NOVEMBER, 1978

THE NEW ZEALAND JOURNAL OF

medical laboratory technology

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

VOLUME 32, No

The New Zealand Journal of Medical Laboratory Technology

Volume 32, No. 3 November, 1978

The JOURNAL is published three times yearly (in March, July and November), and is distributed, without charge, to all financial members of the N.Z.I.M.L.T. (Inc.).

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.

Inquiries regarding advertising rates and copy or blocks for advertising should be addressed to the Advertising Manager, Otago Daily Times, P.O. Box 181, Dunedin.

Communications primarily concerning the Institute should be addressed to the Secretary.

Changes of address should be notified promptly to the Convener of the Membership Sub-commitee, Mr C. S. Curtis, P.O. Box 52, Hamilton.

T. H. Pullar Memorial Address 1978

Plotting a Proper Course

R. T. Kennedy, FNZIMLT, ANZIM

When your Honorary Secretary contacted me on the telephone about delivering this address my first reaction was that this privilege was surely reserved for those oldies such as Philip and Hutchings and that as a youthful member of the jet set I could not be expected to join the ranks of these venerable gentlemen. It was politely implied that I was in fact a member of the geriatric club and I must admit that a recent game of hockey has convinced me that I am not as young as I used to be.

I wish, however, to thank the Council for the honour of inviting me to deliver this address.

I do not ever remember meeting Dr Pullar but it is inevitable as the years pass that the addressers your Council honours will be in this category. I thought that in order to pay my small tribute to Dr Pullar I would give you a brief potted history of the address.

Dr Pullar died on August 29, 1966. At the Council Meeting of April, 1967, on the motion of Kennedy and Fletcher the address was set up, the first being delivered at the Conference in Christchurch in 1967 by that eminent haematologist Dr Fred Gunz. The addressers who followed were Drs Lynch, Williams, Markham, Kenealy, Herdson and Stewart. The first medical technologist was Harry Hutchings in 1974, followed by John Case, Dr Staveley and your immediate past-president and international congress representative, Des Philip.

Some time ago I was discussing with a senior physician in my hospital the number of laboratory tests generated from his area. He was somewhat defensive, having been recently investigated by a select committee of the Medical Audit Department, otherwise known as the MAD Committee. When forced into a corner he stated that he often did not have as much time as he would like to spend with his patients and as he thought he should do something for them, he sent them out for laboratory tests.

The Intensive Care area of Auckland Hospital is a large generator of laboratory tests. Amongst those ordered were daily electrolytes on various body fluids. When questioned about this the physician-in-charge stated that he only wanted the results twice a week but found it easier to instruct the nursing staff to collect all fluids every day and send them to the laboratory.

At a recent meeting a histopathologist noted with concern the falling number of hospital post mortems and said that this had a bad effect on the teaching programme. A colleague replied, using that eight-letter word made famous by Germain Greer which refers to bovine faecal material, if registrars were genuinely interested in a case they would, on their own initiative, follow up a post mortem.

Here is a poem by anon. with some help from Dorothy.

There was a young medic from Gore
Who requested tests by the score,
When told they cost money,
He replied, that is funny,
Why wasn't I told this before.
The prof. at the school didn't say
And the registrar showed me the way
To fill every form in early each mornnig
So the lab. would have work for the day.

Ladies and gentlemen, lest you think that this address is somewhat like the first disjointed 30 minutes of the film "Close Encounters of the Third Kind" let me return you to earth with the serious title of this address, "Plotting a Proper Course".

All of the short stories I have just told you are true and the poem has its serious side. They have been used to illustrate the ease with which laboratory tests can be ordered and the almost complete disregard by some of their costs. You will all be aware of the almost continuous bombardment of articles both in the popular press and the medical literature on health spending. In all developed countries of the world there has been a growing concern of the amount spent on

health. Some of the percentages of gross national products are:

United States of America	8.5 expected to rise to 10 by 1980.
Australia	7.6
Canada and France	7
Germany	9.5
New Zealand	6

The worry to administrators is that all figures are rising. Three United States Presidents have tried to contain health costs. They have not been successful in a country where doctors are getting richer faster than any other occupational class, outstripping lawyers in earnings by two to one, although lawyers are desperately trying to catch up with malpractice suits. It has recently been suggested that a medical bank be set up, in the same way that President Eisenhower set up his soil bank to pay farmers not to grow crops, in which doctors will be paid for not doctoring. The idea being that as many of the people treated by doctors would be better off left alone, the country might save money.

Several factors can be identified as the cause of this situation. They range through too many doctors, too much expected from medicine by the public, private insurance payments, to just bad management. Undoubtedly it is a combination of all these and many more. The one factor, however, that has led to dramatic increases in costs in both the public and private sectors has been that associated with the rise of technology in medicine. Alvin Toffler, the author of "Future Shock", speaks of the general fantastic spurt forward in our lifestyle as being due to technology feeding upon itself. Technology makes more technology possible, he says, as we can see if we look for a moment at the process of innovation. Technological innovation consists of three stages linked together into a self-reinforcing cycle. Firstly, there is the creative feasible idea, second, its practical application and third, its diffusion through society. The process is complete and the loop closed with the diffusion of technology embodying the new idea which in time helps generate new creative ideas. There is evidence today that the time between each phase is shortening, thus technology feeds upon itself. This technology in medicine has resulted in developments which now come heralded with such superlatives as miraculous, wonder, breakthrough, advance of the century and so on. Despite these advances I wonder just how much better off we are. Medical matters surround us in our daily lives whether we wish it or not. The press and television constantly remind us about the wonders of medicine and doubtless it is for this reason that the population at large have come to rely more and more on doctors to look after them and less and less on their own initiative. We may well ask ourselves are we a healthier people for the millions of dollars poured into health?

To find an answer to this question is like searching for the proverbial needle in the haystack. What is health? How do you measure improvements in health? Can you put a cost on a life or assess palliative treatment? Is the cost of screening the population for a disease with an incidence of 1 in 20,000 worthwhile? How much should we spend on preventative medicine as opposed to the 70 percent of the entire health vote presently spent on hospitals?

These and other such profound questions have stretched the minds of many people. If you are a supporter of Ivan Ilich you would agree that large areas of modern medicine are not only useless but quite frankly harmful. For those of us who have been seen the jungle of ironmongery and electronics in our intensive care units, who could argue with a return to death with dignity.

I would suggest to you that despite the vast sums spent all over the world on what is called modern medicine, we are only marginally better off healthwise. As far as hospital medicine is concerned Ilich has gone as far as to say that the age of hospital medicine which from rise to fall has not lasted more than a century and a half is coming to an end. The acute problems of manpower, money, access and control which beset hospitals everywhere can be interpreted as symptoms of a new crisis in the concept of disease.

These provocative statements may not be acceptable to many of you, but I suggest that large parts of the health services, both public and private, are not managed and that there is a lack of aggressive decision making.

