficiency of beta chains, delta and gamma chain synthesis occur to a variable extent but the overall production is insufficient to compensate for the deficiency in beta chains. The deficiency in globin production results in a secondary accumulation of haem that cannot be utilised. In normal cells excess haem stimulates globin synthesis and thereby removes itself by its incorporation into haemoglobin. If globin production is depressed, as in thalassaemia, then the haem that accumulates will eventually inhibit further haem production by a feedback mechanism. The overall effect is a depression of the haem synthetic pathway.

Cells that contain relatively large amounts of Hb A_2 and Hb F will survive longer. Cells poor in Hb A_2 or Hb F contain large amounts of alpha chains causing a precipitate and are rapidly removed from circulation by the spleen or destroyed in the marrow. Thin abnormally shaped cells of thalassaemia have a shortened life span and the resulting chronic haemolysis gives rise to a compensatory over activity of the bone marrow. Many newly produced cells are destroyed even before entering peripheral circulation. Because of the increased volume of bone marrow activity the total number of red cells entering the circulation is still considerable. The resulting degree of anaemia is dependent upon the equilibrium established between increased production and increased destruction of the red cells. Any depression of marrow activity would disturb the delicately balanced state, especially when the body is faced with additional demands as in pregnancy or infection.

Figure 3.—Haemoglobin electrophoresis on cellulose acetate strips. The HbA_2 is increased compared with normal.



β Thalassaemia Major

Two similar conditions of β thalassaemia exist which vary in severity. The major disability is found in the homozygous state, that is, two genes the same (see Figure 2). The clinical picture is severe and major life expectancy is 15-20 years.

The haemoglobin level is very seldom above 70g per litre and unless kept alive by constant transfusions anyone afflicted with β thalassaemia major can be expected to die in childhood.

Serum iron is increased provided no secondary iron deficiency is present. Chronic increase in marrow activity and multiple transfusions result in an over-absorption of iron and the marrow may characteristically show excessive iron deposits. Iron chelating agents are used in therapy to counteract the iron overload and to give satisfactory management of the patient. Due largely to multiple transfusions, the cause of death in thalassaemia major is very often heart failure caused by the build-up of iron in the tissue of cardiac muscle.

Children suffering from this disorder need constant attention because in order to survive they need multiple transfusions and infections must be vigorously treated.

NB. For a child to have thalassaemia major both parents must be diagnosed as having thalassaemia minor.

β Thalassaemia Minor

β Thalassaemia minor appears to be the most frequent form of thalassaemia and is spread all over the world. The gene responsible for this abnormality is inherited as a single trait hence the resulting anaemia is very mild causing little or no disability.

The haemoglobin level is generally between 100 and 120 g/l. However, β thalassaemia minor may develop as a severe anaemia when found in association with malnutrition, parasitic infestations, chronic infections and pregnancy. The disorder is commonly not diagnosed until adolescence or adult life and may be first diagnosed when another member of the family is found to have the disorder, during pregnancy, or, as a routine check.

The primary requirement for the diagnosis of β thalassaemia minor is the exclusion of iron deficiency as the resulting anaemia of each disorder is much the same. Cases of beta thalassaemia minor tend to have a higher red cell count; a lower mean corpuscular haemoglobin concentration index than one might expect in an iron deficient patient with an equivalent haemoglobin level. It would be unwise to make a diagnosis solely on the indices given by an electronic blood counting machine.

A good diagnostic feature of β thalassaemia minor is an increased percentage of Hb A_2 of the total circulating haemoglobin arising from the depressed production of Hb A. The normal level of Hb A_2 is usually in the range of 2.5-3%. In contrast, in β thalassaemia minor the Hb A_2 level may be as high as 6.7%. An exact and visual quantitation of the Hb A_2 level can be performed by elution from cellulose acetate strips.

If Hb A production is depressed, then Hb A_2 production is related to the effectiveness of compensatory Hb F production. If there is a fall in Hb A production and *no* increase in Hb F production then there is relatively high increase in Hb A_2 production.

NB. About half of the reported cases of thalassaemia minor have raised level of Hb F in the range of 2.5%.

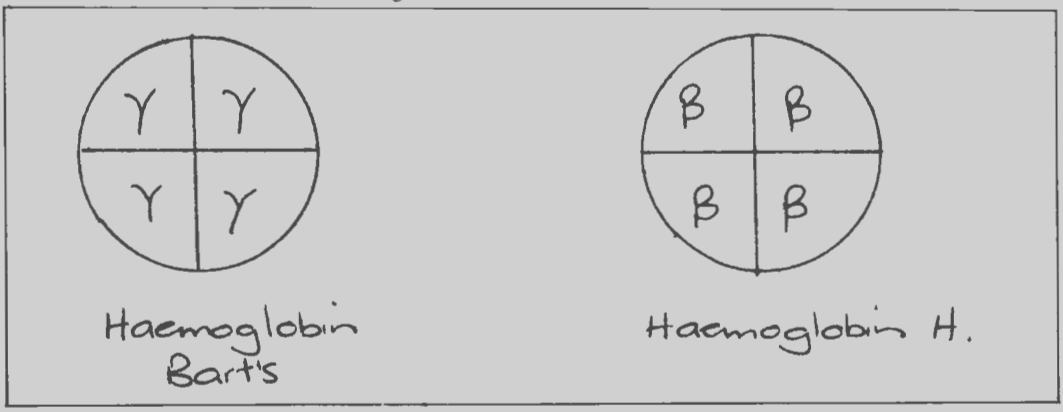
In cases of β thalassaemia minor iron deficiency may develop where the level of Hb A_2 falls. If treated with iron the level of Hb A_2 will rise above the normal range and the diagnosis of β thalassaemia minor can be established.

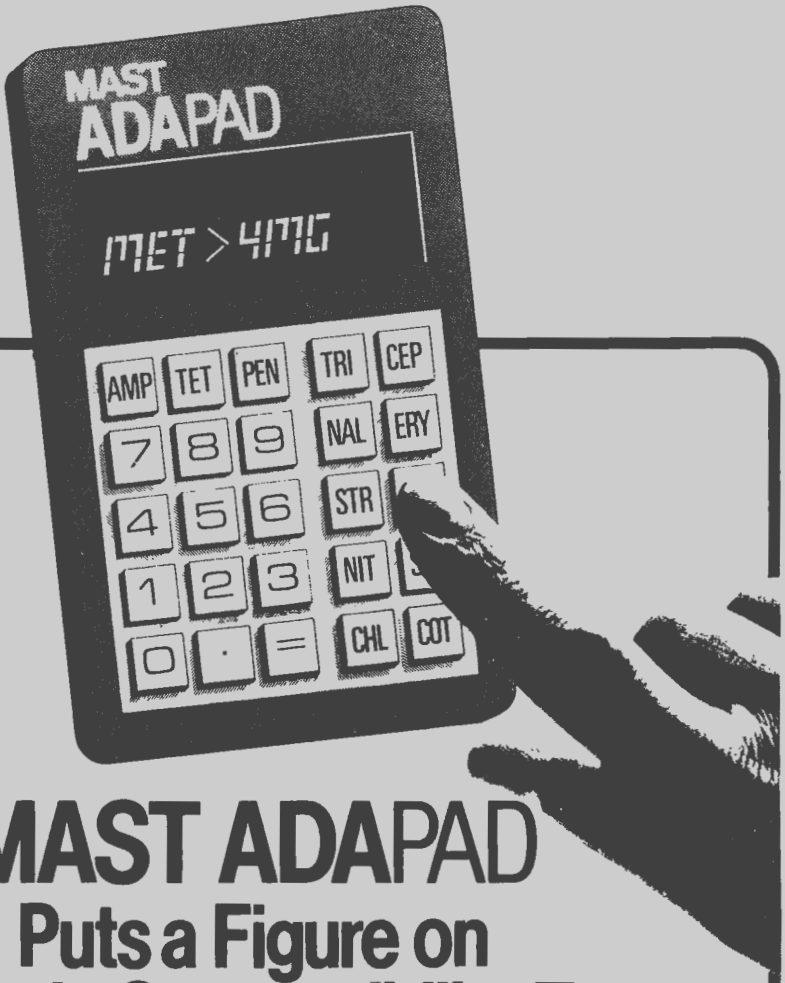
The treatment of β thalassaemia minor consists of treating secondary stresses such as infection and supporting the increased red cell production, especially during pregnancy, with small doses of folic acid and a good protein diet. Blood transfusions should only be given when absolutely necessary. Transfusion is only used to maintain haemoglobin at a comfortable level; most patients do not require transfusion until haemoglobin level drops below 70-80 g/l when disabling symptoms may occur. Iron therapy should be avoided and only used if serum iron level is low.

α Thalassaemia

The alpha thalassaemia syndrome results from a reduced rate of synthesis of the alpha globin chain of the haemoglobin molecule. Overall there is a depression of the production of Hb A_1, A_2 and F as they all contain alpha chains. This condition presents varying degrees of severity. Two varieties are of clinical importance and are

Figure 4.—The unstable tetramers.





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characterised by the formation of unstable tetramers (see Figure 4).

Alpha chains play an important part in securing the stability of a haemoglobin molecule.

Normal foetal haemoglobin ($\alpha_2 \gamma_2$) has a greater affinity for oxygen than normal adult haemoglobin and its predominance in the foetus may be regarded as an adaptation to intrauterine life. If there are insufficient alpha chains to pair with the gamma chains as in alpha thalassaemia, then those gamma chains are liable to form unstable tetramers (γ_4) or Haemoglobin Bart's.

If alpha chain production is totally suppressed then the foetus will be delivered stillborn since the predominant haemoglobin, Hb Bart's cannot effectively release oxygen to the tissue owing to its increased oxygen affinity. This condition represents the homozzgous state for the alpha thalassaemia gene and its known as Haemoglobin Bart's Hydrops Foetalis Syndrome.

Where the newborn is producing some adult haemoglobin, then competition arises for the available alpha chains. Beta units have a much greater attraction for alpha chains than delta and gamma units. Therefore, the few beta units being produced will be fully saturated with alpha chains and the gamma chains will form tetramers$_1$ Hb Bart's. It follows that when there is a shortage of alpha chains Hb F would disappear earlier in life than usual and that Hb A_2 will be decreased. In the older child and adult we see the formation of the tetramer Hb H (β_4) which may total as much as 5-20% of the total haemoglobin in circulation. This condition is known as Haemoglobin H disease and demonstrates a moderately severe anaemia. It is because of the inherent instability of Hb H that inclusion bodies consisting of denatured haemoglobin develop easily within the red cell causing a haemolytic process to occur.

Haemoglobin H disease is relatively uncommon but not rare and the afflicted patient may well have a permanent slight anaemia depicted by Hb level in the region of 100 g/l, easily aggravated by infection or pregnancy. A case of Haemoglobin H disease should remain under medical supervision and be treated in much the same way as β thalassaemia minor. Folic acid therapy is essential in pregnancy and beneficial as a permanent measure.

Alpha-thalassaemia trait may be suspected if the blood count depicts a raised erythrocyte count, low mean corpuscular volume and low mean corpuscular haemoglobin concentration. Again, as in beta thalassaemia iron deficiency must be excluded before the diagnosis of the alpha thalassaemia trait can be made. Confirmation of diagnosis may be provided by finding a positive Hb H preparation. This test depends upon the ability of the redox dye Brilliant Cresyl Blue to cause the precipitation of Hb H to produce inclusion bodies. Visual examination of the preparation is carried out under the oil immersion objective.

The two alpha thalassaemia traits described on the previous page are indeed severe, Haemoglobin Bart's Hydrops Foetalis is lethal representing the homozygous state; haemoglobin H is a much less severe anaemia representing the heterozygous state. Additional traits exist whereby the infant born has a Hb Bart's level in the range of 1-5%. The abnormality is hardly detectable as the patient may show a normal or very slightly anaemia blood picture. Haemoglobin H bodies will only be demonstrated in the occasional red cell after staining. Difficulty in the diagnosis of alpha thalassaemia arises, not only because the condition is symptomless but it is also difficult to recognise haematologically.

The Geographical Distribution of the Thalassaemias

The thalassaemias are a heterogeneous collection of inherited anaemias widely distributed throughout the sub-tropical regions of the world with pockets of high incidence in the Mediterranean countries, the Middle East and South East Asia. It is very difficult to survey the incidence of the thalassaemia gene as the number of reported cases probably is very distant from the number of actual cases.

Technical difficulties arise, especially in the case of alpha thalassaemia, where the carrier state in the adult is either totally or virtually undetectable. Another problem arises because of gene flow resulting from migration between different populations e.g. owing largely to migration (1) there is a significant gene pool of thalassaemia in Australia constituting a significant health problem. Approximately 7% of the people of Greek origin and 5% of the people of Italian origin are heterozygotes for beta thalassaemia. There are now 1,500,000 people in Australia of Greek or Italian origin. Factors that aid in the dispersal of the gene is a tendency for intermarriage, relatively small and concentrated populations and the better diagnosis and treatment of the patient (1976).[1]

Some reports are misleading. In the Caribbean the incidence of thalassaemia was based on its observations in Chinese families only. In China,

beta thalassaemia has been found only in the Cantonese.

Beta thalassaemia is the most widespread abnormality of the haemoglobin production and has been discovered in virtually every population (see Figure 5). It has a high incidence in all areas of the Mediterranean where the observations of this anaemia were first made. Hence beta thalassaemia is also known as the Classical Mediterraenan Anaemia.

Beta thalassaemia is found in Portugal, Spain, Syria, Persia and the Middle East, Afghanistan, Pakistan, India, China, Thailand, Burma, Malaysia, Italy, Greece, the Philippines, New Guinea, Ceylon and Indo-China.

The map below is based on the findings of beta thalassaemia in an appreciable number of native families. It is arbitrary because after intense survey in Britain approximately 100 families have been discovered, yet Britain is not included. Other similar areas of incidence may also warrant inclusion.

Theories suggest that beta thalassaemia arose either in the Mediterranean populations and from there travelled throughout the rest of the world or from China with the Mongol invasion.

There is difficulty in detecting the carrier state of alpha thalassaemia in the adult as assessment of its frequency is limited to the following: the incidence of Hb H disease, the incidence of Bart's Hydrops Foetalis Syndrome, a raised level of Bart's (γ_4) in the cord blood and the presence of alpha thalassaemia interacting with other abnormal haemoglobins.

If we were to assess each separately over the same populations, the results for each would give an entirely different impression of alpha thalassaemia.

Cord blood surveys to detect raised levels of Hb Bart's have demonstrated alpha thalassaemia in Nigeria, Italy, Greece, Thailand, Hong Kong and in American Negroes.

Haemoglobin H disease was first reported in Greece, and has also been found in Italians, Oriental Jews, Indians, Indonesians, Burmese, Thais and Chinese. It has occasionally been found in Swedes, native British and American Negroes. It is remarkably rare in Africans.

Numerous cases of Haemoglobin Bart's Hydrops Foetalis have been described in South East Asia.

It is not possible at this stage to get an overall impression of the distribution of the gene amongst the populations of the world.

Figure 5.—Distribution of Beta Thalassaemia.

Summary

Fundamentally thalassaemia is an inability to produce adequate amounts of either alpha or beta polypeptide chains of normal adult haemoglobin resulting in an imbalanced polypeptide chain formation. In alpha thalassaemia excess beta and gamma chains combine together to form unstable tetramers β_4 (haemoglobin H) and γ_4 (Haemoglobin Bart's). In beta thalassaemia excess alpha chain formation causes free alpha chains to precipitate out in the red cell, resulting in a haemolytic anaemia.

The degree of anaemia is variable but largely dependent on the type and nature of the inherited trait. The overall effect of the anaemia is a depression in the haem synthetic pathway and shortened red cell survival compensated by increased marrow production. This creates an inevitable problem of iron overload and iron deposition in the tissues, which can be slightly reduced with therapy based on iron chelating agents. However, for the well-being of the patient the ill effects of the chronic anaemia are balanced against the hazard of iron overload by transfusion, but limited to the minimum compatible with survival.

The thalassaemia gene is of high incidence in the Mediterranean countries, the Middle East and South East Asia. The gene is dispersed throughout the world because of immigration, the tendency for intermarriage, relatively small and concentrated populations and the better diagnosis and treatment of the patient afflicted with thalassaemia.

There are still questions about thalassaemia that remain unexplained, particularly about the mechanisms that are responsible for the haemoglobin switches. The answer to this question may be of great therapeutic value as it is initially the imbalance of polypeptide chains that causes the anaemia of thalassaemia.

Acknowledgments

The illustration of the distribution of Beta Thalassaemia is taken from *Man's Haemoglobin* by Lehmann, H. and Huntsman, R. G. (1974).

The illustration of the inheritance of Beta Thalassaemia is taken from Thalassaemia, a preventive approach, Mathews, R. N. and Malice, J. (1976), *Medical Journal of Australia*, 2, 8.

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Chemotherapy of Primary Amoebic Meningo-encephalitis (PAM) II. Miconazole and R41,400 (Ketoconazole)

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From a paper read to the NZIMLT Conference Auckland, 1979

Summary

The effectiveness of the imidazole compounds miconazole and R41,400 (Ketoconazole) against *Naegleria fowleri* (MsT) and *N. gruberi* (P1 200f), was tested in vitro, in cell culture and also against *N. fowleri* (MsM) *in vivo* in mice. The results are presented and discussed in relation to recently used drug therapy against *Naegleria* infections.

Introduction

The imidazole group of drugs which includes clotrimazole, R41,400 and miconazole has been shown to be effective in the *in vitro* situation against a number of pathogenic and non-pathogenic strains of *Naegleria*, the causative agent of Primary Amoebic Meningo-encephalitis (PAM) (Anderson & Jamieson, 1972[1]; Jamieson, 1975[9]; Donald, *et al*, 1979[7]).

Miconazole is known already to have antifungal and trichomonicidal activity (Woutters, 1971[12]), and R41,400 is an experimental imidazole which has recently been renamed Ketoconazole. R41,400 differs from most other imidazoles in that it is

water soluble thus reducing the problems of dissolving the drug. This may also have important clinical implications in that solvents or vehicles needed to obtain stable pharmaceutical preparations are not needed (Dixon *et al,* 1978[6]).

In the present study, the *in vitro* effect of the two imidazoles was extended to cover *N. fowleri* (MsT) (pathogen) and *N. gruberi* (P1200f) (non-pathogen) and also the testing of these in cell culture. Miconazole was recently included in the treatment of a nine year old female in California (Seidel *et al,* 1978, pers. comm.) and since the particular role miconazole played in the survival of this case cannot be evaluated the *in vivo* testing of these drugs was included in the programme.

In vivo testing was carried out using *N. fowleri* (MsM) isolated by Cursons *et al,* (1979)[5] from the most recent New Zealand case of PAM. The effectiveness of the drugs to reach and maintain an effective level in the serum was evaluated.

Materials and Methods

AMOEBAE:

Naegleria gruberi (P1200f)—non-pathogen
Naegleria fowleri (MsT)—pathogen
Naegleria fowleri (MsM)—pathogen

N. gruberi (P1200f) and *N. fowleri* (MsT) and (MsM) were grown in CGHV medium (Cursons *et al,* 1979).[4]

DRUGS:

Miconazole was supplied by Ethnor Pty. Ltd. in intravenous (IV) solution containing 10mg.cm^{-3}.