The consequences are waste. Furthermore, if houses are not put in order services will run down, for there is an obvious limit to the slice of the cake that can be made available in any country.

The health services should be regarded as an ancillary industry and administered as such. There is no reason to believe that the highest of humanitarian principles will not survive well in an atmosphere of proper management.

In our own area of medical technology we have a microcosm of the problems confronting the entire health service. The total spending on pathology services, both public and private, is around $30 million per annum, which you will agree is not an insignificant sum. If we were to ask the same questions about value for money we would be faced with the same problems of how to measure our effectiveness. Whilst it may be impossible to measure our contribution to patient care we can examine our own operations from a standpoint of responsible management.

Before developing this theme let me make it clear that I believe when properly used the scientific method in medicine as exemplified in our case by analytical techniques offers a powerful tool to assist in diagnosis and treatment. What concerns me is that through misuse we are helping to propagate the worst aspects of burgeoning technology in medicine.

Laboratories throughout the world have been going through a period of unprecedented growth with figures of 10-20 percent increases per annum being reported. This is particularly so in clinical chemistry and haematology. I am always suspicious when I see such figures quoted, because one is never quite sure on what basis they have been derived. However, assuming they are correct, one may well ask the $64,000 question, "which came first, the chicken or the egg?" By this I mean did the laboratory genuinely respond to demands or did it inflate its own figures by, for instance, the acquisition of multi-channel equipment in chemistry and haematology. Automation in clinical chemistry, and haematology to a lesser extent represents a good example of technology feeding upon technology. The development of single channel analysers of the 1950s through to the sophisticated multichannel machines of the 1970s resulted in the development of a new breed of laboratory worker. This has prompted Astrup to state that the departments more and more seem to resemble supermarkets where the customers just get their articles and where interchange between customers and dealers is reduced to complaints when articles are not available in sufficient amounts or of satisfactory quality. It also started a vicious cycle. Not only did these machines manage the workload efficiently and accurately but they opened the door to a whole new concept of profiling which was supposed to assist medical staff to provide quicker and better diagnosis and also facilitate the detection of pre-symptomatic disease. The great conspiracy had started. Arguments were also produced that this approach was cost justifiable and would help turn-around patients more quickly. Pretty soon people were saying that large block testing was in fact a requirement of medical staff. What was not appreciated at the time was that once these machines were installed they would need upgrading and replacement and this would be increasingly expensive, the newer machines would most likely produce more results, that data-processing facilities would be needed to handle the paper work and that many more tests would be produced than the actual clinical requirement.

The economic arguments in support were extremely shaky to say the least. The height of absurdity has now been reached where one machine can do 20 tests per sample and perhaps 17 will not be reported, so that the requesting doctor can get the three he actually asked for.

I put it to you that in an area such as ours where we cannot demonstrate our total cost effectiveness, that we should be propagating this approach, is totally irresponsible. Whatever the arguments are on cost in relation to multichannel machines, and I am extremely suspicious of most of them, this approach is bad medicine. The laboratory has to accept responsibility for producing a generation of doctors who have had forced on them massive testing programmes and who are now so used to multichannel machines, computer printouts, pre-printed and blocked request forms and easy access to blood collecting facilities, that they cannot be blamed for their lack of ability to use the service with discrimination.

Furthermore, once they get out of the hospital into private practice the whole problem spills over into private pathology and the demands now placed upon them are similar to those placed upon the hospital service.

Not only must clinical chemistry departments be blamed but also haematology departments where the same type of equipment exists. One can also see with the acquisition of white cell/differential machines the propensity for such departments to develop long range diagnosis based on a blood film will be further extended. In microbiology departments there will be requests for gas chromatographs for bacterial identification and automated antibiotic sensitivity equipment. If this is the trend in a country like New Zealand where there are no huge centralised laboratories, I wonder if all training programmes should be scrapped in favour of a button-pushing diploma.

Apart from the contribution of advanced technology to our self-styled increasing workload there are also those associated with bad requesting habits by medical staff. Bad requesting habits are caused by poor training, abrogation of authority for requesting to clerical and nursing staff, lack of awareness of costs, pressure from peers, insufficient interpretative skills, lack of appreciation of the role of the laboratory and so on. Much of the responsibility for this situation squarely rests on the heads of the medical school educators.

If I were asked what I would do to solve these problems, my first suggestion would be to have included in the medical course some down-to-earth and practical teaching on management techniques in relation to medicine. The second thing I would do as a laboratory professional would be to aggressively argue that there should be an active role played by both technologists and pathologists to contain and rationalise the workload. To accept the passive service role, which simply means that the laboratory is there to respond to demands made upon it presumes that clinical staff are well informed and use our service with discrimination. It assumes they understand precision limits, limitations of reference ranges, the various interfering agents, the erroneous results from poorly collected samples and so on. I suggest that this is not the case and in the absence of a discerning consumer it is up to us to take the initiative.

To pursue this policy of workload containment and rationalisation further, the laboratory professionals must also ensure that they are not the guilty party in workload expansion. We have all seen the results when new tests are made available that go unvetted when services are introduced that may not be a requirement of clinical staff and of generally taking the easy way out instead of practising sound management. A decision to increase workloads as part of empire building or for rather naive humanitarian reasons has no place in modern medicine.

This policy, of which I am an advocate, is based on sound common sense and basic management techniques.

When applied in the correct way they provide a powerful and almost irrefutable argument in containing the workload. The second part of the policy of workload rationalisation requires laboratory professionals to cut out the deadwood, duplication and other wasteful practices. Where a hospital is in a steady state with regard to its admissions and outpatient attendances there is no reason why the laboratory workload should grow.

To conclude — this country has several unique features with regard to our profession. It is still not too large for us to know and be able to talk with one another at all levels and although there are occasionally areas of disagreement between technologists and pathologists, we have sufficient respect for each other to be able to work towards a common goal. For the size of the country we are reasonably well equipped and we produce first rate technologists from our training programmes. Accordingly we ought to be able to work together taking into account that there is an obvious limit to the amount of money that can be made available, that all overseas practices are not necessarily desirable and that technological developments should be controlled.

Amongst the best resources we have are our well trained technologists who in many instances do not need replacing with machines and who do not need to be produced at an uncontrolled rate. Given these intentions in combination with the application of sound management should be able to provide an

atmosphere which sets these desirable and achievable goals of a steady state workload and a first class service. This will then provide a basis for reasonably accurate, short and long term planning.

H. G. Wells wrote in 1905, "modern medicine might be compared to a mighty and glamorous ocean liner, with powerful engines and luxurious appointments, but with no compass and an absurdly small rudder, it moves fast but its course has not been plotted. Its ports of call are unending and its destination unknown". I believe we can contribute to the plotting of a proper course.

Ladies and gentlemen, it has been both my pleasure and my privilege to have presented to you the twelfth T. H. Pullar Memorial Address.

Antibiotic Sensitivity Discs. Are They Reliable?

Judith M. Bragger and Helen M. Heffernan
National Health Institute, Wellington

Received for publication, January 1978

Summary

Methods were developed, based on the official methods of the Food and Drug Administration (F.D.A.), for the examination of antibiotic sensitivity discs. Forty-five (45) batches of single discs, 41 from New Zealand manufacturers and four from one United Kingdom manufacturer, were examined for uniformity and potency. Less than 60 percent of the batches tested had potency estimates between 67 percent and 150 percent of labelled potency and only 55 percent met the F.D.A. requirements for uniformity. Overall only 10 (22 percent) of the 45 batches met the F.D.A. requirements for both uniformity and potency.

Introduction

Antibiotic sensitivity discs, used in the diagnostic laboratory to determine the susceptibility of micro-organisms, play an important part in ensuring the rational use of antimicrobial agents. Susceptibility or resistance is frequently determined by reference to standard interpretative tables of inhibition zone diameters. It is, therefore, important not only that the discs contain the stated content but that they produce the inhibition zone-size expected for that content.

Where the control and test organisms are on separate plates with a disc for each plate, as in the Kirby-Bauer (Bauer *et al.*, 1966)[2] and International Collaborative Study (ICS) (Ericsson and Sherns, 1971)[3] methods, there must also be uniformity among the discs in any batch. The interpretative tables for the Kirby-Bauer technique, recommended by the Food and Drug Administration (F.D.A.) (Federal Register, 1972)[5], have been derived from results obtained with discs conforming to the F.D.A. requirements.

While New Zealand has no statutory requirements for sensitivity discs similar to those of the F.D.A., it is of interest to determine whether the discs manufactured in New Zealand meet the F.D.A. requirements. Surveys conducted by the F.D.A. between 1958 and 1961 showed that 25 percent to 66 percent of commercially available discs failed to meet label claims (Wright, 1974)[12].

After the introduction, in 1962, of F.D.A. certification the rejection rate fell to between 1.8 percent to 5 percent. Hill (1966)[8] has previously demonstrated deficiencies in discs manufactured in New Zealand.

The F.D.A. Regulations (Federal Register, 1962[4], 1972[5]) require that the assay method has 95 percent confidence limits no greater than 67 percent to 150 percent of the assay value. Each batch of discs must give an average assay performance between 67 percent and 150 percent of labelled potency, with a uniformity among discs such that the difference between the largest and smallest zone observed is no greater than 2.5 mm. This study examines the uniformity and potency of antibiotic sensitivity discs manufactured in New Zealand.

Materials and Methods

Antimicrobial Agents:

Powders for the preparation of control discs

were obtained from local suppliers and stored at —20°C over desiccant.

Media (Refer to Table I):

A Medium A as formulated in the British Pharmacopoeia 1973 (Appendix A.102), at pH 6.6, 7.8 and 8.1.

B Medium B as formulated in the British Pharmacopoeia 1973 (Appendix A.102).

WT Wellcotest Sensitivity Test Agar (Wellcome CM 49).

Micro-organisms (Refer to Table I):

1. *Bacillus pumilus* NCTC 8241.
2. *Bacillus subtilis* NCTC 8236.
3. *Bordetella bronchiseptica* NCTC 8344.
4. *Escherichia coli* ATCC 25922.
5. *Staphylococcus aureus* ATCC 25923.

B. pumilus, B. subtilis and *Bordetella bronchiseptica* were maintained and the inocula prepared as in the British Pharmacopoeia 1973 (Appendix A.102).

E. coli and *S. aureus* were maintained and the inocula prepared as for the Barry overlay modification of the Kirby-Bauer method of sensitivity testing (Barry *et al.*, 1970)[1].

Assay Plates:

All assays were performed on 305 mm (12 inch) square glass plates. Each plate was placed on a level table and poured with 250 ml of medium, then 150 ml of seeded medium was overlaid. The total depth of agar was 3-4 mm. The plates were left open for 30 minutes to dry.

Sixty-four discs, randomised in an 8 x 8 latin square, were placed on each plate.

Control Discs:

Discs with a diameter of 6.5 mm were punched from Whatman No. 15 paper.

Solutions of each antimicrobial agent were prepared, in the solvents indicated in Table 1, at concentrations 40 times the required content of the discs. The discs were placed on a wire-mesh screen and the antibiotic solution of the appropriate concentration was added to each disc using a 25 microlitre Oxford pipette. The discs were dried on the screen for two hours at 37°C, then used immediately.

Test Discs:

Discs from two New Zealand manufacturers (Manufacturers A and B) were obtained by normal ordering procedures. In addition some penicillin discs were obtained from one United Kingdom manufacturer (Manufacturer C). On receipt all discs were stored in a desiccator at 4°C or —20°C, as specified by the manufacturer.

Batches of single discs of 21 different antibiotics were tested, 21 from Manufacturer A, 20 from Manufacturer B and four from Manufacturer C. Lincomycin was supplied as 2 mcg discs by Manufacturer B and 10 mcg discs by Manufacturer A. Manufacturer A supplied benzyl penicillin as 2, 5 and 10 unit discs. All three were tested. Only one vial from a batch of each type of disc from each manufacturer was tested, making a total of 45 batches.

Assay:

Although the assay methods were based on the official methods of the F.D.A. in most assays the organism chosen differs from that recommended by the F.D.A. It was found that the organisms recommended for the assays of penicillin, methicillin, chloramphenicol and tetracycline all produced zones of inhibition with such indistinct edges that accurate measurement of the zone diameters was very difficult, while those recommended for the assays of erythromycin, neomycin sulphate and streptomycin did not produce linear dose-response lines.

Dose-response relationships were determined with a number of organisms for each antimicrobial. Control discs were prepared to contain 50 percent, 67 percent, 100 percent, 150 percent and 200 percent of the labelled content of the discs to be tested. Eight replicates of each control disc were tested against each organism and a graph of the logarithm of the antimicrobial concentration versus the inhibition zone diameter (dose-response line) was prepared. An organism was selected which gave suitable zones of inhibition, a significant change in the zone diameter between each dose and a linear dose-response line (or the best approach to this). Most of the dose-response lines had some degree of curvature, especially below 67 percent or above 150 percent. The 50 percent and 200 percent doses were included to ensure that neither the 67 percent nor the 150 percent dose fell on a plateau of the dose-response line where there was little or no change in inhibition zone diameter for a further change in antimicrobial concentration.

AUTOMATIC

AVL
AVL
AVL
AVL
AVL
AVL
AVL
AVL
AVL
AVL

GAS CHECK AVL 940

... fully automatic ph/blood gas analyzer requires only 40 µl samples

New!