R41,400 was supplied by Ethnor Pty. Ltd. as a dry powder base and 0.02gm was dissolved in 0.8cm^3 0.1N HCl and made up to 10cm^3 in distilled H_2O.

Both drugs were then diluted further in sterile distilled water to the final concentrations.

IN VITRO:

In vitro studies of the survival of the two amoeba strains in both R41,400 and Miconazole were carried out in 6cm^3 bijou bottles in a total volume of 2.0cm^3.

Stock cultures of amoebae were counted in a haemocytometer so that 0.2cm^3 gave a final concentration of 2-3 $\times$ 10^5 amoebae.cm^{-3}.

The stock drug solutions were diluted so that 0.5cm^3 gave the appropriate final concentration and CGHV medium was then added to give a total volume of 2.0cm^3. All experiments were repeated at least three times in duplicate.

Samples were drawn at 24, 48, 72 and 96 hours and the surviving amoebae counted in a haemocytometer. Where amoeba levels were below 10^4.cm^{-3} an estimate of the number of viable amoeba was made using amoeba saline agar plates (Page, 1967[11]) seeded with *Enterobacter cloacae.* These were incubated for 48 hours (37°C for pathogens and 30°C for non-pathogens) and then examined for viable amoebae.

CELL CULTURE

Once a Vero cell monolayer had been established in Eagles Growth Medium (EGM) the medium was discarded and the monolayer washed with 1.0cm^3 sterile phosphate buffered saline (PBS) (ph 7.6). Eagles Maintenance Medium (EMM) was added to a final volume of 2.0cm^3 i.e. 1.3cm^3 of EMM + 0.5cm^3 of drug + 0.2cm^3 of amoebae.

The inoculum of amoebae was obtained from 24hr exponential axenic cultures of *N. fowleri* (MsT) (routinely passaged in cell culture), the amoebae were counted and diluted with EMM and then added to the cell culture to give final concentrations of 3 $\times$ 10^3.cm^{-3}. Drug solutions were diluted so that 0.5cm^3 gave the appropriate concentrations. Control tubes were included in all experiments with water or diluent replacing the drug.

The tubes were examined every 24 hrs for six days and the presence or absence of cytopathic effects (CPE) or cytotoxic effects (CTE) noted.

After six days the tubes were centrifuged at 1500 rpm for 10 minutes and then after resuspending in Page's amoeba saline (PAS), plated on PAS agar (Page, 1967[11]) and incubated at 37°C for 48 hours after which they were examined for viable amoebae.

IN VIVO (MOUSE PROTECTION):

Young male white mice (Massey Strain) were weighed and then anaesthetisd with 0.6mg Nembutal in a total volume of 0.1cm^3. They were then inoculated intranasally with a solution of *N. fowleri* (MsM) containing 1 $\times$ 10^5 amoebae.cm^{-3}.

The drug treatments were applied first once daily, then twice daily intraperitoneally (IP) and then later intraventricularly (IVent) (Haley *et al,* 1957[8]) at the dosages shown in Table I.

Each experimental batch included controls with, (a) drug and no amoeba, and (b) with amoebae and no drug, each group consisting of 5-10 mice.

Drug therapy was started immediately after inoculation with the amoebae (*N. fowleri* (MsM)) and continued daily (or twice daily) till death (Table I).

On death the brains was removed and death due to amoebae verified by plating the brain on PAS agar seeded with *E. cloaecae*. The plates were incubated at 37°C and examined for viable amoebae after 24 hours.

DRUG SERUM LEVELS:

The assay methods for both drugs were identical except that for R41,400 *Candida piropsilosis* was used, and for miconazole nitrate *C. pseudotropicalis* was used as the assay organism. The methods used were based on Jamieson *et al* (1976).[9] The assay organisms were chosen because they were inhibited by the drug used at levels $\leq 1\mu g.cm^{-3}$.

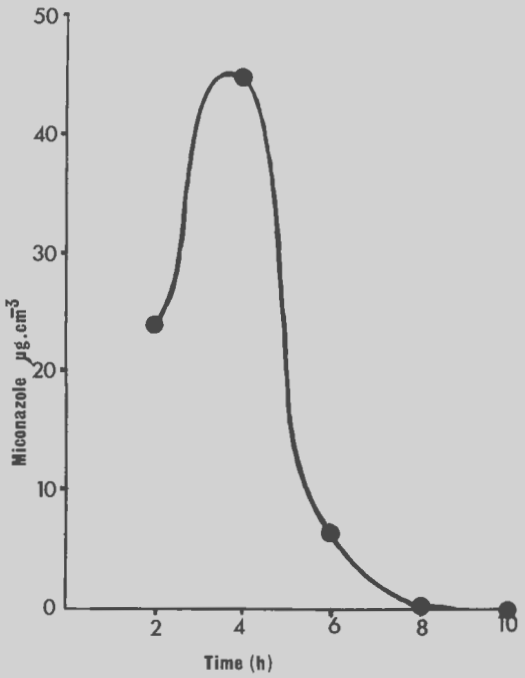
The drugs were administered to 15 mice at a concentration of $60mg.kg^{-1}$ IP, and after 0, 2, 4, 6 and 8 hour periods three mice were sacrificed and their blood pooled. The serum was obtained by placing the blood at 37°C for one hour and then at 5°C for one hour after which the sample was centrifuged at 3000 rpm for 10 minutes.

Dilutions of the drugs were made up in sterile horse serum to final concentrations of 0.5, 10, 25, 50, 75 and 100 $\mu g.cm^{-3}$.

Assay plates were prepared using sabouraud dextrose agar (pH 7.2) in 9cm glass petri dishes. These were spread with $0.5cm^3$ of a 1/50 dilution of the Candida culture grown overnight at 37°C.

Onto antibiotic assay discs (Whatman A. A. 13mm) was placed $0.1cm^3$ of the drug standards or pooled mouse sera at the stated times. The tests were done in duplicate and incubated overnight at 37°C, after which the zones of inhibition were measured using clippers fitted with a vernier scale. A standard curve was drawn from which could be read the concentration of drug present in the pooled mouse sera. Graphs showing the gradual breakdown of the drugs in the blood stream of the mouse were drawn and from then it was possible to ascertain the blood serum levels of the drugs at any time (Figures 1 and 2).

Figure 1.—Blood serum levels of miconazole in mice.



Results

(a) In vitro

(i) Miconazole

It was found that the non-pathogenic *N. gruberi* was susceptible to miconazole having a minimum inhibitory concentration (MIC) of $5\mu g.cm^{-3}$ and a minimum amoebicidal concentration (MAC) of $10\mu g.cm^{-3}$. The pathogenic *N. fowleri* (MsT) showed an initial period of growth followed by inhibition when $5\mu g.cm^{-3}$ was used but the concentration for total inhibition is closer to $10\mu g.cm^{-3}$ and the MAC is $50\mu g.cm^{-3}$. In both species a concentration of $100\mu g.cm^{-3}$ completely sterilised the medium in 48 hours (Figure 3 and 4).

(ii) R41,400

The pathogenic *N. fowleri* (MsT) appeared more susceptible to R41,400, having an MAC of $10\mu g.cm^{-3}$ as opposed to the non-pathogenic *N. gruberi* which was only inhibited by $10\mu g.cm^{-3}$. $50\mu g.cm^{-3}$ was amoebicidal for *N. gruberi* within 48 hours (Figure 5 and 6).

(b) Cell culture

When miconazole was added to the cell culture at the same time as the amoebae, the *N. fowleri* (MsT) was susceptible at $5\mu g.cm^{-3}$ but once a CPE had been established, $10\mu g.cm^{-3}$ was required to halt the progression of the CPE after which no viable amoebae could be recovered. Miconazole was found to be toxic to the Vero cells at a concentration of $5\mu g.cm^{-3}$.

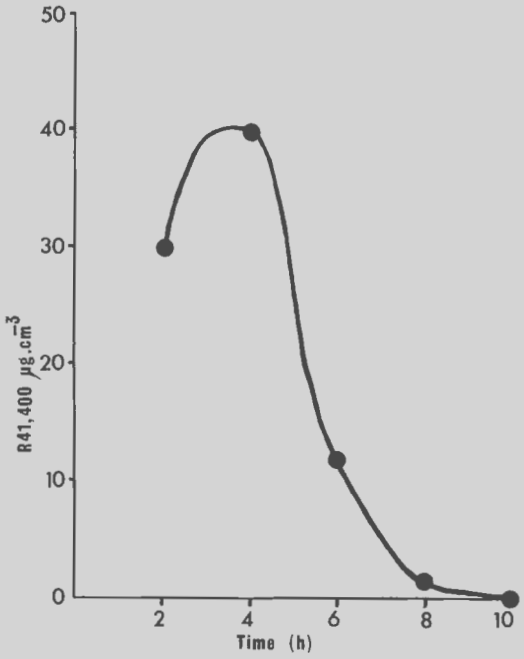
Using R41,400, a concentration of $5\mu g.cm^{-3}$ was inhibitory when added at the same time as the amoebae and also after CPE had been established. However, in both cases viable amoebae were still recoverable and it was only when a drug con-

centration of 10μg.cm^{-3} was used that no viable amoebae were found after a six day incubation period but R41,400 is toxic to the Vero cells at a concentration of 10μg.cm^{-3}. The results of the *in vitro* and cell culture tests are summarised in Table II.

Table I.—Dosages of miconazole and R41,400 injected into mice.

Drug	Method of injection	Drug concentration in mg.kg^{-1}.day^{-1}					
Miconazole	IP	0	15	30	60	120	
	IVent	0	0.1	1.0	2.5		
R41,400	IP	0	5	10	20	60	80
	IVent	0	0.1	1.0	2.5		
	IP (twice daily)	0	5+5	10+10	20+20		

Figure 2.—Blood serum levels of R41,400 in mice.



(c) In vivo (mouse protection)

For both the drugs all the uninfected controls receiving either drug or PAS diluent survived. However, in all infected groups there were no survivors after seven days with the average time of death being 5-6 days, neither drug affording protection against the amoebae.

Figure 3.—The *in vitro* effect of miconazole on *Naegleria gruberi* (P1200f).

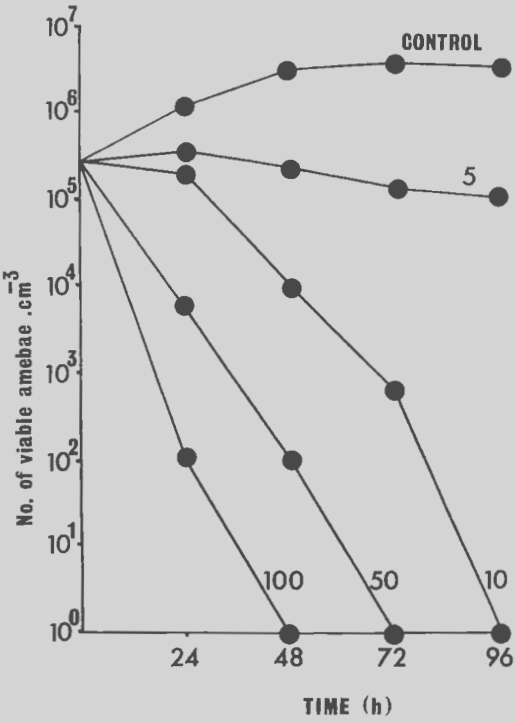


Table II.—Summary of *in vitro* and cell culture results with *N. fowleri* (MsT)

	MIC or MAC in μg.cm^{-3} Miconazole	R41,400
In vitro MAC	50	10
Cell culture		
(i) drug added at zero time MIC	1-5	5
MAC	5	10
(ii) drug added at three days		
MIC	5	5
MAC	10	10
Cytotoxic dose	5	10

MIC—lowest concentration of the test compound which produces obvious reduction in the number of trophozoites over 96 h.

MAC—lowest concentration after exposure to which no living trophozoites could be found after 96 h.

Figure 4.—The *in vitro* effect of miconazole on *Naegleria fowleri* (MsT).

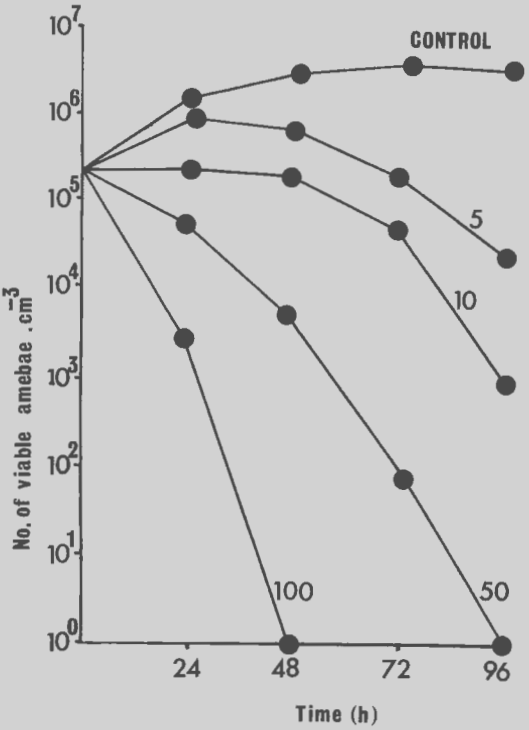
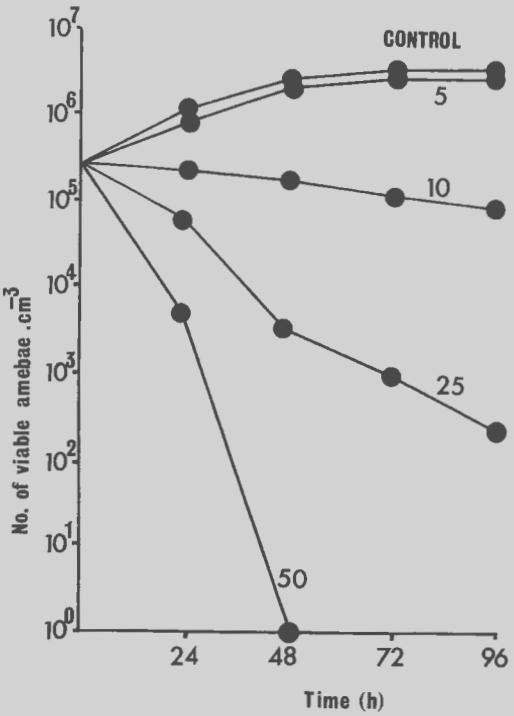


Figure 5.—The *in vitro* effect of R41,400 on *Naegleria gruberi* (P1200f).



Among those mice given IVent drug injections, the average time of death was also 5-6 days and in all dosage groups the time of death was equal to those groups which were inoculated with pathogenic *N. fowleri* (MsM) and given no drug treatment.

(d) Serum assay

The inhibition zone diameters for the standard drug concentrations were measured and a standard curve constructed. The areas of inhibition for each test serum (Figures 7 and 8) were measured and read off the standard curve to give a serum level. The peak serum level of R41,400 was 40μg.cm^{-3} whereas that for miconazole was 45μg.cm^{-3}. The serum level of miconazole decreased rapidly after six hours to 6μg.cm^{-3} and was undetectable after eight hours. R41,400 however, was still detectable at 2μg.cm^{-3} after eight hours (Figures 1 and 2).

Discussion

The *in vitro* studies confirm previous work with miconazole and *Naegleria* spp. The highest dose recommended for human infections is 3600mg.day^{-1} (approximately 54mg.kg^{-1}) given in three IV infusions. The role that this drug played in the survival of a recent Californian PAM case (Siedel *et al,* 1978, pers. comm.) is not clear. In this case miconazole was administered along with amphotericin B, which is currently the most effective drug for *Naegleria* infections (Carter, 1969[2]; Anderson and Jamieson, 1972[1]; Jamieson and Anderson, 1974[10]), and could have acted synergistically with the amphotericin B.

R41,400 is also seen to be effective *in vitro* and in cell culture against pathogenic *N. fowleri* strains. In the *in vivo* situation, however, it was not effective even when given twice daily which would have maintained blood serum levels of the drug at a level and for sufficient time to have equalled *in vitro* amoebicidal levels.

Further, the serum levels achieved in the mice in the first eight hours after injection should have been sufficiently high to inhibit amoebic multiplication. In the well vascularised area of the nasal mucosa, where amoeba are found three days after inoculation (Carter, 1970[3]) there would be

Figure 6.—The in vitro *effect of R41,400 on Naegleria fowleri* (MsT).

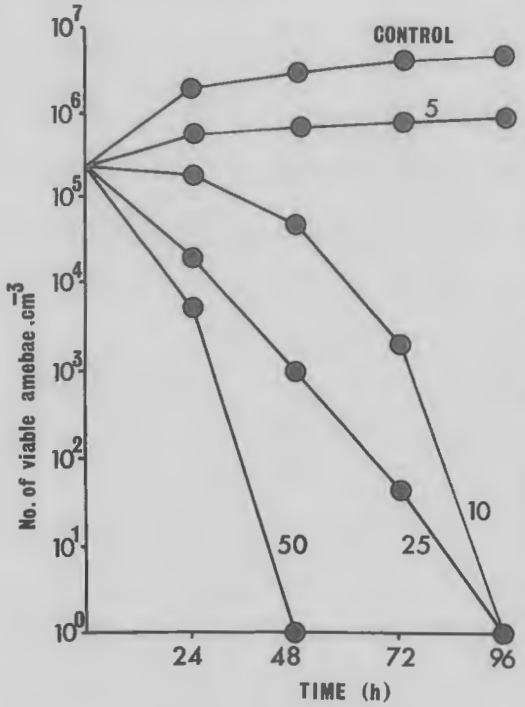


Figure 7.—Inhibition of *Candida piropsilosis* growth by serum samples containing R41,400. Figures indicate time in hours of sampling after initial IP inoculation of 60mg.kg⁻¹.

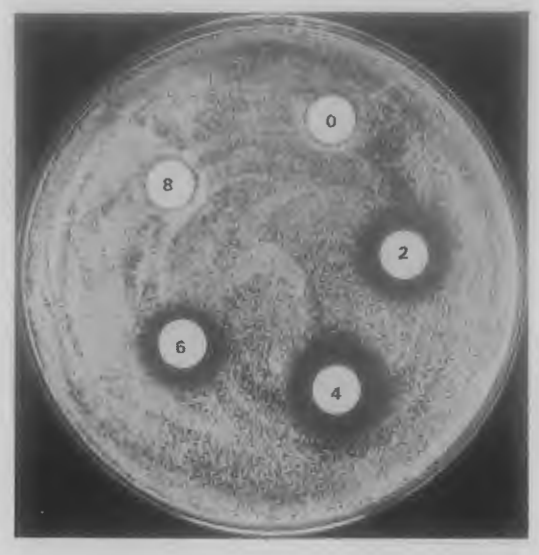
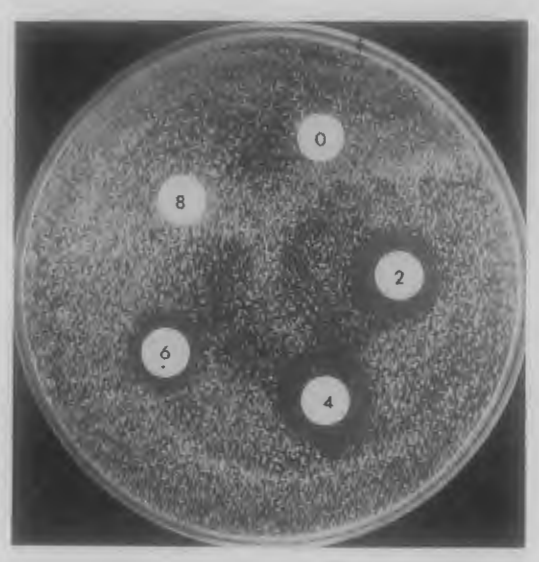


Figure 8.—Inhibition of *Candida pseudotropicalis* growth by serum samples containing miconazole. Figures indicate time in hours of sampling after initial IP inoculation of 60mg.kg⁻¹.



ample exposure of the amoebae to blood containing amoebicidal levels of either R41,400 or miconazole. This is especially so when twice daily doses are given. It is important to remember that patients would be unlikely to receive any treatment until at least 72 hours after infection, by which time the amoebae would have reached the meninges and the brain (Jamieson, 1975[9]).