— blood sample always visible
— fetal hemoglobin switch
— fast analysis: 50 sec
— built-in gas mixer

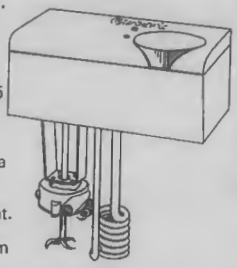
AVL AG Biomedical Instruments
P. O. B. 10, Grabenstrasse 11
CH - 8201 Schaffhausen/Switzerland
Phone: (053) 5 31 13, Telex: 76 358

SELBY-WILTON SCIENTIFIC
Auckland — Wellington — Christchurch — Dunedin

When it's by Grant, it's good! .... and it's guaranteed!

Everything by Grant of Cambridge England has a three year guarantee.

And, new from Grant. New Clip-on control units.



Now available in New Zealand, through Smith Biolab, Grant SU5 and SU6 control units can be used to convert virtually any tank to a thermostatic bath, or to a reservoir for pumping temperature-controlled liquid to other equipment. Two types of control systems, liquid expansion thermostat and all electronic thermistor thermostat are available.

Grant Instruments (Cambridge) Limited offer a comprehensive range of general and specialised Laboratory equipment available through the sole New Zealand Agents Smith Biolab.

- **SPECIALISED LABORATORY EQUIPMENT**
  Copenhagen Seed-Testing Baths.
  Dewpoint cabinet for plant propagation.
  Inspissators for culture media.
  Gerber/Reductase baths for dairy labs.
- **EQUIPMENT FOR BLOOD PRODUCT LABORATORIES**
  Shell Freezers for cryoprecipitate.
  Plasma bag freezers.
  Plasma bag thawing baths.
- **CLINICAL EQUIPMENT**
  Bloodwarming baths for transfusions.
  Perometer blood loss monitor.
  Caloric Test appatarus.
- **TEMPERATURE CONTROL SYSTEMS**
- **UNSTIRRED WATER BATHS**
- **STAINLESS STEEL THERMOSTATIC WATER BATHS**
- **ACCESSORIES FOR STAINLESS STEEL WATER BATHS**
  Refrigerated cooler units.
  Test tube racks, lids, etc.
- **SHAKING BATHS**
- **LOW TEMPERATURE THERMOSTATIC BATHS**
- **HIGH TEMPERATURE THERMOSTATIC BATHS**
- **CIRCULATORS**
  FH flow-heater
  FC flow-coolers.
- **PUMPS AND STIRRERS**
- **SAFETY CUTOUTS**
- **BLOCK THERMOSTATS**
- **THERMOSTATIC CONTROL UNITS**
- **CO_2 INCUBATORS**

Bringing a world of choice as close as your telephone with personal service throughout New Zealand.

SCIENTIFIC DIVISION

with resident representatives in Dunedin, Palmerston North and Hamilton.

SMITH BIOLAB

P.O. Box 36007,
Auckland 9, New Zealand.

Auckland	Ph. 483-039
Wellington	Ph. 683-453
Christchurch	Ph. 63-661

SB 11829

For the assay, control discs were prepared containing 67 percent, 100 percent and 150 percent of the stated content of the test discs. Forty test discs and eight replicates of each of the three control discs were placed on each plate in a latin square design, two plates were used so that a total of 80 discs were tested from each batch. A period of 30 minutes pre-diffusion (60 minutes for polymyxin) was allowed before the plates were incubated at 37°C for 16-18 hours.

The inhibition zone diameters were measured to the nearest 0.1 mm by projection on to a ruled screen.

Analysis of Assay:

Uniformity.

The diameter of the smallest inhibition zone was substracted from the diameter of the largest inhibition zone observed on each plate for the 40 test discs and for each set of eight control discs.

For each assay plate the mean diameter was calculated for the zones of inhibition for the 40 test discs and for each of the three sets of control discs. The standard deviation for the 80 discs tested from each batch of test discs was multiplied by the appropriate t factor for $p = 0.05$ to obtain 95 percent confidence limits for each batch. The standard deviation was calculated for all the control discs in all assays of each antimicrobial and multiplied by the appropriate t factor for $p = 0.05$ to obtain 95 percent confidence limits for the assay of each antimicrobial.

Potency.

From the measured inhibition zones for the 67 percent and 150 percent control discs standard deviations and 95 percent confidence limits were obtained. Using the 95 percent confidence limits the maximum range of permissible inhibition zone diameters was determined for each antimicrobial.

If the potency of the test discs is between 67 percent and 150 percent of labelled potency the mean inhibition zone diameter for the test discs ($\pm$ 95 percent confidence limits) should fall within this range.

Results

Uniformity:

For the test discs the difference observed between the largest and smallest inhibition zones was greater than the F.D.A. allowance of 2.5 mm in 27 of the 45 batches. There were differences of up to 16 mm between the largest and smallest zones produced by discs from a single vial. In two batches from Manufacturer A there were some discs which did not produce measurable zones of inhibition.

Taking the difference between the largest and smallest zones as a measure of uniformity places undue emphasis on a single exceptionally large or small zone or conversely places insufficient emphasis on several very small or large zones. The within-batch variations in inhibition zone diameter (standard deviation x t factor for $p = 0.05$) for the test batches from the three manufacturers and for the control discs prepared by us are shown in Table II.

When these figures are used 25 of the 45 batches have within-batch variations greater than 2.5 mm (Table III).

The differences between the mean diameters of the inhibition zones for the 150 percent and 67 percent control discs for each antimicrobial are shown in Table II for comparison with the within-batch variations. For 14/21 batches from Manufacturer A and 7/20 batches from Manufacturer B the within-batch variation is greater than the difference in zone size between the 150 percent and 67 percent control discs.

Therefore, for these batches there is a more than two-fold difference between the greatest and the least amount of the antimicrobial agent contained in discs from a single batch.

The uniformity among the control discs was such that the greatest difference observed between the largest and smallest inhibition zone diameter within any set of eight replicates on a single plate was 1.5 mm; in 39 of the 45 assays the difference was not greater than 1 mm. The greatest variation at the 95 percent confidence level is 1.5 mm (Table II), only 11 of the 45 batches tested show this degree of uniformity (Table III).

Potency:

When the test discs have a diameter greater than 6.5 mm ($\frac{1}{4}$-inch) the F.D.A. method applies a correction by measuring from the edge of the disc to the edge of the zone

and multiplying by 2. As both New Zealand manufacturers make discs with a diameter greater than 6.5 mm we applied a similar correction; the difference between the diameters of the test and control discs was subtracted from the measured zone size to obtain corrected zone size.

Irrespective of the correction for disc diameter, for more than 40 percent of the batches tested the estimated potency is not between 67 percent and 150 percent of labelled potency (Table IV).

Uniformity and Potency:

Table III shows that 20 batches meet the F.D.A. requirement for uniformity. Only 10 of these batches have potency estimates (after correction for disc diameter) between 67 percent and 150 percent of labelled potency (Table V).

The greatest failings were among the penicillin-containing discs. Table II shows the large within-batch variations for four of the seven penicillin-containing batches from Manufacturer A. The potency estimates were less than 67 percent for five of these batches and none of the seven batches met both F.D.A. requirements. Of the 80 penicillin two-unit discs tested, 11 did not produce measurable inhibition zones: and none of the 80 discs tested produced an inhibition zone as large as the inhibition zones for the 100 percent control discs.