Clotrimazole, another imidazole, also follows the above pattern. It was found to be effective *in vitro* against 18 strains of *N. fowleri* in doses ranging from 0.125 to 0.25μg.cm^{-3} (MAC). It was given to mice twice daily at doses each of 50mg.kg^{-1} and although the serum levels reached 6μg.cm^{-3} three hours after a single dose of 50mg.kg^{-1} it was still ineffective against infection by *N. fowleri* (Jamieson, 1975[9]).

Thus like clotrimazole, miconazole and R41,400 showed promise *in vitro* but they do not protect against amoebae *in vivo*.

Acknowledgments

We wish to thank Roche Products, Ethnor Pty. Ltd., the Medical Research Council and the New Zealand Health Department for financial support of this work.

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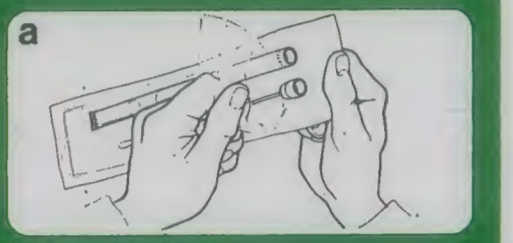
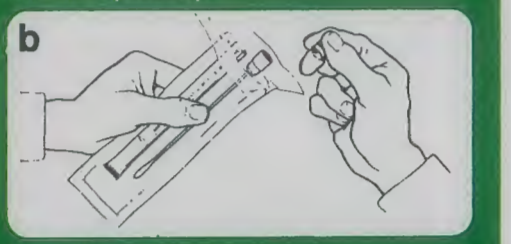
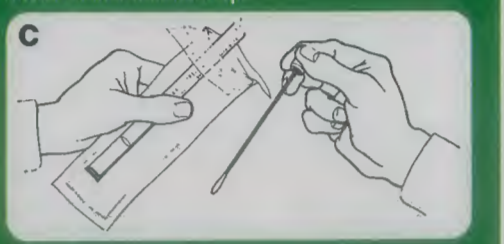


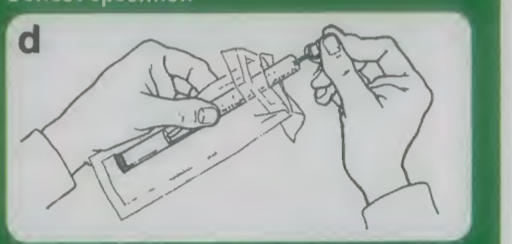
Peel to expose caps



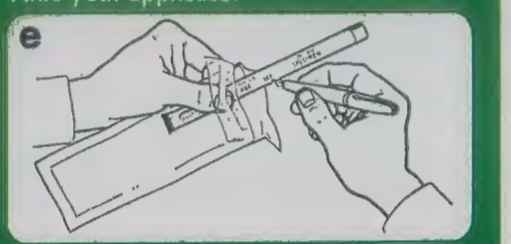
Discard transtube cap



Collect specimen



Tube your applicator



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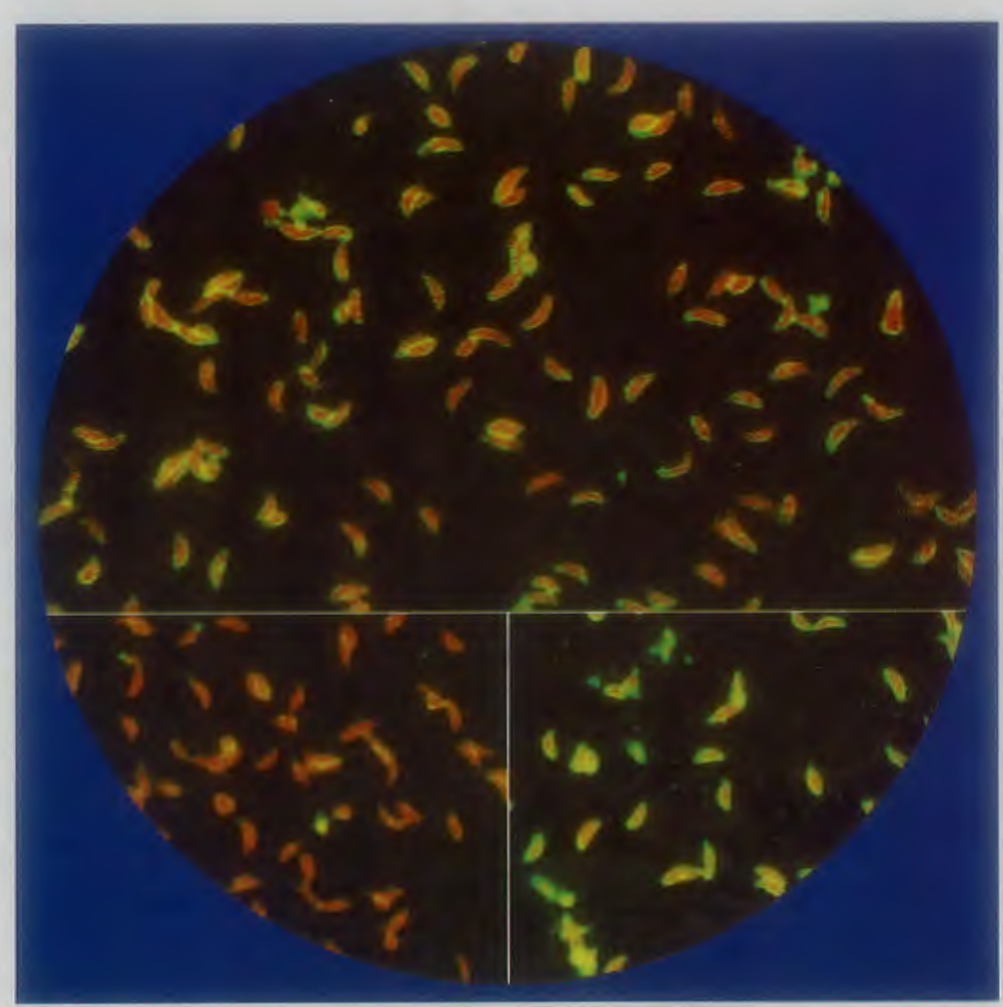

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Staff Selection: Intuition or Assessment?

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Received for Publication, May 1980

Introduction

The single most expensive item on the budget of any laboratory is its staff and successful selection and placement of the human resource is an essential function of effective laboratory administration. Turnover of staff is expensive both in terms of the time involved in procurement and induction and the time required for new employees to develop the skills necessary for adequate task performance. In any work situation there exists, in addition to the formal job related group structures an informal group structure arising in the first instance from simple geographical proximity and reinforced by the sharing of common interests (for example Squash, Bridge, Balinese Dancing), or friendship. Such groups exert powerful forces, both positive and negative, within the organisation. Likert (1974)[4] showed that highly effective groups, where roles were well established, were characterised by a strong loyalty to the members of the group which functioned in a supportive atmosphere, not aggravating conflict and focusing on a common goal. The influence of the informal group is ubiquitous, shaping perceptions and attitudes and ultimately determining productivity. All laboratories will have experienced the problems caused by introducing into this cohesive unit an individual who, for a variety of reasons, is unable to integrate into the existing power structure and remains either on the fringe or as a complete outsider. Unstable social groups, whether created by dissension within the group or by rapid staff flows, produce poorly and lower the overall morale. Such situations may be in part avoidable if a correlation can be found between the 'good' employee and the methods used in staff selection and induction.

Advertising

In the first instance recruitment for a post is usually as the result of an advertisement. Such advertising may be intended to reach the widest possible audience as in newspaper advertising, or it may be more selective as in specific journals and periodicals. By choosing the media and judiciously wording the advertisement a large degree of self-selection is possible. Information about the job, the employer and the minimum job specifications should be included although in the case of more complex posts an invitation to make further enquiries may be necessary. For trainee technologists the minimum specifications are fairly rigidly laid down while those for a technical assistant for example are much more flexible. Statistically selection is improved most by a larger number of people applying but the primary requirement of the advertisement is that while eliciting maximum response it also excludes unsuitable applicants. In our own laboratory it has been found over many years that ex-nurses prove to be particularly good technical assistants for specific posts, giving subsequent long tenure of service and showing a high degree of work motivation, and advertisements are worded with this in mind.

Relevant Data

Assuming then that the advertisement has weeded out the obviously unsuitable, details of applicants are now accumulated on a pre-prepared application blank. Information obtained should be basic, factual and pertain directly to the specifications for the particular job. It should include such details as previous work history, length of tenure, marital status, age and a resume of examinations passed together with the grades obtained. The individual who has held five positions in the last ten years may be a real 'whizz kid' but the chances are (s)he is still moving, as is the individual tied to a particular town until their partner completes university. In some circumstances such individuals may be exactly what is needed to perform a particular task but decisions should only be made after due consideration of all such information. Matters of health are only relevant if they affect the particular task, and if such information is immaterial it should not be sought. Lack of a sense of smell, extreme colour-blindness and defective hearing are all disabilities which may be considered important in the laboratory situation. A physical examination to provide baseline status may be required if the applicant is accepted but this is a separate issue. Questions pertaining to personality may be required for a salesperson but for laboratory staff they could not be considered directly applicable. Following recent legislation discrimination on the basis of race, creed, nationality, or religion is prohibited and information relating to any of these areas may not be sought either directly or by inference. If adequate research has been done to establish relationships between biological data and subsequent job success a weighted application form may be prepared. (See example Figure 1.) It is generally accepted that character references, by their very nature, are of little value as the applicant will undoubtedly selected referees biased in their favour. A check on previous work experience in the form of a questionnaire to the previous employer, or a telephone call will yield more accurate and valuable information. Not only is more information available by the latter method but people are inclined to speak more freely than they would be prepared to commit themselves in writing.

Figure 1: Sample Weighted Application Blank for Technical Assistant

Item	Short Term	Long Term	Weight
Age	%	%	
16-18	32	10	−3
18-20	43	37	−1
20-22	15	10	−2
22+	10	43	+4
Marital Status			
Married	42	61	+1
Single	58	39	−1
Education			
U.E.	42	31	−1
Bursary	49	23	−2
Nursing	9	46	+4
Years on last job			
Less than 1	42	20	−2
1-2	12	31	+3
2-3	28	13	−2
More than 3	18	36	+2
Years of experience			
0	46	20	−2
Less than 1	8	0	−4
1-2	23	20	0
2-3	18	12	−3
More than 3	6	48	+4

Data could have been compiled from previous applications. It is expressed as a percentage. The weightings are arbitrary but based on the percentages.

The Interview

On the basis of the information obtained in the application blanks a short list of candidates is prepared and the third step in the process is the employment interview—highly subjective and frequently inexact. Too often laboratory managers find that the impressions gained in interviewing have little correlation to subsequent worker performance. The interviewee who appears efficient, pleasant and altogether suitable but who follows up with shoddy substandard work is infinitely more difficult to displace from a position than (s)he is to appoint. Bull (1973)[1] has designed a personnel selection system, The Verifier, which aims to minimise errors of judgment by reducing all the information gathered to a mathematical equation producing the optimum combination of predictor variables. While not suggesting that such computerised techniques are necessary to laboratories it is certainly essential to structure and direct the form of the interview, and to understand its limitations. Interviewers, depending on their background and experience, weigh incoming information differently and tend to make decisions early. It is accepted that interviewers usually make a decision to accept or reject within the first half

of the interview, and Webster (1959)[6] put the time of decision making at less than four minutes! Articles frequently appear in magazines (particularly in times of high unemployment) directing applicants on how to present themselves for interviewing and ways to influence the judgment of the interviewer. They are told to arrive early, enter confidently, dress in a particular manner, be informed about the organisation and have pre-prepared answers to particular queries. This reflects the degree to which it is acknowledged that opinions can be swayed by details which may have no direct bearing on the ability to do the job. Kolb (1974)[3] refers to the halo effect where a general impression is used to evaluate specific traits, and to the distortion in perceptions created by stereotyping. An unfortunate experience with one individual with a particular attribute totally irrelevant to job performance may forever jeopardise the chances of all other applicants possessing the same attribute, although the interviewer may be quite unconscious of their bias. American research has shown that interviewers in general prefer tall people over short, thin people over fat, and are even influenced by such unrelated traits as hair colour (the dumb blond stereotype?) and name. Such unconscious prejudices are very difficult to control.

How then can the technique of interviewing be improved so that the results obtained are better than chance? Study of unsuccessful incumbents coupled with data from termination reports and perhaps even post-exit questionnaires would permit compilation of a list of relevant questions. Similarly the facets which identify successful employees should be identified and a degree of correlation looked for. This is not a short term task as statistically the larger the population the more valid the results would be and an inter-laboratory survey would obviously provide maximum correlation. The past has been called the key to the future and should be fully utilised. According to the latest figure available out of 104 NZCS candidates for 1979 only 59 passed, and this does not include those who have dropped out before getting this far. Since generally speaking their academic qualifications are impeccable is some other important motivational factor being overlooked in the selection process? Formal questions based on an adequate job description and other relevant data would give a degree of standardisation. All interviewees should be asked the ame questions under the same conditions and using the same weighing criteria. The questions must be reliable, that is, producing consistent results, and valid, that is, of value in predicting job success. This does not mean that the interview should be completely directed, but the basic structure should be adhered to. In general the more senior the appointment the longer and less formal direction is required in the interview. Notes should always be taken as subsequent recall of data, even short term, is very unreliable. The interviewer should be familiar with all the material contained in the application blank and regardless of first impressions should make every effort to suspend judgment until the interview is over. A comfortable private setting is essential, as far as possible free from interruption and with sufficient time allotted. Delegation of tasks is as much a managerial function as appointment of staff and any matters requiring attention should be referred to another senior member of staff. It is important that the interviewer establish a sense of rapport early and the atmosphere encourages the applicant to speak freely—a liking for people is a distinct advantage! In fairness to the applicant an indication of what future action to expect should be given and the interview brought to an obvious close so they are not left wondering what to do next. Once the applicant has left an immediate written evaluation should be made but no decision reached until all the applicants have been interviewed.

Induction

The highest turnover of staff in any organisation occurs during the first six months and it is important having made the selection that laboratories initiate a planned comprehensive induction programme (Figure 2). Job satisfaction depends on motivation (personal satisfaction) and administrative factors (wages, facilities, etc.). If the new employee is to function effectively they must identify with the goals of the organisation. This presupposes a knowledge of the organisational structure, the people in it and the actual job. They need to be instructed on how to answer the phone, who to go with inquiries, where the facilities are, how to fill in the time sheet, what to do if sick and a host of other details. The manager must maintain contact with the new employee, remember their name and use it, and ensure that someone specific is assigned to the task of subsequent instruction. How often does the new person arrive to a bustling bewildering Monday morning where everyone seems to be frantically busy at a host of completely incomprehensible tasks and so much information is thrust at them that by the end of the day they are convinced that they will never be able to cope? After hearing several

technical assistants in our laboratory discussing how near they came to leaving after the first week we now have an induction process which ensures that they learn only one simple job at a time and are not expected to run before they can walk. Failure to do proper induction negates the entire selection process and results in disappointed disgruntled employees and an increased labour turnover that could have been avoided. Time and effort invested in a planned system of staff selection and induction will pay its rewards in a stable organisation where employees feel a sense of belonging and loyalty and turnover and absenteeism are acceptably low.

Figure 2: Sample Induction Training Record

Name: *Date Commenced:*
Position: *Date Completed:*
Department:

1. *Organisational Information*
   a. Service provided
   b. Management structure
   c. Other departments
2. *General Welfare*
   a. Canteen and facilities
   b. Lockers and toilets
   c. Tea breaks
   d. Uniform
   e. Medical service
   f. Sports/social facilities
3. *Introduction to Department*
   a. Supervision
   b. The job
4. *Conditions of Employment*
   a. Hours of work
   b. Holidays
   c. Sickness
   d. Educative facilities
   e. Grievance procedure
5. *Housekeeping*
   a. Work areas
   b. Waste disposal
6. *Safety Procedures*
   a. Fire safety
   b. First aid facilities
7. *Wage structure*
   a. Terminology
   b. Wage scales
   c. Pay procedures
   d. Superannuation

Conclusion

An attempt to summarise the salient points of such large fields as selection of staff and induction must be of a general nature. Personnel management is a vital but often overlooked facet of laboratory management and a systematic approach, with due consideration given to the importance of personal attitudes and their influence on the outcome is essential. Close examination of our own methods and their validity, as evidenced by the results should stimulate us to rethink and if necessary modify our procedures.

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The Enz (or is it the Beginning?)

Once upon a time there was an enzyme who lived in a land called Tissue Cell. This enzyme had one big problem: he was schizophrenic—which is why all his frienz called him Split Enz.

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Just before he left, his best friend and confidant (whose real name was L-alanine 2-oxoglutarate amino transferase—but who was

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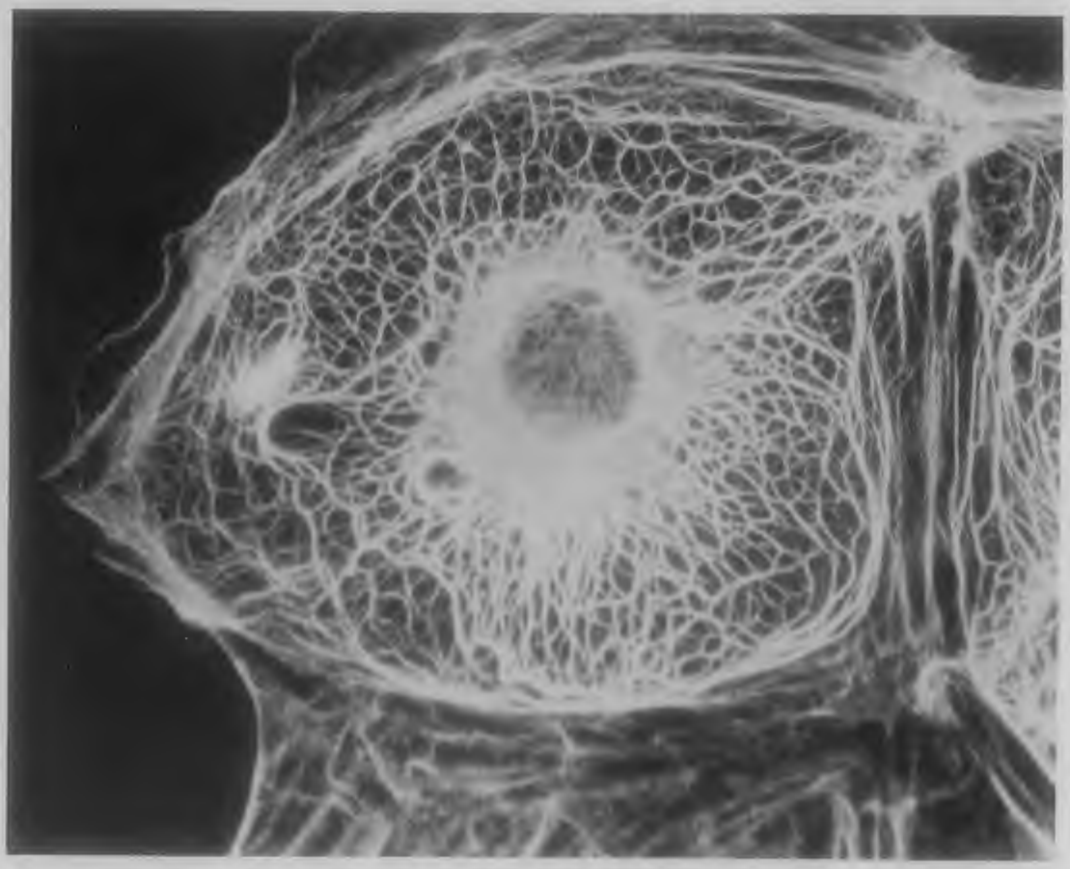

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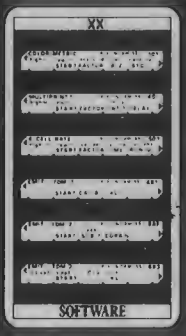

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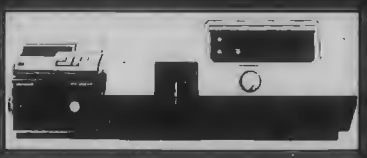

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known to all as "The Fenz") warned him about bad enzymes he might come across. He told Split Enz not to associate with the "Shady Lady" of the nuclear metropolis—Loose Enz, who had been known to lead young enzymes astray by saying "Let me catalyse *your* reaction!" Nor was he to go near the enzyme by the name of Rear Enz, who sold pornographic material. Especially was he to keep away from the well-known con-man: Sticky Enz, who could talk enzymes into investing all their activity in non-existent substrates.

Promising faithfully to do as The Fenz had told him, Split Enz set off. Soon he arrived at the nuclear body; but before he had time to prepare himself for what lay ahead, he was sucked inside through one of the open nuclear poregates. Taken by surprise, and confused by the noise and bustle of the place, Split Enz did not see a messenger RNA come hurtling towards him until it was too late. Down he fell and hit his sulphydryl group against the edge of a chromosome. He began to have one of his enzileptic fits—the most frenzied one he'd ever had, and was rushed to the local hospital—"On The Menz".

When he finally came round, he asked the doctor when he would be able to leave. (How he longed for the simple life of converting A into C; and B into D again).

"That all depenz," he was told. "We're sending you to an enzymologist called Mind Benz—he might be able to sort you out". The next day, Split Enz went to be analysed. As he went in, he bumped into another enzyme, muttering to himself, coming out. "Who's that?" he asked.

"Oh, just another one of my clienz; Nerve Enz", said Mind Benz. "He's quite neurotic—he thinks there's more to life than just this Tissue Cell. He says there are more of them outside and that we're all part of something much bigger. He keeps asking where all our nutrients come from. Well, everything knows they're supplied by the All Powerful Trans Enz. Just another one of those cretenz if you ask me.

Anyway, back to your case, "You see," he said assuming a professional voice, "One tenz to let all of one's inhibitors get on top of one. What one has to do is cleanz one's mind of them and start again. Here; take two of these tablets in a glass of protoplasm every day except for weekenz".

Split Enz left with hope in his heart. At last, a positive solution. Yes, he could feel it working already. He knew that someday he would be *one* personality—in other words, he would make enz meet.

Written by Kathleen Mayes,
Nelson Hospital Laboratory,
Private Bag,
Nelson.

Technical Communications

HB_sAg and Anti-HB_s Found in Laboratory and Ancillary Staff

Heptitis B infection in laboratory workers constitutes a small but significant occupational risk. In England, approximately 0.5-1% of all cases of Hepatitis B reported, are in laboratory workers (Public Health Laboratory Service 1975).

There is an increased incidence of the disease seen in laboratory staff as compared to other groups of workers. Numerous studies indicate that contact with blood and other pathological specimens is more important than direct contact with the patient. For example, staff in one U.S. plasma processing unit were tested for anti-HB_S Taylor, *et al* (1974)[2]. Of 51 staff who had no contact with blood, 18% had anti-HB_s 64 staff who had some contact with blood, 55% had anti-HB_s 78 staff who had direct contact with blood, 81% had anti-HB_s. Another study compared the incidence of anti-HB_s between groups of healthcare workers. Leere, *et al* (1975).[1] Laboratory staff, overall, had the highest incidence of seropositivity—20. 3%, with nurses 11.2% positive, and administrative staff 6.1%. 40% of the clinical chemistry staff subgroup were seropositive. (N.B. diagnostic and quality control sera may also be infective even in the absence of HB_sAg detectable by a sensitive radioimmunossay technique).

A recent report, in Dtsch. Med. Wochenschr; noted different rates of HB_sAg detected in qualified (4.7% positive) and student (0%) laboratory staff; and anti-HB_s—36.1% in qualified staff as compared to 6.6% of students. Records of tests performed on staff members in this laboratory were checked to compare with these findings. Staff tested included those accidentially inoculated, and those exposed to contaminated material, from 1977 until 1979. All were tested for HB_sAg and anti-HB_s by radioimmunoassay, and serial tests at the time of inoculation, six weeks and four months later, were performed where laboratory accidents involving HB_sAg contaminated material had been reported. As a comparison, of 2425 new donors tested by RPHA for HB_sAg, 0.16% were positive (results

confirmed by RIA). 82 of the new donors were tested for anti-HB_s by RIA, because of a past history of hepatitis, contact with a heaptitis case, or apparently positive HB_sAg screening tests—of these 0.53% had anti-HB_s. The results are as follows: of 69 staff tested, none were HB_sAg positive at any time. However, it is obvious that, at some stage, exposure to HB_sAg must have occurred as anti-HB_s was requently present (see Table).

ML 22

Years Laboratory Work		< 5		> 5		
	No. Tested	Anti-HBs Positive	Positive	No. Tested	Anti-HBs Positive	% Positive
Technologists Technicians & Trainees	24	1	4.2	21	2	9.5
Donor & Laboratory Collection Staff	4	0	0	12	0	0
Pathology Registrars	—	—	—	5	0	0
Laboratory Clerical Staff	3	0	0	—	—	—
Total Staff	31	1	3.2	38	2	5.3

Summary

The numbers tested in each category are relatively small but the results obtained do not confirm the findings reported in Dtsch. Med. Wochenschr. 103: 1065-67 (June 30, 1978). However, it can be seen that seropositivity for anti-HB_s in this survey was confined to those directly involved in blood, serum and plasma separation and testing procedures.

Teresa A. Cleary, L. M. Milligan,
Immunohaematology Department,
Diagnostic Laboratories,
Dunedin Hospital.

January 1980

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BCP Albumin and the Gilford 3500

Due to the relatively costly 'made up' Bromo Cresol green (BCG) reagent available for the estimation of serum albumin levels on discrete analysers, we have been looking for a less costly alternative. Following the publication of an article (1978)[3] concerning Bromo Cresol purple (BCP) as a substitute for BCG as the basis for a dye binding method, we attempted to adapt the BCP reagent described, designed for continuous flow analysis, to discrete analysis on our GILFORD 3500.

As the 'working' reagent is apparently unstable when stored for any length of time, we decided to keep it in a two component form. The two solutions could be added together to produce any required volume. This suited as well, as our reagent consumption is not large and would require volumes of only 100-200 ml per week (the advised storage life of the working reagent).

The two component solutions are:

1. Stock BCP solution. 40 mmol/l in absolute ethanol (0.54g BCP, BDH indicator grade in 25.0ml absolute ethanol). Stored in an opaque plastic container at 4°C, its life is a minimum of three months.

2. Acetate Buffer solution. 6.03g/l Sodium Acetate (BDH 'AR' grade) anhydrous, dissolved in approximately 800ml deionised water. 10.0ml Acetic Acid (15.0ml glacial CH_3COOH, diluted to 100ml with deionised water) is added along with 1.0ml BRIJ 35 (25g/100ml). The pH is adjusted to 5.2 ± 0.05 (with acetic acid solution of 0.5mol/l Sodium Hydroxide). Stored at R.T. in a plastic container.

The working solution is made by adding 0.10ml of stock BCP solution to each 100ml acetate buffer solution. This working solution is filtered before use.

The GILFORD 3500 is programmed with the Albumin card (designed for BCG reagent) with the following parameters changed from the original printout.

DISPENSER A—Sample 5μl (5% STOP)
Reagent 1.00ml (40% STOP)
Wavelength 600nm.

Samples were run in parallel with the BCG method on the GILFORD 3500 over a month. Regression analysis gave the following results:

Slope 1.131
y = -5.356
r = 0.987
n = 51

Day to day CV% at 40.5gm/l = 2.2%, (n = 26) and at 20.0 gm/l = 1.4% (n = 17).

We have found the reagent outlined above very successful in our particular application—that is, assay of relatively small numbers of samples—without excessive wastage due to reagent deterioration. Our internal quality control

indicates that the quality of results has not suffered, although we do now have a problem with the Wellcome external survey. (The BCP method will not measure bovine albumin due to an apparent reduction if its affinity for the dye). There have been other recent communications (1979),[1, 2] indicating that the accuracy of the BCP method is superior to that of the BCG method, and that the degree of interference, due to a number of factors, is of less consequence.

We would recommend the BCP reagent for use on the GILFORD 3500 on the basis of cost and performance, when compared to the BCG method.

December 1979

D. M. Fallas,
Laboratory,
Thames Hospital.

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Correspondence

Errors Arising from Non-mixing of Thawed Specimens

Sir,—Although most laboratory workers realise that poor mixing of frozen specimens after thawing leads to errors, we wonder if they are equally aware of the extent of such errors. Recently, we carried out an experiment on urine samples, following the method used by Omang and Vellar.[1] A thoroughly mixed urine sample was dispensed into four 10 ml stoppered polypropylene tubes and frozen for 60 hours. The frozen aliquots were thawed by standing undisturbed at room temperature for four hours. One of the aliquots was thoroughly mixed by repeated inversions (control). Small portions were aspirated from the top, middle and bottom of each tube for analysis on an AAII Autoanalyser. The median result of each triplicate analysis is presented in the table.

MEDIAN RESULTS OF TRIPLICATE ANALYSES

Concentrations:

	Na *mmol/l*	K *mmol/l*	Urea *mmol/l*	Creatinine *mmol/l*	Albumin *g/l*
Top	34	16	54	1.9	0.30
Middle	84	33	126	4.4	0.70
Bottom	141	52	198	6.8	1.21
Control	86	33	125	4.1	0.74

Fractions of Control Value:

	Na	K	Urea	Creatinine	Albumin
Top	0.40	0.48	0.43	0.43	0.41
Middle	0.98	1.00	1.01	1.07	0.96
Bottom	1.64	1.58	1.58	1.66	1.66

It should be noted that the concentration distribution pattern is the same for all of the analytes tested, and errors of the order of 60% could be introduced by neglecting to thoroughly mix thawed specimens.

May 1979.

M. H. Abernethy,
T. A. Walmsley,
Clinical Biochemistry,
Christchurch Hospital.

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Book Reviews

Hazardous Chemicals. A Manual for Schools and Colleges. Published by Oliver and Boyd, Edinburgh, for the Scottish Schools Science Equipment Research Centre and obtained from Penguin Books (NZ) Ltd., C.P.O. Box 4019, Auckland 1. Price $NZ13.95.

The foreword states that the Scottish Schools Science Research Centre offers a service of constructive and practical advice to schools and has done so since 1964. With the introduction of the Health and Safety at Work Act in Britain, attention has quite rightly been focused on the question of safety in science laboratories. The contents have been gathered from practical professional contributors.

This is a ringbound reference book arranged in alphabetical order. Consequently there is no need for numbered pages. There are some 200 entries,

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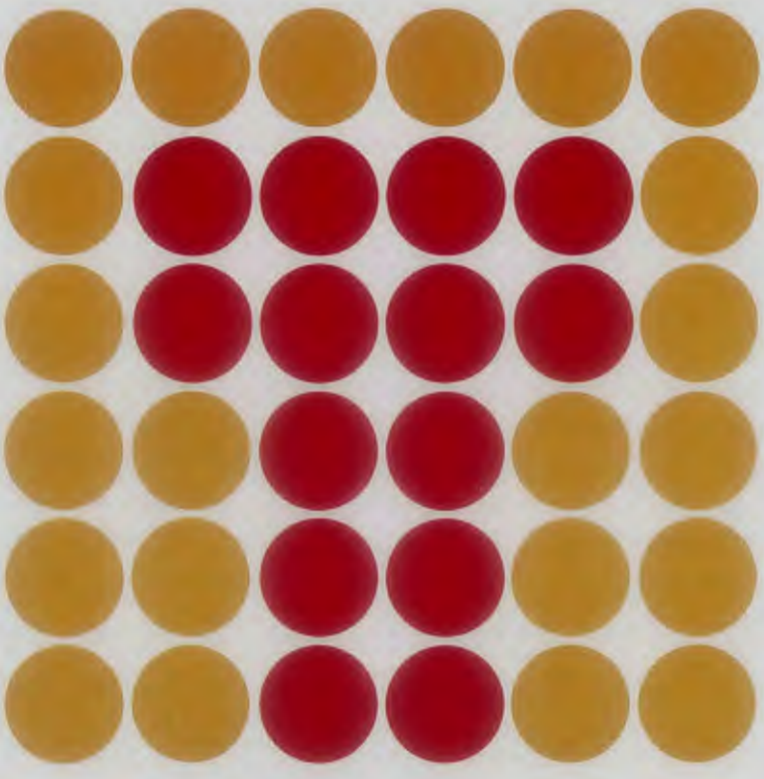

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Introduction

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Eighteen clinical investigations have assessed the value of the LANCER TennaGen Assay in over 5,700 subjects and analyzed over 7,500 samples.[3] It has proved to be a simple, rapid, sensitive and reproducible *in vitro* test.

The assay is compatible with routine laboratory procedures and can be performed with minimal personnel training. It requires no major investment in specialized equipment. The product has a shelf life of 18 months when stored at 4-8° C.

The LANCER TennaGen Assay is a valuable aid in

- **Diagnosis of cancer**
- **Management of therapy for gastrointestinal and lung cancer**
- **Monitoring for recurrence of disease**

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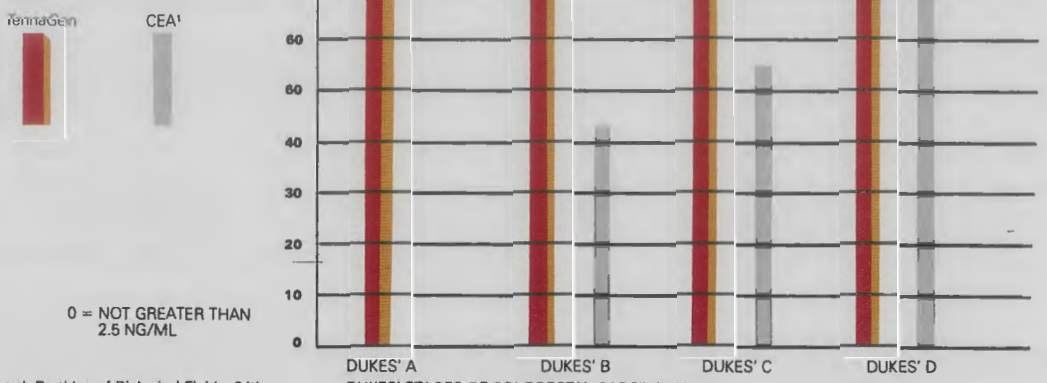

0 = NOT GREATER THAN 2.5 NG/ML

[1]Hirai, H., et al, Protides of Biological Fluids, 24th Colloquium 1976, p. 621 (51).

each on a separate page. The substance is at the top of the page in bold type. First aid given lower down the page is also in bold type and is clearly set out in simple sentences.

The other details provided are synonyms, chemical formulae and a series of subheadings namely: Hazards, Incompatibility, Handling, Storage, Disposal and Spillage.

There is an extensive introduction which gives advice on the handling of toxic chemicals, fire precautions, defines Threshold Limit Values and Short Term Exposure Limits for workers handling toxic substances and discusses carcinogens. There is also a bibliography.

As this book is aimed at science laboratories it is inevitable that a number of chemicals and solvents specifically used in clinical biochemistry laboratories are not listed. With this reservation one can say that this is a well designed ready reference manual for which there is a need in the laboratory and that it would be a useful adjunct to the first aid kit.

Janice Parker.

Diagnostic Parasitology. Clinical Laboratory Manual. Lynne Shore Garcia, A.B., M.T., IASCP, and Lawrence R. Ash, Ph.D. Second Edition. Published by the C. V. Mosby Company 1979. Obtained from N. M. Peryer Ltd. Christchurch. 174 pages soft covered and spirally bound. Price $NZ21.70.

This comprehensive volume comprises 12 chapters: Collection and preservation of faecal specimens; Macroscopic and microscopic examination of faecal specimens, including concentration techniques; Permanent stained smears, dealing with the trichrome and iron-haematoxylin staining techniques; Special techniques for stool examination, covers techniques not usually contemplated by routine diagnostic laboratories, namely cultures of larval-stage nematodes, egg studies and search for tapeworm scolex. Separate chapters cover: Examination of other specimens from the intestinal tract and urogenital tract dealing with pinworm, sigmoidoscopy material, duodenal contents and urogenital specimens; Sputum, aspirates and biopsy material; Procedures for detecting blood parasites; Parasite recovery comprising culture methods, animal inoculation and Xenodiagnosis. Once again this chapter is not applicable to a routine diagnostic laboratory. No technical details are documented in the chapter on Serodiagnosis of parasitic diseases rather the tests available for the specific parasitic diseases, the tests of choice and the applicability of procedures listed.

Fixation and preparation of parasite specimens is followed by the largest section in the manual: Parasite identification. The majority of the illustrations are black and white, the only colour plates pertaining to the genus *Plasmodium*. Use of tabulated charts summarising life cycles, geographical distribution, parasite morphology and size aid in identification. The final chapter is concerned with Quality Control procedures for diagnostic parasitology followed by a useful glossary.

With this manual, the authors have provided a valuable addition to the laboratory shelf, but it is a book which requires to be supplemented with a standard parasitology reference work.

Margaret E. Berry.

Recent Advances in Infection, Number One (1979). Edited by David Reeves and Alasdair Geddes. 226 pages. Published by Churchill Livingstone and obtained from N. M. Peryer Ltd, Christchurch. Price $35.20.