Similarly, 5/80 cloxacillin 5 mcg discs from Manufacturer A did not produce measurable inhibition zones while 5/80 produced inhibition zones as large as the inhibition zones for the 150 percent control discs. Overall, only 2/21 batches from Manufacturer A met both F.D.A. requirements (Table V). While the within-batch variations were not so large for discs from Manufacturers B and C, only 8/20 batches (2/5 penicillins) from Manufacturer B and none of the four penicillin-containing batches from Manufacturer C met both requirements of the F.D.A. (Table V). Table VI shows the ranges of inhibition zone diameters observed on a single assay plate for discs from some batches.

For all assays the 95 percent confidence limits were within 67 percent to 150 percent of the assay value. However, it can be seen from Table II that for some assays (gentamicin and neomycin sulphate in particular) the slope of the dose-response line (change in inhibition zone size between the 67 percent and 150 percent doses) is not sufficient to allow limits narrower than 67 percent to 150 percent.

Discussion

The most common fault is a lack of uniformity within batches, 55 percent of the batches tested have within-batch variances greater than the 2.5 mm allowed by the F.D.A. Regulations. The tolerance of 2.5 mm is generous when it is noted that we achieved a much smaller maximum variance, 1.5 mm, for the control discs that we made. Kirshbaum, Kramer and Arret (1960)[9] comment that manufacturing methods and machinery should be able to make discs at least as uniformly as they can be made by hand.

However, less than 25 percent of the manufacturers' batches have within-batch variances less than or equal to 1.5 mm.

This lack of uniformity must be particularly disconcerting for laboratories using susceptibility testing methods such as the Kirby-Bauer or I.C.S. recommendations. The use of a control organism in these methods provides a check on technique and on the potency of the batch of discs but gives no indication of the variation between discs. The Stokes method (Stokes, 1968)[10] does provide a control over the performance of individual discs and should be the method of choice when using discs that do not meet the requirements of the F.D.A.

The F.D.A. Regulations define the paper quality and the disc diameter to be used for the control discs in the assay. In order to estimate the content of the test discs the following assumptions must be made; that the release of the antimicrobials from the test discs is identical to the release from the control discs, that the correction for any difference in the size of the paper discs is valid, and that the dose-response relationship is linear. The latter is not true for a number of the antimicrobials that we assayed, especially for those in which the potency of the test discs falls outside the 67 percent to 150 percent limits. The potency estimates in this report, therefore, indicate only how the

Table I Details for performance of assay

Labelled Content of Discs Tested		Solvent for the Preparation of Control Discs	Medium	Organism
Ampicillin	25 mcg	*phosphate buffer, pH6.0 water	A,pH6.6	E. coli
Bacitracin	10 units	*0.1 N HCl water	A,pH6.6	S. aureus
Carbenicillin	100 mcg	water	A,pH6.6	B. subtilis
Cephaloridine	15 mcg	water	A,pH6.6	E. coli
Cephalothin	30 mcg	water	A,pH6.6	E. coli
Chloramphenicol	30 mcg	methanol	A,pH6.6	B. subtilis
Cloxacillin	5 mcg	water	A,pH6.0	B. pumilus
Erythromycin	15 mcg	methanol	A,pH7.8	B. pumilus
Gentamicin	10 mcg	water	A,pH7.8	B. subtilis
Lincomycin	2, 10 mcg	water	A,pH7.8	B. pumilus
Methicillin	10 mcg	water	A,pH6.6	B. subtilis
Nalidixic Acid	30 mcg	† 1 N NaOH water	A,pH7.8	B. pumilus
Neomycin Sulphate	30 "mcg"	water	A,pH8.1	B. subtilis
Penicillin 2, 5, 10 units		water	A,pH6.6	B. subtilis
Polymyxin B Sulphate	300 units	water	P	Bordetella bronchiseptica
Streptomycin	10 mcg	water	A,pH7.8	B. subtilis
Sulphafurazole	250 mcg	† 0.1 N NaOH water	WT	E. coli
Sulphamethoxazole	250 mcg	† 0.1 N NaOH water	WT	E. coli
Tetracycline	30 mcg	methanol	A,pH6.6	S. aureus
Triacetyloleandomycin	15 mcg	methanol	A,pH7.8	B. pumilus
Trimethoprim	1.25 mcg	methanol	WT	E. coli

* to dissolve
† NaOH added dropwise to effect solution in water

Table III Uniformity of test discs compared to 1.5 [illegible] variation allowed [illegible] and 1.5 [illegible] variation observed for control discs.

Manufacturer	Number of Batches of Test Discs with Variation [illegible] of [illegible]				Total Number of Batches Tested
	[illegible]	[illegible]	[illegible]	[illegible]	
A	[illegible]	[illegible]	[illegible]	[illegible]	21
B	[illegible]	[illegible]	[illegible]	[illegible]	20
C	[illegible]	[illegible]		[illegible]	[illegible]
All	[illegible]	[illegible]	[illegible]	[illegible]	45

Table IV Potency estimates for all batches of test discs relative to the control discs.

Manufacturer	Number of Batches of Test Discs with Potency Estimate (p = 0.05)			Total Number of Batches Tested
	< 67%	67-150%	> 150%	
A	5 (9)*	14 (11)	2 (1)	21
B	0 (4)	8 (14)	12 (2)	20
C	0 (0)	1 (1)	3 (3)	4
All	5 (13)	23 (26)	17 (6)	45

The figures in brackets are the results obtained after the correction is made for the differences between the diameters of the paper discs used by the manufacturers and those used for the control discs.

Table II Uniformity of test and control discs and range allowed by 67-150 % limits

Labelled Content of Discs Tested		Within batch variation in Inhibition Zone Diameter (mm) [Std deviation x t factor for p = 0.05]				Difference between the Means of the Inhibition Zone Diameters for the 150% and 67% Control Discs (mm)
		Test Discs Manufacturer			Control Discs	
		A	B	C		
Ampicillin	25 mcg	13.8	1.3	4.8	1.1	6.1
Carbenicillin	100 mcg	5.2	1.3	1.6	.6	3.5
Cloxacillin	5 mcg	16.0	1.2	2.3	.7	5.7
Methicillin	10 mcg	5.9	3.0	1.7	.7	5.0
Penicillin	2 units	21.6			1.3	6.7
"	5 "	10.9			1.0	5.4
"	10 "	2.3	4.7		.8	3.8
Bacitracin	10 "	3.9	1.5		.6	3.2
Cephalothin	30 mcg	6.5	2.3		.7	4.0
Cephaloridine	15 mcg		1.9		1.3	6.5
Chloramphenicol	30 mcg	8.4	8.7		1.5	8.0
Erythromycin	15 mcg	3.5	5.2		.7	3.0
Gentamicin	10 mcg	1.1	1.1		.5	2.2
Lincomycin	2 mcg		.8		.8	4.6
"	10 mcg	1.9			.6	3.1
Nalidixic Acid	30 mcg	3.7	10.3		.7	5.3
Neomycin	30 mcg	2.3	.9		.5	2.2
Polymyxin B	300 units	4.2	1.0		.5	2.6
Streptomycin	10 mcg	2.9	0.9		.6	2.7
Sulphafurazole	250 mcg	7.8	8.0		1.4	6.7
Sulphamethoxazole	250 mcg		5.3		.9	5.2
Tetracycline	30 mcg	1.9	1.4		1.0	3.0
Trimethoprim	1.25 mcg	5.7			1.1	7.0
Triacetyloleandomycin	15 mcg	3.5	4.8		.7	4.0