This is the first of a new series of review articles covering new areas and topics of current interest in infection and clinical microbiology. Originally this topic and others were found in 'Recent Advances in Clinical Pathology' but due to advances and expansion in the microbiology of infections it was decided to create a new series.

This book consists of fourteen chapters each presented by different authors and covering a wide range of subjects.

Due to the emergence of new antimicrobial agents in recent years it isn't surprising that five chapters are devoted to antibiotics and trends in resistance following their use. The first chapter deals with antimicrobial resistance. Recently there has been an emergence of resistance in strains which have been sensitive to an antibiotic for many years. Pneumococci and gonococci and these organisms and many others are comprehensively dealt with.

There is a review of new antibiotics, particularly those agents which have been introduced in the past five years. This is an extremely useful chapter considering the confusing array of antibiotics and their derivatives on the market.

It has only recently been realised that Campylobacters are a major cause of diarrhoea in man and no contemporary work would be complete without mentioning this group. The isolation and cultivation of Campylobacters, the biology of

these and anaerobic spiral bacteria and their role in animal diseases is discussed.

The chapter on the detection of bacterial antigens outlines rapid methods such as countercurrent immunoelectrophoresis, coagglutination, and the *Limulus lysate* test all of which may be useful for the demonstration of bacterial components in serious bacterial infections.

Other chapters include Quality Control in microbiology, Infections with Obligate Anaerobes and Meningococcal diseases; Pathogenesis and Prevention to name but a few.

This is a well presented, well referenced book providing up-to-date information on a variety of topics. It cannot help but provide invaluable assistance to all those trying to keep abreast of advances in this field. Maree Johnstone.

Electrophoresis. A Survey of Techniques and Applications. Part A: Techniques. Edited by Z. Deyl, Physiological Institute, Czechoslovak Academy of Sciences, Prague, Czechoslovakia. Co-editors: F. Everaerts, Z. Prusik and P. J. Svendsen from Elsevier Scientific Publishing Company, P.O. Box 211, Amsterdam, The Netherlands. In the USA: C/o Elsevier/North-Holland Inc., 52 Vanderbilt Ave., New York, NY 10017.

This, the first volume in a two-part set, deals with the principles, theory and instrumentation of modern electromigration techniques. The second part of the set will be concerned with the detailed applications of electromigration methods to diverse categories of compounds, although to a limited extent some applications are discussed in Part A.

Several electromigration methods for both analytical and preparative separations have become standard procedures. These are discussed in the book together with newer developments in the field. Hints are included to overcome the difficulties which often arise from the lack of suitable equipment. Adequate theoretical background of the individual techniques is given.

In each chapter practical realisations of different techniques are discussed and examples are presented to demonstrate the limits of each method. The mathematical and physicochemical background is arranged so as to make it as coherent as possible for both non-professionals, such as postgraduate students, and experts using electromigration techniques.

CONTENTS: Preface; Foreword; Introduction. Chapters: 1. Theory of electromigration processes. 2. Classification of electromigration methods. 3. Evaluation of the results of electrophoretic separations. 4. Molecular size and shape in electrophoresis. 5. Zone electrophoresis (except gel-type techniques and immunoelectrophoresis). 6. Gel-type techniques. 7. Quantitative immunoelectrophoresis. 8. Moving boundary electrophoresis in narrow-bore tubes. 9. Isoelectric focusing. 10. Analytical isotachophoresis. 11. Continuous flow-through electrophoresis. 12. Continuous flow deviation electrophoresis. 13. Preparative electrophoresis in gel media. 14. Preparative electrophoresis in columns. 15. Preparative isoelectric focusing. 16. Preparative isotachophoresis. 17. Preparative isotachophoresis on the micro scale. List of frequently occurring symbols. Subject Index.

Basic Concepts in Anatomy and Physiology. A Programmed Presentation. Catherine Parker Anthony and Gary A. Thibodeau; 4th Edition. C. V. Mosby Company. 214 pages, ring-bound soft cover, illustrated. Obtained from N. M. Peryer Ltd. C.P.O. Box 833, Christchurch 1. Price $12.95.

The concept of programmed information can be described as the presentation of small pieces of information arranged in a planned sequence. These are called frames. Information conveyed in outlined boxes or in diagrams or implicit in the text has to be learned in order to fill in blank spaces in the text. The missing words or phrases are given at the side of the page and are concealed by an 'L'-shaped cardboard former. The intention is to enable answers to be checked after filling them in. So much for the mechanics of the system. Will it work? My own experience was that it calls for considerable self-discipline not to have a 'peek' at the answer! However this does defeat the object of the exercise.

It seems that the book was produced to assist in nursing training and the level of attainment is fairly simple. The chapter headings are Cells; Communication control and integration; Transportation; Energy supply and waste excretion; Survival of the species; Maintenance of fluid, electrolytes and acid-base balance. Filling in the missing

spaces has an element of play about it and may well add interest and incentive. I do get an impression of rote learning and this hardly seems a feasible approach to something like the Krebs' cycle. It is difficult to see how this book would fit into the medical technologist's curriculum. It would not help prepare for the NZCS (paramedical) exam, except as an introductory text.

The authors do stress that the programmed approach has limitations and should be used to supplement conventional textbooks and I would agree with this. R. D. Allan.

Abstracts

Contributors: Margaret Berry, E. R. Crutch, Shirley Gainsford, N. J. Langford and L. M. Milligan

HAEMATOLOGY

Heparin and Partial Thromboplastin Time: an International Survey. Poller, L., Thomson, J. M. and Yee, K. R. (1980), *Br J. Haemat* **44**, 161.

The reliability of routine partial thromboplastin time (PTT) methods in the measurement of the anticoagulant effect of Leparin has been assessed in a study involving over 300 hospitals in the U.K. and overseas. Commercial PTT methods were relatively insensitive to heparin, added in vitro, compared with the standardised PPT method tested by the same laboratories. The value of a sensitive reference preparation for the calibration of routine PTT reagents used in heparin control is demonstrated. E.R.C.

Use of an Inexpensive Programmable Calculator for Computation of Platelet Counts from Particle Counts. Herod, E., Farrington, A. M., Urmston, A., Ball, M., and MacIver, J. E. (1980), *Medical Laboratory Sciences* **37**, 39.

A method is described for calculating whole blood platelet counts from particle counts, using an inexpensive programmable calculator, and resulting in a reduction in unpredictable errors. E.R.C.

The Factor VIII Comples in Von Willebrand's Disease Using a Modified Technique for the Quantification of Von Willebrand Factor. Marshall, Lorraine R. and Herrmann, R. P. (1979), *Aust. J. Med. Technol.* **10**, 137.

The authors describe a new technique using platelets and measuring ristocetin-induced aggreation in an aggregometer for determining Von Willebrand factor. The level of Von Willebrand factor appeared to reflect the clinical severity of the condition more closely than either the factor VIII procoagulant activity or the factor VIII related antigen. E.R.C.

A Modified Activated Partial Thromboplastin Technique to Monitor Heparin Therapy Using a Platelet Aggregometer. Bailey, P. E. and Thom, J. (1980), *Aust. J. Med. Lab. Sci.* **1**, 23.

The authors describe a modified partial thromboplastin for the control of heparin therapy based on the use of a platelet aggregometer to detect the end point. E.R.C.

Functional and Metabolic Studies of Polymorphonuclear Leucocytes in the Congentital Pelger—Huet Anomaly. Johnson, Christine, A., Bass, D. A., Trillo, A. A., Snyder, Melinda and DeChatelet, L. R. (1980), *Blood* **55**, 466.

Neutrophils from two individuals with congenital Pelger-Huet anomaly were examined. The quantitative leucocyte enzyme activities were normal, as was chemotaxis, random migration and bactericidal activity. E.R.C.

The Complement System of the Newborn Infant. Drew, J. H. and Arroyave, C. M. (1980), *Biol. Neonate.* **37**, 209.

Whole complement activity (CH_5O), and levels of some components of the classical (Clq, C_4, C_3) and alternate (factor B and properdin) pathways were determined in 55 non-infected and 11 infected newborn infants. Normal newborn infants were lower than adults in all complement measurements, preterm infants being significantly lower than term infants. Because of the high incidence of C_3 spilt products in infected infants, incorporating a test to determine their presence may be of benefit in the diagnosis of the presence of infection in newborn infants. E.R.C.

Recommendation for Reference Method for Determination by Centrifugation of Packed Cell Volume of Blood. International committee for standardisation in haematology expert panel on blood cell sizing (1980), *J. clin. Pathol.* **33**, 1.

This paper details the reference method for determining packed cell volumes. The technique uses the macrohaematocrit or Wintrobe tube. E.R.C.

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Evaluation of the Honeywell ACS 1000 Leucocyte Differential Counter. Clowes, Margaret, Giles, C., Ibbotson, R. M. and Johnson, P. H. (1980), *J. clin. Pathol.* **33,** 145.

The Honeywell ACS 1000 is a relatively inexpensive differential white cell counter, which is only partially automated. This article might be of some local interest as a number of laboratories in New Zealand have had an instrument for evaluation. E.R.C.

Interlaboratory Comparison of Serum Vitamin B12 Assay. Mollin, D. L., Hoffbrand, A. V., Ward, P. G. and Lewis, S. M. (1980), *J. clin Pathol.* **33,** 243.

The results have been compared of microbiological and radioisotope dilution assay of serum Vitamin B12 by participants in national interlaboratory trials in Britain. In general, radioisotope dilution gave higher results than microbiological assay. E.R.C.

Automated Differential Leucocyte Counters. An Evaluation of the Hemalog D and a Comparison with the Hematrek. Bain, B. J., Neil, P. J., Scott, D., Scott, T. K. and Innis, M. D. (1980), *Pathology* **12,** 83.

Two papers are published comparing the Hemalog D and Hematrek. The first includes the principles of operation; reproducibility and accuracy on normal blood samples, and the second is an evaluation of performance on routine blood samples from hospital patients at the Princess Alexandra Hospital in Brisbane. E.R.C.

Acquired, Transient Factor X (Stuart Factor) Deficiency in a Patient with Mycoplasma Pneumonial Infection. Peuscher, F. W., Van Aken, W. G., Van Mourik, J. A., Swaak, A. J. G., Sie, L. H. and Statius Van Eps, L. W. (1979), *Scan. J. Haematol.* **23,** 257.

The authors describe a severe haemorrhagic diathesis due to acquired deficiency of factor X. The clinical and serological features of this case indicated mycoplasma pneumonial infection. E.R.C.

Monequivalence of Automated and Manual Haematocrit and Erythrocyte Indices. Fairbanks, U. F. (1980), *Am. J. clin. Pathol.* **73,** 55.

Dr Fairbanks compares automated and manual haematocrit and erythrocyte indices and concludes that the manual results appear to be inherently less reliable than those obtained by automated methods. E.R.C.

MICROBIOLOGY

Evaluation of Enzyme-Linked Immunosorbent Assay for the Serodiagnosis of Amoebiasis. Yang, J., and Kennedy Marie T., (1979), *J. Clin. Mic.* **10,** 778.

A paper describing the standard micro-ELISA technique and its reliability and application for the detection of antibodies to *Entamoeba histolytica*. Highly sensitive, specific and reproducible results were obtained. Comparison of the ELISA and IFA and IHA techniques showed that the former was slightly more sensitive than the two latter methods. An ELISA titre of 1:100 was regarded as specific in the detection of antibodies to *E. histolytica*. M.E.B.

Serology of Legionnaires Disease: Comparison of Indirect Fluorescent Antibody, Immune Adherence Haemagglutination and Indirect Haemagglutination Tests. Lennett, D. A., Lennette, Evelyne T., Wentworth, Berttina B., French, M. L. V. and Lattimer, G. L. (1979), *J. clin. Mic.* **10,** 876.

Most infections of *Legionella pneumophila* have been diagnosed by serology. Cultivation is difficult and slow although improved media for recovery are being developed. An IAHA test for the measurement of antibodies to Legionnaires disease was developed and evaluated. Its sensitivity was compared to that of the IFA test and the IHA technique. The sensitivity of the three tests appeared to be similar with the IFA test giving slightly higher titres. However the IFA test may give false positive results. Although the IHA test is equal to the IAHA test in sensitivity and specificity, it may be somewhat less versatile as the antigen sensitised cells must be specially prepared. Both the IHA and IAHA tests appear to be satisfactory alternatives of IFA test for Legionnaires disease. M.E.B.

Identification of Diaminopimelic Acid in Legionnaires Disease Bacterium. Guerrant, G. O., Lambert, M. S., and Moss, C. W. (1979), *J. clin. Mic.* **10,** 815.

Diaminopimelic acid is a unique amino acid of the bacterial cell wall. It was found to be a component of the cell wall of *Legionella pneumophila* thus providing additional evidence that this organism is a bacterium. The presence of this amino acid was determined by gas liquid chromatography and confirmed by gas chromatography—mass spectrometry. M.E.B.

Endophthalmitis due to Salmonella enteritidis. Corman, L. I., Poirier, R. H., Littlefield, Christine, A., and Sumaya, C. V. (1979), *J. of Paediatrics.* **99,** 1001.

Salmonella enteriditis Group D bioserotype Panama was isolated from an exudate from the anterior chamber of the right eye of a seven week old boy. A preceding history of diarrhoea suggests that Salmonella bacteremia occurred following an initial gastroenteritis. No Salmonella was isolated from the blood cultures, CSF or faeces, however antibiotics had been administered prior to culture of specimens. The authors have been unable to find previous reports of Salmonella species causing endophthalmitis, but meningitis and osteomyelitis have been associated with Salmonella gastroenteritis and young infants may be at particularly high risk for developing these complications. M.E.B.

Pseudo-Leptospires in Blood Culture. Rahman, M., and Macis, F. R. (1979), *J. clin. Path.* **32,** 1226.

Spiral filaments seen in blood cultures of two patients with fever and jaundice were intially thought to be Leptospires. These were later proved to be artefacts. The Leptospirosis Reference Laboratory in London did not confirm the findings and serological tests were negative. The authors conclude that dark ground examination of blood cultures for leptospires should not be undertaken in routine laboratories with only limited experience of leptospires. M.E.B.

Grouping of Streptococci by Streptex. Waitkins, Sheena, A., Ratcliffe, J. G., Anderson, R. D., and Roberts, D. (1979), *J. clin. Path.* **32,** 1234.

Streptex is a commercially available kit for the identification of Lancefield groups A, B, C, D, F, and G. Wellcome Laboratories have modified the coagglutination system by substituting polystyrene latex particles for Staphylococcal protein A, and using the enzyme pronase for the antigen extraction. The authors in general found the streptex reactions not always easily readable and identification was based on the strongest agglutination noted. Weak reactions required repetition and only 5 of 19 group D grouped satisfactorily. Streptex performed poorly for those group D other than *Strep faecalis.* M.E.B.

Vibrio Alginolyticus Infections in Humans. Schmidt, U., Chmel, H. and Cobbs, C. (1979), *J. clin. Mic.* **10,** 666.

This paper is a report on two cases of infection caused by Vibrio alginolyticus and a review of other human infections. S.G.

Comparison of a Slide Coagglutination Technique with the Minitek System for Confirmation of Neisseria Gonorrhoeae. Hampton, K. D., Stallings, R. A. and Wasilauskas, B. L. (1979), *J. clin. Mic.* **10,** 290.

When the Phadebact gonococcus test was used to directly test colonies of N. gonorrhoeae, reactions were noninterpretable. However if colonies were heated in distilled water first definitive results were obtained and the Phadebact test compared favourably with Minitek in the identification of N. gonorrhoeae. S.G.

Culture Diagnosis of Meningococcal Carriers. Yield from Different Sites and Influence of Storage in Transport Medium. Olcess, P., Kjellander, J., Danielsson, D., and Lindquist, B. L. (1979), *J. clin. Path.* **32,** 1222.

A comparison in culture yield of meningococci from throat swabs and nasopharyngeal specimens in 178 persons revealed 44 carriers. All of these were detected by culture of throat swabs while 34% would have remained undiagnosed if only nasopharyngeal specimens had been examined. Storage of throat swabs in a transport medium for 24 hours before culture gave a negative culture for meningococci in 41% of the carriers. M.E.B.

Recent Observations on the Serology of Syphilis. Lager, A., Schmidt, B., Spendlingwimmer, I., and Horn, F. (1980), *Brit. J. Ven. Dis.* **56,** 12.

Recent observations in syphilis serology reveal a common trend in the use of the AMHA-TP (automated version of the microhaemagglutination assay) and the VDRL for screening purposes, reactive results being confirmed by FTA-Abs. The importance of the use of the haemagglutination technique as a screen is stressed. In a survey of 7474 sera the VDRL alone failed to indicate reactivity in 56.54% of sera which were reactive to both AMHA-TP and FTA-Abs. This article also deals with the haemagglutination technique in relation to CSF specimens. M.E.B.

Streptococcus M G—Intermedius (Streptococci Milleri) Septic Arthritis in a Patient with Rheumatoid Arthritis. Houston, B. D., Crouch, M., and Finch, R. G. (1980), *J. of Rheumatology* **7,** 89.

A case of Streptococcus M G—Intermedius (*S. milleri*) Septic arthritis in a patient with rheumatoid arthritis is presented. The unusual nature of this infection and the difficulties with the identification of *S. milleri* are discussed.

The growth requirements, colonial morphology and antibiotic susceptibility of his organism are described. Lancefield grouping of *S. milleri* may demonstrate group A, C, F or G antigens. A typing scheme described by Ottens & Winkler permits recognition of six serotypes I-VI. Differences in nomenclature has also been a source of confusion in the identification of this organism. M.E.B.

A Comparison of Five Methods for the Detection of Trichomonas Vaginalis in Clinical Specimens. Levett, P. N. (1980), *Med. lab. Sci.* **37,** 85.

The author compared five methods for the detection of Trichomonas vaginalis in high vaginal swabs. These included wet preparations, culture and staining with Leishmans, Diff Quik and acridine orange. The acridine orange stain gave the most positive results. S.G.

Identification of Viridans Streptococci on the Minitek Miniaturised System. Holloway, Y., Schaareman, M. and Dankert, J. (1979), *J. clin. Path.* **32,** 1168.

Using the Minitek system and applying a liquid paraffin overlay and incubation in an atmosphere of CO_2, viridans streptococci were identified earlier than with the conventional system. Results agreed with the conventional methods of Colman and Williams and compared well with Cowan and Steeles scheme. S.G.

A Rapid Bile Solubility Test for Pneumococci. Howden, R. (1979), *J. clin. Path.* **32,** 1293.

A reliable and simple test for identifying pneumococci is described. After incubation in an anaerobic atmosphere with 10% CO_2 to produce large colonies, a loopful of bile salt is placed on suspected pneumococcal colonies. Lysis of the pneumococcal colonies is seen after 15 minutes further incubation. S.G.

Cultivation of Pneumocystis carinii with WI-38 Cells. Bartlett, Marilyn, S., Verbanac, Patricia, A., and Smith, J. W. (1979), *J. clin. Mic.* **10,** 796.

Pneumocystis carinii has been successfully cultured with WI-38 human embryonic lung fibroblasts. Inoculum was obtained from infected lungs of cortisone-treated Sprague-Dawley rats. Successful cultivation has also been achieved with MRC-5 cells and with embryonic chicken epithelial cells. WI-38 is a readily available cell line but a continuous culture has not been achieved. This cell line is equal or superior to the MRC-5 line. Four attempts to culture infected human lung were unsuccessful. M.E.B.