Table V Potency estimates [illegible] zone diameters [illegible] test batches [illegible]

Manufacturer	Number of Batches with Variation (p = 0.05) in inhibition zone diameter < [illegible]	Number of Batches with Potency Estimate (p = [illegible])		
		< 67%	67-150%	> 150%
A	[illegible]	[illegible]		0
B	[illegible]		[illegible]	1
C	[illegible]			3
All	[illegible]	[illegible]	[illegible]	4

Table VI Measured diameters of inhibition zones for discs from some batches

	Number of Discs with Measured Diameter of Inhibition Zone					Number of Discs Tested	Range of Inhibition Zone Sizes for 67% to 150% Control Discs (mm)
	<12	12-16	16-20	20-24	24-28mm		
Ampicillin 25 mcg							19 - 25
Manufacturer A		1	26	1	12	40	
B					40	40	
C				12	28	40	
Cloxacillin 5 mcg							19 - 24
Manufacturer A	5	11	13	8	3	40	
B				1	39	40	
C				5	35	40	
Penicillin 2 units							24 - 31
Manufacturer A	9	6	10	7	8	40	
Nalidixic Acid 30 mcg							17 - 22
Manufacturer A			27	13		40	
B		4	1	26	9	40	

test discs performed by comparison with our control discs prepared to contain 67 percent, 100 percent and 150 percent of the labelled content of the test discs. The results are shown for both corrected and uncorrected inhibition zone sizes as we believe that in a clinical laboratory it would not be usual for corrections to be made before the measured inhibition zone diameters were compared with standard tables for the interpretation of sensitivity tests. Since the two New Zealand manufacturers make discs with diameters of approximately 8 mm and 9 mm it is expected that the inhibition zone diameters will be correspondingly larger than those for the 6.5 mm diameter control discs. When the correction for disc diameter is made the estimated potency is between 67 percent and 150 percent for 26 of the 45 batches tested. The discs from the U.K. manufacturer (Manufacturer C) all have potency estimates greater than 100 percent. This may be a demonstration of greater release of the antimicrobials from the paper used in the manufacture of these discs.

Only 22 percent of the batches tested met the F.D.A. requirement for both uniformity and potency; 9.5 percent of the batches from Manufacturer A, 40 percent of the batches from Manufacturer B and none of the four batches from Manufacturer C. The penicillin-containing discs were particularly unreliable; only two of the 16 batches tested met both requirements. We can offer no explanation for the enormous within-batch variations observed in the penicillin-containing discs from Manufacturer A.

It is difficult to understand why cloxacillin discs are manufactured. It has often been stated (Hewitt, Coe and Parker, 1969[7]; Garrod and Waterworth, 1971[6]: Stokes and Waterworth, 1972[11]) that disc tests using cloxacillin are unreliable. For the penicillinase-resistant penicillins the recommended procedures for methicillin discs should be followed and the results taken to apply to cloxacillin.

The F.D.A. restricts the number of antimicrobial agents that may be marketed as antibiotic sensitivity discs and defines the contents to be used (Federal Register, 1972)[5]. There is a need for similar restrictions in New Zealand.

Other major faults noted were: production of non-circular inhibition zones, desiccant mixed in with the discs, labelling in micrograms where "units" should be used, the same batch numbers for discs containing different

antimicrobials, and discs labelled " cephaloridine " found to contain cephalothin.

Overall, the single discs manufactured in New Zealand are not reliable as regards content or uniformity and they cannot be recommended for use in susceptibility testing methods with standard interpretative tables. Since inter-laboratory comparisons are meaningless without adherence to standard methods, an assessment of the distribution of antimicrobial resistant organisms in New Zealand will not be possible until standardisation of the potency and quality of the discs is achieved.

Acknowledgments

The authors wish to thank the pharmaceutical companies who provided antibiotics for use as laboratory standards.

Published with the authority of the Director-General of Health, Department of Health, Wellington, New Zealand.

REFERENCES

1. Barry, A. L., Garcia, F. and Thrupp, L. D. (1970), *Am. J. clin. Path.* **54,** 149.
2. Bauer, A. W., Kirby, W. M. M., Sherris, J. C. and Turck, M. (1966), *Am. J. clin. Path.* **45,** 493.
3. Ericsson, H. M. and Sherris, J. C. (1971), *Acta path. et micro. Scand. Section B,* Suppl. 217.
4. *Federal Register.* (1962), **27,** pt. 147, 13221.
5. *Federal Register.* (1972), **37,** pt. 147, 20525.
6. Garrod, L. P. and Waterworth, Pamela M. (1971), *J. clin. Path.* **24,** 779.
7. Hewitt, J. H., Coe, A. W. and Parker, M. T. (1969), *J. med. Micro.* **2,** 443.
8. Hill, G. J. (1966), *N.Z.J. med. Lab. Technol.* **20,** 70.
9. Kirshbaum, A., Kramer, J. and Arret, B. (1960), *Antibiot. and Chemother.* **10,** 249.
10. Stokes, E. Joan. (1968), Clinical Bacteriology, 3rd ed. p. 179. London, Edward Arnold.
11. Stokes, E. Joan and Waterworth, Pamela M. (1972), *Assoc. clin. Path.* Broadsheet 55.
12. Wright, W. W. (1974), IN: Current Techniques for Antibiotic Susceptibility Testing, ed. Balows, A. p. 26. Springfield, Thomas.

A Review of Gastroenteritis on Nauru

Anne L. R. Southern, ANZIMLT
Nauru General Hospital, Republic of Nauru

Received for publication, June 1978

Introduction

The Republic of Nauru is a small, very isolated atoll, 12 miles in circumference, lying in the Central Pacific 26 miles south of the Equator at 166° 55′ E. The climate is tropical with variable and irregular rainfall.

The economy of the island relies entirely upon the mining of phosphate deposits in the central portion of the island which in cross section looks rather like a fried egg, the yolk being the " topside " phosphate deposits, the white being the coastal fringe where the entire population of approximately 7,200 live. Depending upon the rainfall pattern the island may either have a lush tropical vegetation or appear dry and scorched. The topsoil layer is both too thin degree, hence most food requirements are met through importation. There is little indigenous animal or bird life. The reef encircling the atoll is a continuation of the coastal fringe covered with jagged outcrops of weathered coral " pinnacles " and terminates abruptly with a drop to approximately 1,500 foot depth of water.

Gastroenteritis on Nauru is a significant problem causing the hospitalisation of some 100 persons per year from among the Nauruan population alone.

Nauru is served by two hospitals, one for the Nauruan population, plus expatriate employees of the republic, the other for the Gilbertese, Tuvaluans, Chinese and European employees of the Phosphate Corporation. For the purpose of this paper, relevant statistics have been drawn from the records of the Nauru General Hospital only as it was felt that inclusion of laboratory data from the Phosphate Corporation (NPC) hospital, often non-specific and incomplete, would introduce a large unknown factor. However, reference will be made to areas under NPC control where they have a direct effect on the island community as a whole; specifically, water supply and waste disposal.

TABLE I.

	1975		1976		1977	
	No.	% of the Total	No.	% of the Total	No.	% of the Total.
JAN	10	1.2	9	8.0	16	15.0
FEB	19	3.7	10	9.0	11	12.0
MAR	8	6.8	23	19.0	10	7.0
APR	5	7.0	3	5.0	7	7.0
MAY	6	6.0	3	4.0	6	5.0
JUN	2	2.0	2	3.0	4	3.8
JUL	0	0	7	6.0	8	8.0
AUG	5	5.0	10	9.0	6	7.0
SEP	8	7.9	14	10.0	3	3.0
OCT	8	6.0	10	11.0	14	15.0
NOV	6	4.0	5	5.0	10	9.0
DEC	9	6.0	3	3.0	10	11.0
TOTAL	86	7.0	99	8.0	105	10.0

TABLE II.

AGE AND INCIDENCE.

AGE GROUP	% of the Population	Cases	% of Total Admissions.
1 Month	12.0%	5	2%
1 - 6 Months		51	17%
7 - 12 Months		98	34 %
1 - 2 Years		32	11%
2 - 5 Years		28	10%
5 - 10 Years	14.0%	13	4%
11 - 20 Years	26.9%	25	9%
21 - 45 Years	35.1%	20	7%
45 Years	12.0%	18	6%
TOTAL:		290	74%

Relevant Data

Table I. Illustrates the number of admissions per month covering the years 1975, 1976 and 1977 for which the presenting feature was gastroenteritis. The figures have also been interpreted as a percentage of the total number of admissions for the month.

Table II. Illustrates the age group versus incidence relationship.

During this three-year period, four deaths occurred among this group of patients. In two of these, the cause of death in one case was fulminating hepatitis, and in the other Hirschprung's disease. However, in the remaining two, a 66-year-old woman with pre-existing heart condition, and a two-week-old baby, the gastroenteritis was felt to be a major factor. All four deaths occurred in 1977.

During 1977 two separate but most probably related outbreaks of typhoid fever occurred. While the figures for January to March, 1977, and October to December, 1977, may well reflect some undiagnosed cases of typhoid, all confirmed cases have been eliminated from these statistics for two reasons. Firstly, the dominant feature of the typhoid presentations were fever and headache, with only a small number of younger children having associated gastroenteritis. Secondly, the typhoid outbreak has been the subject of a separate report by Dr T. Kuberski, S.P.C. Epidemiologist, released in March, 1978.

The most vulnerable age groups are the small children up to 5 years, with a peak in the 6-12 months group. However, it must be pointed out that 88 percent of the Nauruan population is under the age of 45, therefore the figures for the older group representing 16 percent of the admission for that group is still significantly high.

Study of past laboratory records indicate that some 70 percent of the gastroenteritis cases have one or more demonstrable faecal pathogens.

In very young children up to one year by far the most common organism isolated is *Staphylococcus aureus*. Pathogenic *E. coli* of several different strains are relatively common in the 0-3-year age group, with intestinal parasites widespread. Order of frequency for parasites is as follows: *Trichuris trichiura, Giardia lamblia, Ascaris lumbricoides.*

Multiple infestations occur with or without concurrent bacterial pathogens.

After two years of age by far the most common bacterial pathogen is *Shigella flexneri* type 2 (*S. sonnei* and *S. boydii* have both been found but are not significant). Salmonellae are frequently identified, of several different serotypes, parasitic patterns follow much the same as the younger groups but also amoebic infestations although, not common, begin to appear.

In the adult population, *Trichuris trichiura, Ascaris lumbricoides* and *Giardia lamblia* are widespread, and many adults carry amoebic cysts and active amoebiasis is common.

Again, *Shigella flexneri* is more common than salmonella although it is of interest to note the recent improvement made with the laboratory stool culture techniques has revealed a far wider range of Salmonella species than was once believed. Salmonella isolates made over the last 15 months include:

Unlocking the Problem Heart

A Comprehensive Combination From MERCK

Revealing:

The Follow-up

LDH
For extended monitoring throughout clinical course

α-HBDH
For specific confirmation of heart muscle as the source of elevated LDH activity

Revealing:

The Diagnosis

CK-MB.
CPK
GOT

In the diagnosis of myocardial infarction, activities of these enzymes rise significantly within 6 hours. If both remain normal, angina pectoris is suspected

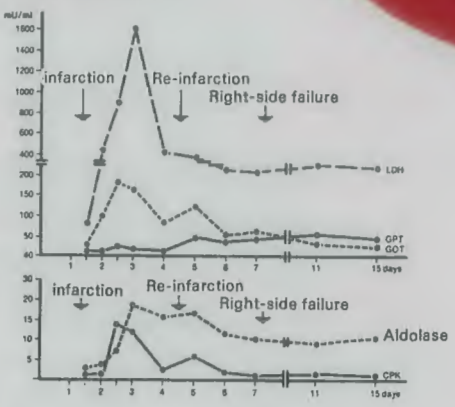
Revealing:

The Complications

GPT

Determined along with CPK and GOT to elucidate possible right ventricular failure with liver involvement, noted in a sharp rise of liver-specific GPT activity

Serum Enzyme Activities in Myocardial Infarction



The Sensitive Six — The Security of 6 Enzymes

In the diagnosis, prognosis and monitorina of myocardial infarction, you can rely on **6** enzyme assays to maintain linearity throughout the higher ranges of activity.
Each reagent is manufactured with the meticulous research oriented care pioneered by MERCK in the production of pure biochemicals.
And that means the utmost in specificity, sensitivity, stability and reproducibility.

E. Merck, Darmstadt
Represented by BDH (NZ) Ltd.

Sole N.Z. Distributors
GENERAL DIAGNOSTICS [NEW ZEALAND] LTD.
206 THE PARADE, ISLAND BAY, WELLINGTON, 2. P.O.BOX 7170 WELLINGTON SOUTH,
CABLES & TELEGRAMS: DIAGNOSTIC. TELEX: GENDIAG NZ 3859. TELEPHONE 836-255.