IMMUNOHAEMATOLOGY

Identification of genotypes of Blood Group A and B. Yoshida, Akira (1980), *Blood* **55,** 1.

The human blood groups (ABO) are known to be determined by the terminal Glycosyl residues attached to common carbohydrate chains of the red cell surface. This article describes a biochemical method for positively identifying the genotypes of these blood groups. L.M.M.

In Vitrol Tests for Distinguishing Possible Immune-Mediated Aplastic Anaemia from Transfusion-Induced Sensitisation. Torok-Storb, Beverley, Sieff, C., Storb, R., Adamson, J. and Thomas, D. E. (1980), *Blood* **55,** 2.

It has been reported that lymphocytes from patients with aplastic anaemia suppress *in vitro* growth of haemopoietic colonies from healthy HLA- nonidentical unrelated individuals and have suggested that in some cases, the aplastic anaemia may have an immune aetiology. Further study will determine whether the two methods described in this article will be useful for identifying patients at risk of graft rejection. L.M.M.

Autotransfusion on Surgical Practice. Adhoute, B. G., Nahboo, K., Lancelle, D., Mora, M., Rouvier, R., Bleyn, J. and Orsoni, P. (1979), *Cardiovasc. Re. Centre Bulletin* **18,** 2.

This article presents results collected from 58 vascular surgery cases where autotransfusion of intraoperatively collected blood was employed. The clinical results obtained, confirm laboratory studies on the quality of autotransfused blood. The authors claim that this technique of autotransfusion is simple, safe and inexpensive. L.M.M.

Successful Transfusion of Platelets Cryopreserved for more than three years. Daly, P. A., Schiffer, C. A., Aiswer, J. and Wiernik, P. H. (1979), *Blood* **54,** 5.

In order to determine the duration of storage for cryopreserved platelets, 14 transfusions of random donor, pooled platelets, stored in the vapour phase liquid nitrogen for three years were analysed. These transfusions were controlled using fresh, pooled platelets infused into the same patients at a later stage. Results obtained, suggest that platelets could be cryopreserved for some time and these satisfactorily infused. L.M.M.

Preparation of Stable Intermediate-purity Factor VIII Concentrate with a note on High-purity Factor VIII. Margolis, J. and Rhoades, P. (1979), *Vox. Sang.* **36,** 369.

Cryoprecipitate was prepared by a rapid thawing technique and was pooled in large batches. These pooled batches were washed with ice-cold tris-citrate-NaCl solution. After dissolving it was absorbed with A (OH) 3 and Kaolin and cleared by centrifugation. The supernatant diluted with 5% dextrose was passed repeatedly through a bed of Celite filters and lyophilised. This crude factor VIII concentrate was also suitable material for the preparation of high purity factor VIII. L.M.M.

An Improved Procedure for Accurate Assays of Factor VIII. Margolis, J. (1979), *Pathology* **11,** 149.

An improved one stage method for accurate assays of Factor VIII combines highly reproducible end points with elimination of temporal drift and of subjective factors involved in graphic analysis. L.M.M.

Effect of Blood Transfusions on Survival of Cadaver and living Related Renal Transplant. Oei, L. S., Thompson, J. S. and Corry, R. (1979), *Transplantation* **28,** 6.

The effect of a Blood Transfusion was analysed in a number of renal transplant patients. The association of blood transfusion with HLA genotyping and poor risk recipients was analysed. L.M.M.

Anti-Rh 39—A New specificity Rh System Antibody. Issitt, P. D., Pavone, B. G. and Shapiro, M. (1979), *Transfusion* **19,** 4.

Two examples of an auto-antibody that defines a previously unrecognised Rh system antigen are described. L.M.M.

CLINICAL BIOCHEMISTRY

Surfactant Inhibition of Cholesterol Oxidase. Miner-Williams, M. (1980), *Clin. Chim. Acta.* **101,** 77.

A study of the effects of some common surfactants on the enzymatic cholesterol estimation using cholesterol oxidase, showing that not all surfactants are suitable for use with this assay. Tween 20 and Triton X-405 inhibit the activity of the enzyme completely, and with others the effects may vary with concentration. N.L.

The Real and Apparent Plasma Oxalate. Akcay, T., and Rose, A. G. (1980), *Clin. Chim. Acta.* **101,** 305.

A modification of the Hallson and Rose enzymatic method for urinary oxalate is described for plasma. Results obtained were suspected to be too high due to the possible conversion of Glyoxalate to oxalate. This was corrected for using inhibitors to the reaction. It is concluded that previously quoted normal figures for *in vitro* determination of Plasma Oxalate are too high and that those published for *in vivo* isotopic methods are probably correct. N.L.

Gas-Chromatographic Estimation of Urinary Oxalate and its Comparison with a Colorimetric Method. Farrington, C. J., and Chalmers, A. H. (1979), *Clin. Chem.* **25,** 1993.

Described is a specific gas chromatographic method which has been tested for specificity and has double internal standardisation. A comparison is made with the colorimetric method of Hodgkinson and Williams. N.L.

Evaluation of a Nephelometric Assay for Haptoglobin and its Clinical Usefulness. Van Lente, F., Marchand, A., and Galen, R. S. (1979), *Clin. Chem.* **25,** 2007.

An assay for Haptoglobin using a laser Nephelometer is evaluated. The assay is shown to be sensitive with good within run, and between run precision. The method shows good correlation with the electrophoresis method. N.L.

Determination of High Density Lipoprotein Cholesterol: Comparison of two precipitation methods and their applicability to clinical samples. Boni, L, and Hendrikx, A. (1980), *Clin. Chim. Acta.* **102,** 41.

Precipitation methods for HDL-Cholesterol using Sodium phosphotungstate-Magnesium Chloride and Sodium dextran sulphate-Magnesium Chloride are compared. Both are shown to give similar values. Effects of Triglyceride and Cholesterol increases and food intake on the two methods are considered. N.L.

Serum α_2-Macroglobulin Levels in Diabetes. James, K., Merriman, J., Gray, R. S., Duncan, Y. P., and Herd, R. (1980), *J. clin. Path.* **33,** 163.

α_2 macroglobulin levels determined by radial immunodiffusion in diabetics are found to be significantly higher than found in age and sex-matched controls. N.L.

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Biochemical tumour markers. M. Legge, Perinatal Biochemistry Unit, Women's Hospital, Christchurch.

An overview will be presented on the author's current experience with biochemical tumour markers and their use in detecting and monitoring tumours.

Information on the use of alpha-fetoprotein, human chorionic gonadotrophin, B-1-glycoprotein, human placental lactogen and glucose phosphate isomerase will be presented in relation to the identification and screening of tumours.

An application of computer assisted analysis in a Clinical Laboratory. Jon Atkinson, Diagnostic Laboratory, Auckland.

A technical note describing the use of a Data General Nova II mini computer interfaced to clinical laboratory analysers. The system operates in both Biochemistry and Haematology, however, the Haematology Coulter "S" Diff/Terminal interfaces will only be mentioned briefly.

The Biochemistry system operates a Technicon SMA 12/60 and a two channel AA II glucose/urea autoanalyser, handling a large workload of patient specimens in a private laboratory.

Manual data entry is also available via teleprinter terminal next to both analysers. The mini computer is on-line to a large, high speed computer which accepts verified results for processing of doctors' reports. The computer greatly simplifies workflow and data handling for laboratory staff which would otherwise be a mammoth task.

An unusual case of Neonatal Jaundice. Mrs S. Smithson, Pathology Department, Wanganui Hospital.

By virtue of definition cases of rare disease occur only infrequently, especially in the smaller centres. When a case does present itself, early diagnosis is often important in order to prevent death or permanent brain damage in an infant. This case study shows how such a diagnosis was easily established using basic technology and instrumentation, and serves as a reminder of some elementary precautions that can be overlooked in a busy laboratory.

T Units for Enzyme Determination. D. Reilly, Diagnostic Laboratory, Auckland.

This is a proposal for uniform reporting of enzyme determination. All enzymes chemistry values are corrected so that the upper limit of normal is 100.

e.g. AST upper limit is 40
factor is 100/40 = 2.5

Each test value in the usual units is multipled by 2.5. In T Units, the normal range would be up to 100.

An obvious advantage is that all laboratories would have the same normal range, regardless of method which must simplify interpretation by physicians who visit several hospitals with different methods and normal ranges.

Programmable calculations in Clinical Chemistry. E. M. Johnston, Department Clinical Chemistry, Auckland Hospital.

A brief description of experiences with currently available benchtop calculator systems with particular emphasis on their application in process control, data logging and general laboratory computing functions. The advantages of developing own software against firm programme, manufacturer supplied instrumentation.

Urine N-Aceyl Glucosaminidase (N.A.G.) in Renal Diseases. Mr R. Siebers, Chemical Pathology Department, Wellington Hospital.

N.A.G. is a lysosomal enzyme widely distributed in tissues and high activities are present in lysosomes from renal tubular epithelium.

An increase in excretion occurs with renal tubular damage and measurement of N.A.G. is a sensitive early indicator of such damage.

In our laboratory, we are trying to determine of N.A.G. excretion can be used as an early indicator of renal transplant rejection and a study is underway to determine renal involvement in rheumatoid arthritis, gout and S.L.E. It is intended to present preliminary results of these studies.

Seminal Fluid Analysis—Should we move into the twentieth century? M. Legge, Perinatal Biochemistry Unit, Women's Hospital, Christchurch.

Abstracts of Papers NZIMLT Conference 1979

H.P.L.C.—Its increasing importance in Bioanalytical Chemistry. Mr D. Scott, Waters Associates Pty Ltd.

Nearly twice as many articles on L.C. were published in the journal *Clinical Chemistry* in 1977, as in the previous year.[1] Many review chapters and some books have also been published. Some general considerations, such as equipment and techniques together with new and innovative separations will be discussed in an attempt to account for the increasing importance of HPLC in the Clinical Laboratory.

REFERENCE

1. Hercules, Hieftje, and Syndner, Contemporary topics in Analytical, and Clinical Chemistry, Vol 2, 1978.

Therapeutic Drug Monitoring. Mr G. Broad, Medical Laboratory, Hamilton.

A short review on the evolution of pharmacology and therapeutic drug monitoring is presented.

Meaningful use of serum and/or body fluid drug concentration levels is then considered with the following facets outlined:

1. Patient compliance
2. Drug absorption
3. Drug transportation
4. Drug utilisation
5. Biotransformation
6. Excretion

Protein Quantitation: Discrete Analyser V. Laser. D. J. Haines, Department of Immunology, Hamilton Medical Laboratory.

The routine quantitation of specific proteins has led to two separate techniques (discrete turbidometric analysis and nephelometry) being proposed as the successor to current methodology.

The purpose of this discussion topic is hopefully to obtain a general impression amongst those present as to the direction in which specific quantitation is moving in this country.

Polyacrylamide Disc Gel Electrophoresis of CSF and serum as an aid in the diagnosis of Multiple Sclerosis. Anne Mason, Chemical Pathology Department, Wellington Hospital.

The paper will include an introduction covering briefly the presence of unique bands in the CSF of many multiple sclerosis patients and the techniques used in past years to help in the laboratory diagnosis of multiple sclerosis.

The paper will then go on to describe a modification of Thompson *et al* technique developed at Wellington Public Hospital in assessing oligoclonal bands in CSF, including the results of a survey of 33 controls and 132 patients.

Improved Total Iron Binding Capacity Determination in Commercial Quality Control Programmes. Mr R. Shirley, Medical Laboratory, Hamilton.

An Auto Analyser method for total Iron Binding capacity was found to give consistently high values in commercial Quality Control Programmes. Values obtained from lyophilised sera of human or bovine origin were found to be pH dependent.

A simple pH modification in the iron saturation process greatly improves survey performance.

Antiepileptic Drug Analysis by EMIT. Mr G. Broad, Medical Laboratory, Hamilton.

Techniques available for drug quantitation will be reviewed.

EMIT procedures, routinely used on a series 300 Centifichem for Phenytoin and Carbazepam will be critically examined. Patients results obtained over a two year period will be presented and discussed.

The Agony Now—The Ecstasy When? Mr J. Powell, Chemical Pathology Department, Green Lane Hospital.

The development of the SMA process control module of NCLCS at the Green Lane Hospital prototype site is followed from its inception to the present time. Aspects such as design, philosophy, hardware, software, human interaction and problem resolution are considered in detail.

Balancing the quality control budget. Jan Parker, Biochemistry Department, Dunedin Hospital.

Consumption of control sera and its cost. Preparation and storage of beef sera. Calibration of SMA 660 for urea and electroytes using beef pool. Beef pool as drift control for liver function

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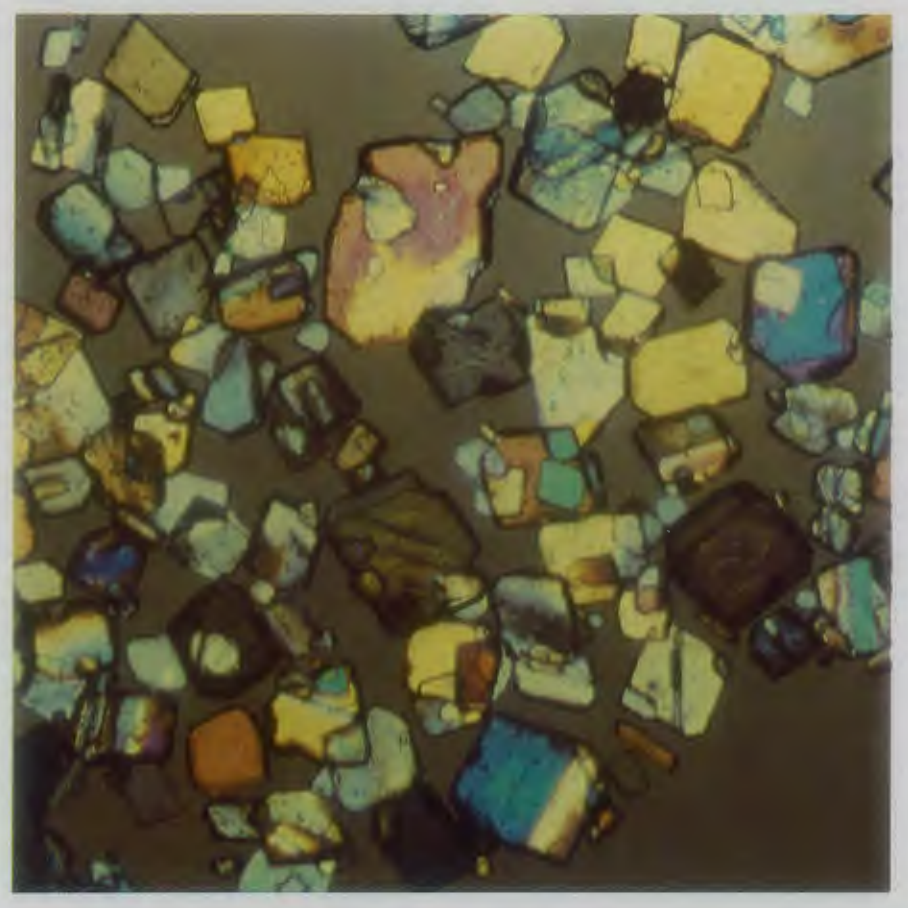

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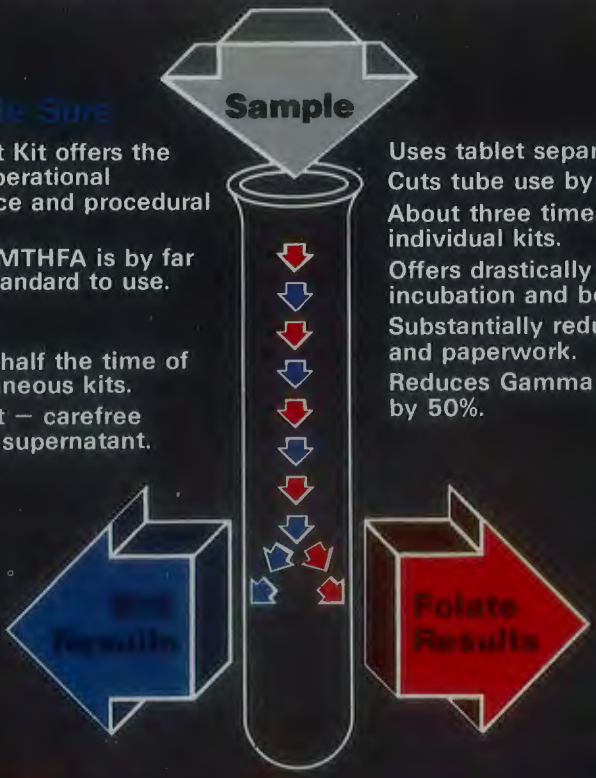

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Seminal fluid analysis has traditionally been based on a number of empirical observations such as counts, motility, staining etc. Such techniques are usually based on a single "experienced" observer and quality control is poor. We have recently been investigating the use of specific biochemical techniques to determine whether sperm are capable of fertilisation.

It is possible that biochemical analysis of seminal fluid will replace the more traditional techniques in current use. Details on such possible techniques will be presented.

Characterisation of Immune-complex-like activity in Human Sera. G. Smith, J. D. K. North and I. J. Simpson, Department of Medicine, University of Auckland Medical School.

Circulating immune-complexes are frequently demonstrable in human sera, and are thought to be responsible for tissue injury in some diseases. Although there are several satisfactory methods for the detection of circulating immune-complexes, it is now necessary to attempt to define the physical characteristics and concentrations of immune-complexes which produce disease.

Currently we are using four techniques for the detection of immune-complex-like material in human sera: the Clq deviation test, the Clq solid phase, Clq binding activity and a conglutinin binding activity. These assays all rely on the ability of the complex to fix complement. They will be described briefly.

It has been found that the Clq deviation test detects only very high molecular weight complexes. The other tests show reactivity with complexes with a variety of molecular sizes. Sera that are positive with the Clq deviation test have all been shown to have a very high molecular weight fraction on Sephrose 4B chromatography. This fraction is not lipid and cannot be digested with D.N.Ase. Positive fractions from gel filtration are being studied with immuno-diffusion and polyacrylamide gel electrophoresis.

An attempt is being made to correlate disease activity with the concentration, size and immunoglobulin composition of the detected complexes.

Our changing biochemical environment. E. K. Fletcher, Department of Clinical Chemistry, Taranaki Base Hospital.

Physiologists, biochemists and microbiologists have described man's ever improving ability to live in harmony with his external environment. Coincidental with this has been man's tendency to meddle with his internal environment. He is becoming more and more reliant on chemical support through drugs. The impact of this is just beginning to be seen. There may be a need to rewrite the textbooks. A review of the trends of the last decade and examination of where laboratory medicine might go from here is viewed from the stool at the biochemistry bench.

H.P.L.C. in the Biochemistry Laboratory. Mr D. Scott, Waters Associates Pty. Ltd.

High Performance Liquid Chromatography offers a reasonably simple, inexpensive and rugged capability to satisfy many of the current needs of clinical analysis, including reagent characterisation, research, reference samples, reference methodology, genetic screening, paediatric chemistry, speciality testing and routine analysis. Some routine assays will be discussed in practical terms, together with a description of new column technology.

Vitamin B12 and Folate Estimations by a Dual Radioisotope Kit. R. K. Anderson, Diagnostic Laboratory, Auckland.

Radioisotopic methods are now well established for measurement of serum vitamin B12 and folate but some workers still express doubt about the vitamin B12 estimations.

Past experience at Auckland Hospital has shown that some sera give normal vitamin B12 results by RIA methods when clinical, haematological and microbiological assay findings indicate vitamin B12 deficiency. For this reason, the Auckland Hospital Laboratory has continued with microbiological assays.

In 1978 a dual isotope kit for vitamin B12 and folate assay became commercially available. Improved methodology and potential savings in time and expense encouraged us to evaluate this kit.

The performance of the kit was checked by standard methods and found to be satisfactory. Normal ranges were established and sera obtained from hospital patients were tested using the dual RIA kit. These results were compared with values obtained from standard microbiological assays.

Although comparisons were good, discrepancies occurred. The RIA kit failed to detect one low vitamin B12 and six low folates.

A case of Flame Cell Myeloma. Miss K. M. Schollum, Haematology Department, Green Lane Hospital.

A case history of a 63 year old man who has flame cell (non-secretory) myeloma. This is a rare type of myeloma—1.2% of all myeloma cases—characterised by decreased immunoglobulins, no urine protein or Bence Jones protein, normal serum electrophoresis and the presence in the bone marrow of plasma cells with flame-like appearances. These cells are more commonly seen in IgA myeloma. The cells are capable of producing protein but not of secreting it thereby giving the "flame-like" appearance in the cytoplasm of the cell where the protein is stored. It is likely that this is the first case of flame cell myeloma in New Zealand.

Serial CFU-c assays using soft-agar technique in acute Myeloblastic and Lymphoblastic Leukaemia. B. F. Postlewaight, Department of Haematology, Auckland Hospital.

The *in vitro* colony-forming ability of bone marrow in acute leukaemia has been extensively studied at the time of diagnosis and clinical remission. In the acute leukaemias, the *in vitro* growth and pattern of granulocyte-committed stem cells is invariably abnormal. In both groups, colony-forming ability returns to normal levels with a normal cluster to colony ratio when remission is obtained.

Evidence has accumulated which indicates that in patients with acute granulocytic leukaemia, a variable number of cluster and colony-forming cells may be derived from leukaemic cells. Thus, excessive cluster formation with decreased colony formation is often associated with the emergence of leukaemic clones in the marrow. This pattern has previously been thought to be in contrast to acute lymphoblastic leukaemia, since there is no evidence to indicate that marrow elements other than granulocyte-committed precursors proliferate in this culture system.

Data from our laboratory concerning quantitative changes in cluster formation appear to assume a significance which has not been understood, particularly when results are interpreted.

The Diagnostic use of Cytogenetics and Cell Culture in Preleukaemic Syndromes. Mrs J. Bunn, Department of Haematology, Auckland Hospital.

A wide variety of haematological abnormalities can precede the development of acute leukaemia.

These include refractory anaemia with hypocellular marrow, pancytopenia, leucopenia and thrombocytopenia, or the occurrence in the blood of small numbers of blast cells.

The diagnosis of acute leukaemia is not always straightforward on morphological grounds alone and ancillary aids such as cytogenetic studies and cell culture preparations have been used to provide additional information.

The purpose of this paper is to review this group of pre-leukaemic patients for whom diagnosis presents a difficulty and to a lesser extent determine the relative importance of identifying chromosomes individually, such as in banding, in these cases.

An unusual case of Hb-H disease. J. E. Lucas, Haematology Department, Dunedin Hospital.

A brief resume of the Thalassaemias is presented, followed by a case report of a child with Hb-H disease caused by an unusual and unsuspected genetic combination.

An evaluation of the Coulter Counter Model S-Plus. P. A. Martin, B. K. Smith and D. J. Nicol, Department of Haematology, Royal Perth Hospital, Western Australia.

In order to cope with increasing workloads in the haematology laboratory automation has been a necessary development.

One of the most successful automated simultaneous multiple parameter analysers, the Coulter Counter Model S, was introduced in 1968. Since then widespread acceptance of this and similar automated systems from other manufacturers have greatly improved speed, precision and accuracy in the laboratory.

More recently the increase in dependence on the platelet count as a diagnostic of prognostic indicator has led to the development of automated or semi-automated stand alone systems for this test. Inclusion of the platelet count into a multiparameter system was a logical step, and the first such instrument with the Technicon Hemalog-8. In 1978 a Coulter Counter (Model S-Plus) with a simultaneous platelet counting facility was introduced.

In the Model S-Plus, basic methods for measurement of the various parameters remain unchanged from previous models, using refinements of the original Coulter principle in combination with an automatic diluting and mixing system for specimen processing.

As with the red and white cell counts, the platelet count is performed by size differentiation using a whole blood suspension. If insufficient numbers of platelets are counted the machine automatically recounts the suspension until a

statistically adequate number have been counted. This significantly increases the precision of platelet counting, especially in the important lower range (below 50 × 10^9/l). Counts of this order increase the processing time from a standard 35 secs up to 50 secs.

The machine also provides information with regard to red cell and platelet size distribution and is capable of being fully interfaced to a computer system. As well, monitoring of the machine functions is improved by use of microprocessors.

The precision of the Model S-Plus is equivalent to that of the Model S-Senior for the estimation of haemoglobin, red cell and white cell parameters. The platelet count shows excellent agreement with both manual and semi-automated systems.

The extended repertoire of this new machine makes it an excellent acquisition for any large routine haematology laboratory.

The use of a desk top computer to interface a Coulter Counter Model S-Plus to a large hospital computer system. D. J. Nicol, R. E. Davis, D. Drew, B. K. Smith and P. A. Martin, Department of Haematology, Royal Perth Hospital, Western Australia.

Automatic data capture from multiparameter analyser is faster and more accurate than manual keyboard entry. A Hewlett Packard Model 9835A desk top computer has been used to interface a Coulter Counter Model S Plus to a comprehensive haematology computer system.

The desk top computer (DTC) is programmed to enable operation in data capture or data transmit mode. It can also be used as a general system terminal.

In data capture mode, blood is aspirated into the Coulter S-Plus and a three digit specimen identifier is entered on the DTC keyboard together with a significant part of the patient's hospital record number. Results are displayed on the DTC screen as soon as generated. The Coulter S-Plus printers are not routinely used. Range checks within the DTC programme cause inverse video highlighting of specimen numbers whose results are out of range. Control blood specimens are entered against a special code. Twenty sets of results can be accumulated on the DTC screen and constitute one batch. Editing facilities allow the deletion of single sets of data, blocks of data or whole batches. Once edited, batches are written to the DTC tape cartridge. Robust means are calculated on each batch as part of the quality control programme, and printed on the DTC "tally roll" printer prior to writing the batch to tape.

Data transmit mode can be selected at any time and batches of results sent to the main frame computer (Control Data Corp. Cyber 171). To increase efficiency, only parameters actually measured by the analyser are sent, all calculated values being determined by the main computer. Specimen identifying numbers pertaining to sets of results successfully transferred to patient cumulative disc files are printed on the DTC printer. Data rejected because of specimen identifier mismatch with previously registered information, are printed on the DTC printer with an appropriate message.

The DTC programme incorporates a backup procedure for production of hard copy results on the "tally roll" printer which can serve as interim reports in the event of failure of the main system.

Normal values of Auckland children. R. T. Sheldon, Department of Haematology, Auckland Hospital.

A need to establish normal New Zealand childhood haematological values prompted this two year study. Values have been broken down into yearly segments from two to thirteen years and three monthly from one month to twenty-four months. All work was carried out using the Coulter ZF6 system.

Platelet Uptake of Dopamine. J. F. Speed, Department of Nuclear Medicine, Waikato Hospital.

It has been reported that dopamine (along with many other substances) is actively transported across the platelet membrane, and as this is a phenomenon which is shared by amine containing cells in the brain and sympathetic synaptosomes, it is thought that platelet studies may be of value in the assessment of some neurological conditions.

This paper is concerned with the technical problems associated with setting up an assay for platelet uptake studies using 14C labelled dopamine. Previous reports are discussed briefly to illustrate the difficulties associated with reproducing other workers' results, technical findings will be presented, and preliminary clinical studies will be presented.

Post-Transfusion Purpura. Miss C. Hickton, Haematology Department, Christchurch Hospital.

A woman presented with thrombocytopenia some days post-transfusion. Platelet antibodies were detected in her plasma using a platelet aggregation method.

The antibody was later identified as anti $P1^{A1}$.

An interesting case of bleeding—? Bernard Soulier Syndrome. Mrs M. Lyne, Department of Haematology, Auckland Hospital.

A case study of a young man with a long history of chronic illness and bleeding. The results of investigations performed over the last 16 years, together with recent data collected are reviewed.

A review of laboratory control in treatment of Factor VIII deficiencies. S. W. Wilson, Haematology Department, Dunedin Hospital.

This paper is a review of current methods of treatment, the variety of blood products available, and the problems involved in management and control of the hereditary Factor VIII deficiencies—Haemophilia A and Von Willebrand's Disease.

A case of acquired Factor VIII deficiency. B. R. Bishop and Dr A. E. White, Haematology Department, Dunedin Hospital.

The paper presents an unusual case of acquired Factor VIII deficiency due to an inhibitor, secondary to diffuse carcinoma.

A short history, haematological results and discussion, is followed by further clinical and histological evidence.

An unusual coagulation finding in Typhoid Fever. Miss C. Hickton, Haematology Department, Christchurch Hospital.

Prolonged coagulation results in a patient with typhoid fever were thought to be due to D.I.C. However, further investigation proved this not to be so and the possibility of an acquired Fletcher Factor deficiency is discussed.

A strange Haemolytic Phenomenon. Mr M. R. Clarke, Base Hospital, Whangarei.

A crossmatch and antibody screen on an intensive care patient showed an unusual haemolysis pattern in the indirect saline-Coombs' test. All cell specimens incubated with this patient's serum were haemolysed by the addition of broad spectrum Coombs' reagent but haemolysis did not occur with albumin-Coombs' of enzyme-Coombs' techniques.

The blood specimen had been taken while the patient was receiving an infusion of "INTRALIPID 20%" and was markedly lipaemic.

A case of Multiple Antibody Production stimulated by Pregnancy and Intrauterine Transfusion. Mrs L. B. Pinder, Auckland Blood Transfusion Centre.

The case of Mrs C. G. is followed from the initial antibody screen of her third pregnancy to her child's final exchange transfusion, some 23 weeks later. During this period she received three intrauterine transfusions and five different antibodies were detected. The nature of these antibodies and the probable reasons for this production are discussed. The problems of providing sufficient compatible blood to cover the transfusion requirements at each stage of the case are reviewed.

A red cell panel diluting fluid. D. J. Wilson, Christchurch Hospital.

A new solution in which a washed red cell panel may be suspended and stored as a working cell suspension for four weeks is described.

Results of pH, haemolysis and antigen strength throughout the four week storage period are presented and comparisons with other red cell storage solutions are made.

An evaluation of Platelet Filters. Miss K. F. Smith, Auckland Blood Transfusion Centre.

An *in vitro* study is presented which indicates that platelets are not lost during filtration and platelet recoveries were the same with all filters under study.

NIPS in New Zealand. R. J. Austin, Taranaki Base Hospital, New Plymouth.

Five National Immunohaematology Proficiency Surveys involving 51 laboratories have now been completed. This paper presents for discussion some statistics from these surveys and trends that are becoming evident.

A survey of recent Asian refugee immigrants. M. Wynn, Diagnostic Laboratory, Auckland.

The results of a recent survey of approximately 200 refugee immigrants from South East Asia are presented. Blood, urine and faecal specimens were examined.

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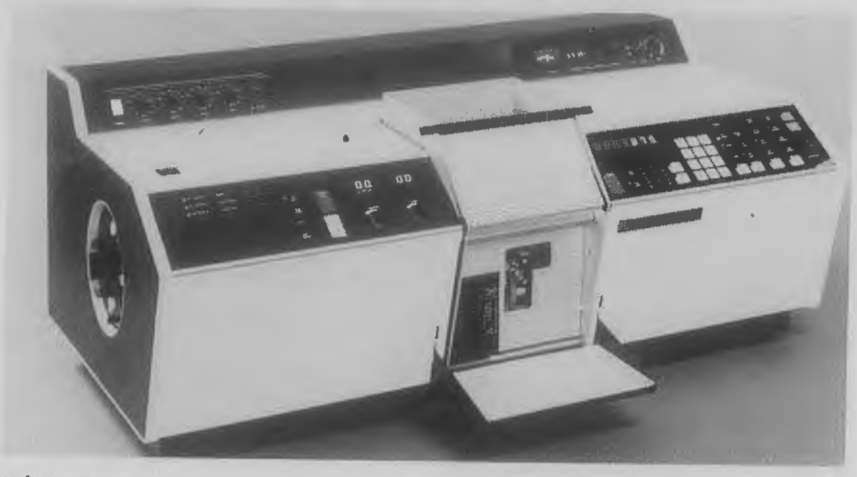

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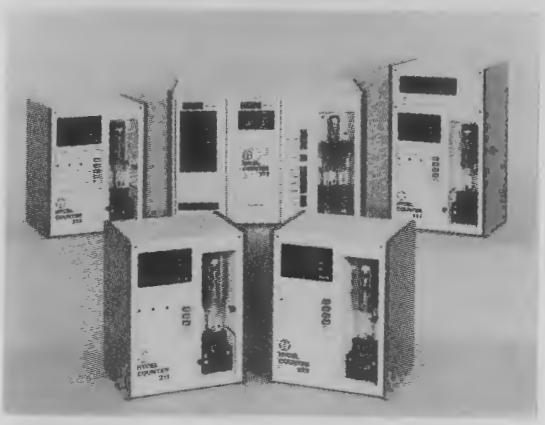

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Significant bacteriuria was detected in approximately 4% of patients. A gonococcus was isolated from one urine specimen and a urethral swab from that patient was also positive.

Haemoglobin electrophoresis indicated thalassaemia traits in a small number of patients.

The importance of receiving three faecal specimens from each person is highlighted. In many cases, parasites were only demonstrated in one sample. The typhoid carrier was identified from the second specimen and would have been missed if only one had been submitted.

Campylobacter Enteritis in New Zealand. Lynley A. Watson, Heather J. L. Brooks, Department of Microbiology and Genetics, Massey University. G. Scrimgeour, Pathology Laboratory, Palmerston North Hospital.

During a three month survey Campylobacter jejuni was isolated by selective culture from the faeces of six out of 122 patients with acute diarrhoea. The incidence of campylobacter enteritis in New Zealand was previously unknown but the overall isolation rate of 5% was comparable to that obtained in similar studies in other countries. For selection and isolation of C. jejuni faecal specimens were inoculated onto 5% blood agar containing an antibiotic supplement and incubated under reduced oxygen tension. Diarrhoea and cramping abdominal pain lasting 2-5 days were the main symptoms of infection, but two patients had a prolonged illness. Campylobacters are a recently recognised cause of acute enteritis and the results of this survey indicate a high incidence in New Zealand.

Campylobacter a "new" pathogen. L. R. Taylor, Bacteriology Department, Princess Mary Hospital for Children, Auckland.

Literature has had reports of Campylobacter and Vibrio as human pathogens over many years. The advent of the organism as a frequent isolate in human disease stems from the development of suitably inhibitory media and the recognition of its microaerophilic character.

This paper discusses the ease with which a routine laboratory can effectively screen for Campylobacter with little extra effort. It demonstrates the characteristic biochemical and colonial morphology which make it easy to find. The frequency of isolation fully justifies the effort in any laboratory at present screening for other bowel pathogens.

A review of Shigella Sonnei Colicine typing. D. M. Norris, National Health Institute.

Colicine typing has not been carried out routinely at the National Health Institute. After the large number of cases occurred in the Auckland area in 1978 representative cultures received at the Institute were colicine typed. Cultures received from 1972 have been typed and the results will be briefly reviewed.

Thyroid Antibodies in a normal New Zealand population. J. Y. Bullock, Department of Medicine, University of Auckland School of Medicine.

The occurrence of autoantibodies in a normal New Zealand population was evaluated in a recent survey, 1641 healthy males and 959 healthy females being investigated. The antibodies tested for were as follows: Antinuclear, thyroid microsomal, parietal cell, mitochondrial, smooth muscle, reticulin and, in the females only, adrenal and salivary gland antibodies. As has been observed in other population surveys and notable in the New Zealand population, there is an increased incidence of autoantibodies with age; the rise being seen in both sexes. This age-related increase is evident for most of the individual autoantibodies, the average increase being slightly higher for females than for males.

The most commonly detected autoantibodies were those against reticulin and thyroid microsomes, thyroid microsomal antibodies were observed in almost 20% of women over age 60.

Where possible, relevant ancillary investigations were performed on all autoantibody positive sera.

This paper will discuss the findings of investigations of thyroid function of 52 females, positive to thyroid microsomal autoantibodies, with ages in the range of 23-65 years.

Evaluation of 5 Thyroid H.A. test kits. J. A. Woodcock, Immunology Department, Auckland Hospital.

A number of different tests are available for the determination of microsomal and thyroglobulin antibodies in thyroid disease.

Two microsomal antibody haemoglutination

kits and three thyroglobulin antibody haemoglutination kits were compared on 140 blood samples with a view to maintaining sensitivity throughout.

Screening positive A.N.A. sera for double-stranded DNA antibodies. G. R. McLeay, Immunology Department, Auckland Hospital.

Sera with antinuclear antibodies from a titre of 1:16 upwards were tested for the presence of double-stranded DNA antibodies using the metaphase F.A. technique.

This was done to determine whether this is a useful practice for an immunology laboratory to undertake as a routine screening process for systemic lupus erythematosis in addition to clinical assessment.

The demonstration of oligoclonal bands in CSF. R. D. Allan, Chemical Pathology Department, Dunedin Hospital.

The expression oligoclonal bands was coined to describe a pattern of discrete bands appearing in the gamma region of CSF after zone electrophoresis on agarose plates.

These patterns appear in over 90 percent of clinically definite multiple sclerosis cases and smaller percentages in less definite manifestations. They also appear in other diseases such as optic neuritis, Guillain Barre syndrome, neurosyphilis, subacute sclerosing panencephalitis and chronic infections of the CNS. These diseases can usually be detected and eliminated in the differential diagnosis and demonstration of oligoclonal bands can offer strong supporting evidence of multiple sclerosis.

The technique or originally called for CSF concentrated to more than 50g/l. Later techniques such as immunofixation on agarose and polyacrylamide electrophoresis offered the possibility of performing the technique with small volumes of unconcentrated CSF.

We have not been conspicuously successful in our attempts to demonstrate these bands and would welcome advice.

A survey of Airborne Pollen and Spores in Auckland: Its use in the diagnosis of seasonal allergies. Jennifer Hillas BSc, Department of Medicine, University of Auckland School of Medicine.

A survey of airborne pollen and spores is being undertaken in Auckland, the initial results will be presented. Even at the height of the flowering seasons, meteorological factors influence greatly the concentration of pollen and spores in the atmosphere. Consideration of these factors is, therefore, essential when assessing the allergic patient's symptoms and treatment.

A flowering calendar for Auckland and common anemophilous plants, many of which produce allergenic pollen, has been prepared.

Allergy testing: Value for effort. M. W. Roberts, Immunology Department, Auckland Hospital.

We perform large numbers of skin tests for immediate of Type I hypersensitivity reaction due to IgE antibodies. We are able to compare a proportion of our skin test results with serum RAST levels for specific allergen IgE and we find good correlation between these techniques, showing the value of the prick test in all patients with symptoms of bronchial asthma, allergic rhinitis or urticaria.

Mean agreement between RAST and positive prick test is 91%.

Photographing fluorescent stained specimens. R. A. Lynch, Immunology Department, Auckland Hospital.

Rapid quenching of many fluorescent dyes presents a problem in successful photomicrography.

Sophisticated pulsed laser light sources have been recently introduced to overcome this problem but such devices are relatively expensive. An alternative intermittent light from a conventional mercury vapour lamp is discussed.

The clinical application of lymphocyte function tests. M. G. Cullinane, J. M. Drummond, M. R. Gatman, Immunology Department, Auckland Hospital.

Peripheral blood lymphocytes, despite their homogeneous morphological appearances, have been divided into four distinct sub-populations. These are T lymphocytes, B lymphocytes, K's and Nulls. T and B lymphocytes are identified by their specific surface markers and K and Null lymphocytes are calculated from these results.

The identification of these sub-populations has proven very useful in the diagnosis of lymphoproliferative disorders, and malignancies of lymphoid tissue.

A brief summary of the 2000 patients seen in this department will be given.

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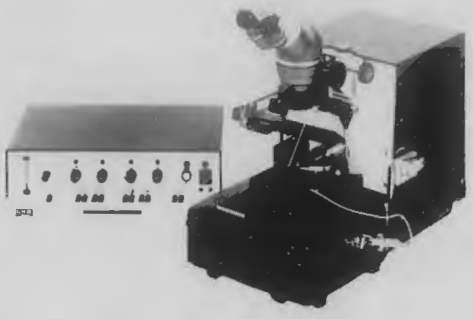

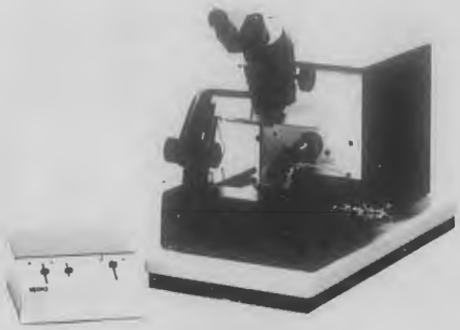

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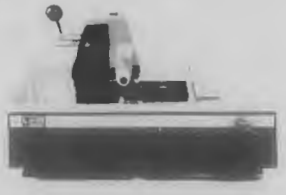

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LKB disposable knives for microtomy

- LKB HistoKnifeMaker for the laboratory preparation of glass knives for microtomy.
- Simple operation, needs no training.
- 25 mm and 38 mm knives can be made reproducibly.
- Knives fit most of the commercially available microtomes.

NEW

LKB Ultrotome V – a practical mediumpriced ultramicrotome

- Simple finger-tip slide controls for the regulation of cutting speed and section thickness.
- The new thermal advance system produces long ribbons of serial sections in the thickness range 5-200 nm.
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NEW

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LKB MultiPlate – wax dispenser for simple attachment of Trufs to knives, hot-plate for drying and staining semi-thin sections.

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Suppression of the cell-mediated immune response in infectious disease. J. Nelson and E. Marshall, Department of Medicine, Auckland Hospital.

The cellular and humoral basis of immunity to many infectious diseases has been well characterised but there are many anomalous responses, one of which is the depression of cell-mediated immune response associated with many infections.

Mononuclear phogocytic cells have been suggested to have an immuno-regulatory role and the results of experiments investigating the influence of these cells on a cell-mediated immune response will be discussed.

The investigation of patients with recurrent infections. Dr C. S. Hosking, Medical Officer to the Immunology Laboratory, Royal Children's Hospital, Melbourne, Australia.

Fringe Benefits of Diagnostic Cytology. D. Whitaker, Department of Pathology, Queen Elizabeth II Medical Centre, Perth, Western Australia.

Diagnostic cytology is mainly concerned with the screening and evaluation of smears made from various body sites with a view to finding malignant cells to confirm a diagnosis of cancer.

On occasion, the technique may provide significant information in establishing a diagnosis of non-malignant disease. This additional information has been called the "fringe-benefit" of cytology and examples of such findings are recorded here.

The range of non-malignant disease studied was wide and included conditions more likely to be primarily investigated in other laboratory disciplines. By far the most numerous fringe benefit diagnoses were made in the microbiological field.

Some fringe benefit diagnoses were made directly from the observation of a precise change in the cells or cellular patterns, however, many diagnoses were made by studying the background in which the cells occurred. Examples of such conditions are demonstrated.

It can be seen that over a period of time routine cytodiagnosis may provide much valuable information in addition to the detection of malignant cells, and that this may often be of importance diagnostically.

Guide to reticulin staining. N. D. Johnston, Histology Department, Green Lane Hospital.

A lazy man's method of reticulin staining is described, which uses fewer reagents and less time than the usual methods.

Paraffin embedding related to Neuropathology. Dr B. Synek, Auckland Hospital.

This paper will comprise a brief review of the advantages and disadvantages of paraffin embedding for the processing of neural tissues. Various modifications of traditional staining techniques which can be used on paraffin sections to demonstrate a variety of structures will be discussed.

Management of ophthalmic specimens for Histopathology. R. J. Patterson, Histology Department, Auckland Hospital.

The histology of eyes is a specialised procedure. It does not necessarily require extra equipment but does need extra care. The purpose of this paper is to review the treatment of eyes from collection to staining. Various methods of embedding are discussed and the paper is directed primarily at those with little experience of this type of specimen.

Aspects of eye pathology. Dr G. Hitchcock, Medical Laboratory, Grafton, Auckland.

An illustrated talk on some pathologically interesting eye cases.

A "same day service" for Curettings. Mrs M. Sorenson, Histology Department, National Women's Hospital.

National Women's, being the type of hospital it is, we deal mainly in gynaecological histology. In the course of their work, our medical staff do a large number of diagnostic dilation and curettage operations. To enhance patient turnover, we provide a "same day service" for these specimens where possible.

'In vitro' antimicrobial susceptibility of Neisseria meningitidis from 1975. M. J. Green and P. F. M. Cawley, National Health Institute.

Isolates of N. meningitidis are referred to the National Health Institute for confirmation of identification and serogrouping. Since 1975, the

susceptibility of these isolates to penicillin, sulphadiazine, rifampicin and minocycline has been determined as part of a surveillance programme to detect emerging antimicrobial resistance in groups of organisms of public health importance.

The antimicrobial susceptibility and serogrouping of the isolates will be discussed with reference to the health districts from which they were referred.

Cephalosporins, Enterobacteriaceae and sensitivity testing. Joan Lynch and Graham Cameron.

As part of a larger survey, 443 isolates of members of the family Enterobacteriaceae were tested for sentivity to Cephalosporin antibiotics by disc diffusion and plate M.I.C. methods. The correlation between the zone sizes produced and the M.I.C.'s of these organisms was found to be unacceptable. As a result, the disc test is shown to be an unreliable method or predicting the sensitivity of members of this family to Cephalosporin antibiotics.

Staphylococcus aureus, β-lactamase production and sensitivity testing. G. Camerson, I. Te Wiata, Microbiology Department, Auckland Hospital.

The resistance of Staphylococcus aureus to benzylpenicillin is dependent upon the production of β-lactamase. Any method used routinely for the sensivity testing of Staphylococcus aureus to benzylpenicillin must be able to demonstrate this phenomenon clearly.

100 isolates of Staphylococcus aureus were tested for penicillin sensitivity by disc diffusion and plate replicater method. This paper describes the results obtained and discusses the implications.

Drug Therapy of primary Amoebic Meningo-Encephalitis (PAM). C. Elmsly, J. J. Donald, E. A. Keys and T. J. Brown, Department of Microbiology and Genetics, Massey Univesity.

Miconazole a substituted phenyl innidazole and R41400, a new synthesised member of the innidazole group, which has not yet been released commercially, have been tested against *Naegleria fowleri* (MsT, MsM) and *N. gruberi* (P1200f) *in vitro*, and against *N. fowleri* (MsT, MsM) in cell culture and *in vivo*.

In vitro tests with Miconazole showed with P1200f on MIC of $5\mu g.cm^{-3}$ and MAC of $10\mu g.cm^{-3}$ whereas with MsT the MIC is $10\mu g.cm^{-3}$ and MAC is $50\mu g.cm^{-3}$, and with R41400 against P1200f MIC was $10\mu g.cm^{-3}$ and this concentration was the MAC for MsT. The MAC for P1200f was $50\mu g.cm^{-3}$.

In cell culture the effectiveness of the drugs was judged by their ability to prevent cytopathic effects (CPE) due to the amoebae. Cognizance was also taken of the cytotoxic effect (CTE) on the monolayer of the drug itself. In the cases of both drugs $10\mu g.cm^{-3}$ sterilised the cell culture but also caused CTE.

Intra-peritoneal infections into infected mice have been ineffective. Intra-ventricular application of the drugs has been started to defeat the blood/brain barrier which is impermeable to many compounds.

A "look" at the New Zealand proficiency test programme in microbiology. D. M. Norris, S. Gubbins, National Health Institute.

A discussion on how the programme is carried out and a general comparison of the way in which the laboratories of different sizes have performed will be given.

Semen analysis for virgins. John Aitkin, Princess Margaret Hospital, Christchurch.

The establishment of a service for seminal analysis is described.

The methods currently used in semen appraisal and some of the difficulties experienced in analysis are outlined.

Antibody-coated Bacteria: A method for localising urinary tract infection. Heather J. L. Brooks, Department of Microbiology and Genetics, Massey University.

A simple test which distinguishes between infections confined to the bladder and kidney infections is of clinical value. Such a test was devised by Thomas *et al* (1974) and has marked advantages over more invasive procedures such as ureteric catheterisation. The test is based on the finding that bacteria which localise in the kidney become coated in antibody, whilst those which localise in the bladder do not. Antibody-coated bacteria may be detected using fluorescent anti-human gamma globulin. Since its genesis, the "antibody-coated bacteria" test has been severely

criticised. False positive results appear to be particularly common in children due to the presence of antibody-coated contaminants in voided urine specimens.

The present investigation was undertaken to assess the incidence of antibody-coated bacteria in urine specimens from adult, female patients with bacteriuria due to *Escherichia coli* and from healthy women. A semi-quantitative approach was used which appears to be of value in distinguishing between true cases of kidney infection and contamination of voided urine specimens with extraneous antibody-coated organisms.

Laboratory experiences with Cryptococcosis in Auckland. D. Parr, V. Wills, Dr D. Bremner, Microbiology Department, Auckland Hospital.

Cryptococcosis is a comparatively rare disease in New Zealand. There have been 15 cases in Auckland in the past 10 years. The possibility of an increased incidence especially among the immunologically incompetent population must be kept in mind. The disease most commonly presents as a low grade meningitis, sometimes with involvement of other organs but may present with obscure symptoms so a diagnosis of cryptococcosis is not always primarily considered. The need for well alerted laboratory staff to aid in this diagnosis is essential.

A brief review is given of some recent cases at Auckland Hospital, laboratory procedures including the latex agglutination test for cryptococcal antigen are discussed, and attention is drawn to difficulties which have been encountered in our experience with *Cryptococcus neoformans* infections.

ERRATUM

N.Z. J. med. Lab. Technol. (1980), **34,** 15. National Immunohaematology Proficiency Survey (NIPS). A Summary of Results.

One of the co-authors was incorrectly designated J. Austin. This should have been R. J. Austin. Roger Austin wishes me to correct this error lest there should be confusion with the illustrious lady author, Jane Austen, now deceased, who wrote, Emma, Northanger Abbey, Pride and Prejudice and other novels. *I did correct it once, but it reappeared!*

Editor.

INDEX TO ADVERTISERS

Contents

Articles

Directions for Contributors

Original papers on topics related to medical laboratory science will be considered for publication. The original manuscript and one copy are required. Manuscripts should be typed on one side of the paper only, have 1 in margins and be double spaced. Give the author's name with initials or one first name if desired. Indicate the address of the laboratory where the work was carried out. Only use capitals where grammatically indicated and not for headings. Underline only where italics are required.

In general, papers other than reviews should consist of a short summary capable of standing alone as an abstract; an Introduction (outlining the problem and the proposed solution); Material and Methods; Results and Discussion.

Illustrations

Figures; cover graphs, photographs and drawings. The latter should be in black ink on stout paper. They should be about twice the size of the intended reproduction. Number consecutively with arabic numerals (1, 2, etc.) and identify on the back. Legends are typed on a separate sheet.

Tables are typed separately and numbered with roman numerals (I, II etc.).

Nomenclature and Units

Scientific names of micro-organisms should conform with Bergey's Manual of Determinative Bacteriology. The first time an organism is mentioned the full generic name should be given and underlined to indicate that it is to be printed in italics. Subsequently it may be abbreviated. Trivial or common names are printed in roman, e.g., staphylococci, and should not be underlined.

To conform with the Systemes Internationale D'Unites or SI units it is recommended that the following prefixes and abbreviations be employed.

Length: m, cm, mm, μm, nm.
Area: m^2, cm^2, mm^2, μm^2.
Volume: litre, ml, μl, nl, pl ('litre' in full avoids confusion with 'l')
Mass: kg, g, mg, μg, ng, pg
Mass concentrations: mol/litre, mmol/litre, μmol/litre, nmol/litre.
Temperature: Express as °C.
Time: s, min, h, d, a. The latter two symbols which stand for day and year respectively are best expressed in full to avoid confusion.
Density: kg/litre (relative density replaces 'specfic gravity')
Clearance: litre/s, ml/s

N.B.:

1. The symbol for a unit is unaltered in the plural and should not be followed by a full stop, e.g., 5 cm not 5 cm. nor 5 cms.

2. No space should be left between the symbol for a prefix and the unit. A space is left between the symbols in derived units,

e.g., ms = millisecond
m s = metre x second

Where ambiguity could arise words should be written in full.

3. **Numbers.** The decimal is indicated by a full stop. Commas are not used to divide large numbers but a space is left after every third digit.

A zero should precede numbers less than unity. Units which give a number between 0.1 and 1000 should be chosen when possible.

References should be listed alphabetically by author, at the end of the article and numbered in order. All authors' names must be listed with initials; year of publication in brackets; journal title abbreviated according to the World List of Scientific Periodicals. (In general nouns have capitals, adjectives do not and conjunctions are omitted. Previous journals may be consulted.) The title is underlined to indicate italics. This is followed by the volume number underlined with a wavy line to indicate bold type and finally the first page number.

Citations in the text are given the author's name using et al. if more than one, the year and the reference number as a superscript. Thus: Lowe *et al.* (1978)[1]

Proofs

When time permits, authors will be given the opportunity to correct proofs before publication, but not to insert new material. Proofs must be returned within three days of receipt.

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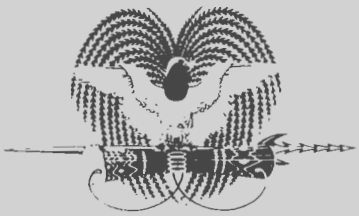

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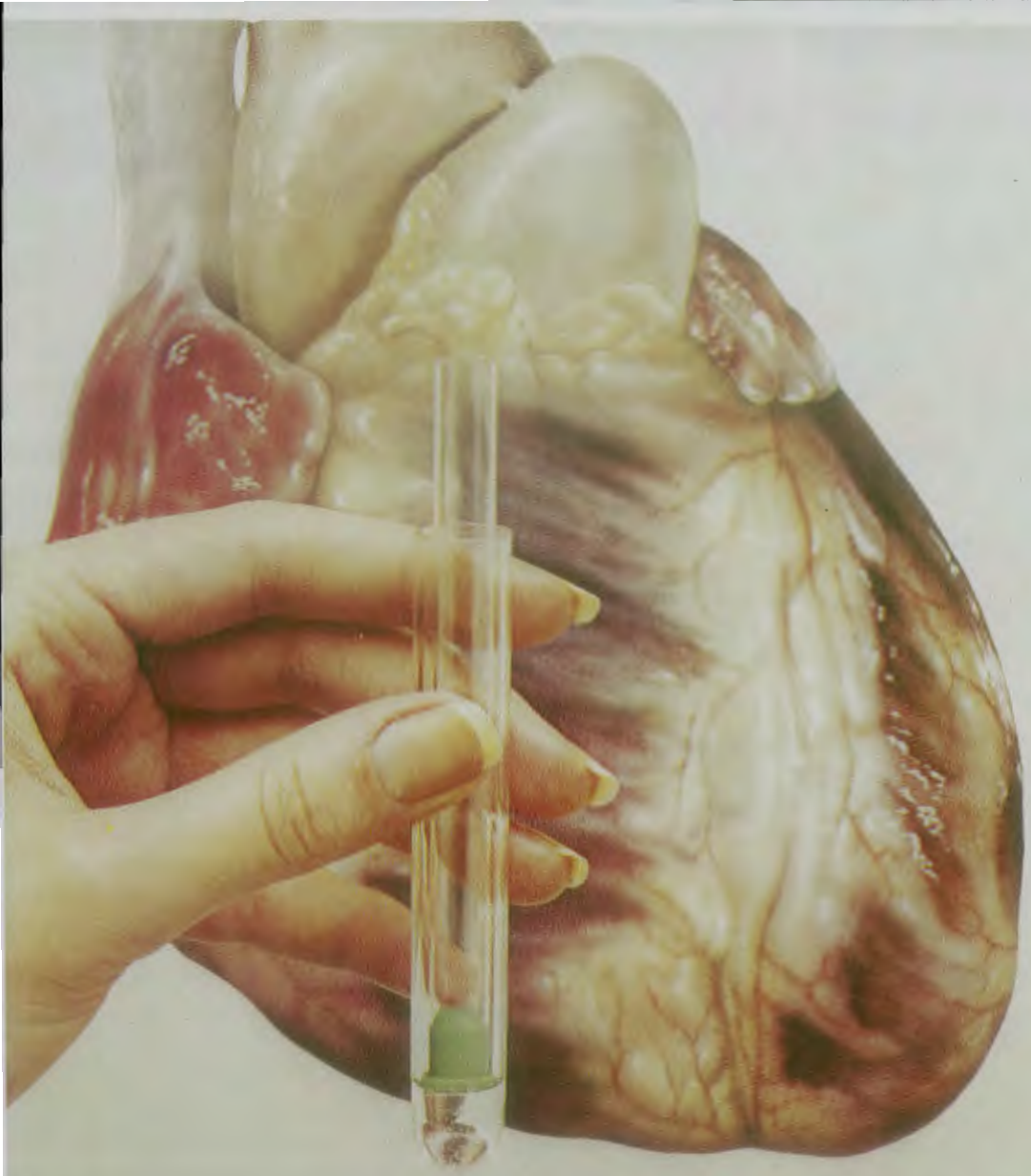

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