1207

1. *S. typhi (vi).*
2. *S. typhimurium.*
3. *S. enteritidis.*
4. *S. seftenberg.*
5. *S. agona.*
6. *S. weltevreden.*
7. *S. oslo.*

The last two, *S. oslo and S. weltevreden,* appear to be widespread and have been isolated not only from faeces but also from blood cultures: the only two, apart from *S. typhi,* to have caused salmonella septicaemia to date.

The high incidence of *Staphylococcus aureus* isolated in the young babies presenting with gastroenteritis and feeding problems, probably reflects the low availability of domestic facilities in Nauruan houses. Only one-quarter of the households have hot water, stoves and refrigerators, hence storage and sterilisation of milk feed, bottles and teats, etc., is unsatisfactory. Even among older children, in whom no obvious pathogen can be demonstrated, staphylococcal food poisoning is often highly suspect, because of the practice of cooking large batches of food at one time and leaving it, inadequately protected.

Vibrios of any sort have never been demonstarted since routine screening of all stool cultures began at the time of the Tarawa outbreak of cholera.

The only case of hookworm seen during the period covered by this survey was a transient Gilbertese.

Laboratory Diagnosis

The diagnostic facility utilised most fully is the laboratory service. Abdominal x-rays may be used occasionally should obstruction be suspected, and one case of a severe infestation of *Entamoeba histolytica* in a small child was only revealed by sigmoidoscopy.

Serial stools from all cases of gastroenteritis/diarrhoea/P.U.O. are routinely screened as follows:

(1) Direct microscopy for parasites using both concentration technique and simple moist film.

(2) Culture on the following range of media:
   (a) Salmonella/Shigella Agar (SS).
   (b) Desoxycholate citrate (DCA) both selective media for salmonella and shigella.
   (c) Selenite — F Broth., an enrichment broth for salmonella, later plated on to SS and MacConkey Agar.
   (d) T.C.B.S. — selective media for vibrios.
   (e) Salt broth — later plated on to azide blood agar—for staph infection in the three-year age group.

(3) All salmonella, shigella and pathogenic *E. coli* isolates are confirmed serologically using specific Wellcome Antisera.

(4) Viral cultures are not performed, viral gastroenteritis is assumed by exclusion of other pathogens.

(5) If P.U.O. is the presenting feature full blood count, urinalysis and blood culture are routinely performed on admission, as well as stool culture.

(6) A full range of biochemical tests are available, the relevant ones to this subject being electrolyte balance by flame photometry.

Management

Phase 1. Correction of water and electrolyte balance. Most often necessary in the very young and old. Laboratory electrolyte checks utilised to guard against over or under hydration.
   (a) Mild cases — correction is oral using "Oresol" containing sodium chloride, bicarbonate, potassium chloride and glucose given in water. If diarrhoea had ceased but oral tolerance is poor it may be given rectally.
   (b) Severe cases — intravenous therapy using gastric replacement solution or Hartman's solution.
   (c) A symptomatic soothing agent such as Kaomagma is necessary.

Phase 2. Treatment depending on the nature of the pathological agent identified by the laboratory. Antibiotics are not given in self limiting conditions, i.e., viral and staphylococcal food poisoning.
   (1) Round worm — Combantrin, vanquin, Piperazine
   (2) Flagellates — Mintezol, Flagyl, Piperazine

(3) Amoebae — Flagyl and tetracycline-chloroquin.

Pathogenic *E. coli,* staphs according to *in vitro* sensitivity testing of organisms. Salmonellae, shigellae, with chloromycetin or Septrin. Of interest is that two recent salmonella isolates, one *S. typhi* and one *S. weltevreden* have been resistant to both chloromycetin and Septrin but have responded well to Amoxyl.

All antibiotics are given in standard doses according to body weight.

Current and Proposed Control Measures

Water Supply and Purification — Annual rainfall on Nauru can vary from 12-180 inches per annum. No ground water is available for domestic use, therefore the only two sources are: Rainfall, Imported supplies.

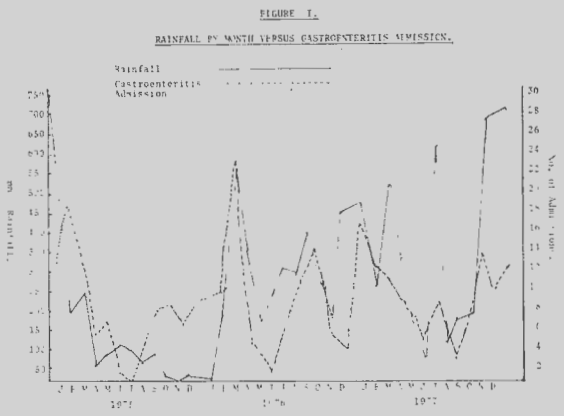
Figure 1. Illustrates an interesting correlation between monthly rainfall and incidence of gastroenteritis, particularly obvious when heavy rainfall follows a dry period. 1974 was virtually a drought year, nine months of that year having 3 or less inches of rainfall, most if not all water at this time was imported. In December, 1974, the rain began, and by February, 1975, when this survey began, the numbers of recorded gastro cases were high. Possible explanation of this may be apparent after clarification of the specifics concerning the Nauruan supply system, considered under two headings, low and high rainfall periods.

Low rainfall periods.

The entire supply for the total island population of 7,254 must be imported from various sources. Control of purity of this water is relatively simple. Not only is it cleared both chemically and bacteriologically prior to shipment, but on arrival pumped to a specific holding reservoir, there to await clearances before release to the main reservoirs. From these, domestic deliveries are made via closed tankers.

Standard of water storage tanks vary greatly from steel enclosed million gallon reservoir, underground concrete storage, to domestic installations of varying capacity, either concrete or steel.

Many Nauruan households utilise old 5,000 gal. steel "pontoon" tanks, often



in a poor state of repair, to eke out periods necessary between tanker deliveries. Many amateur plumbers connect up series of old tanks, using unsuitable connections and poor protective coverings. The installations are particularly vulnerable to contamination. Suspected supplies are, at present, checked by the laboratory on a demand basis, cleaned, repaired and chlorinated as necessary. However, even though individual supplies may be quite severely contaminated with faecal *E. coli,* the problem is largely restricted to the immediate household.

Under the Nauruan rehousing programme already under way, all tanks installed are 10,000 gallons enclosed steel.

High rainfall periods

Over the last two years, all water supplies have been from rainfall. As each individual house has its own catchment the situation remains unchanged in that poorly maintained roofs, guttering, pipes and tanks may lead to contamination locally. However, the problem alters radically when viewed from the aspect of replenishing the main reservoirs for use whenever necessary. This must be presented in detail.

The sole catchment area for the reservoirs is the high density housing area accommodating the Gilbertese and Chinese workers "location".

This area contains 120 blocks of eight flats, presently housing 2,370 persons. Each block of flats is served for their own use from four ground level concrete

tanks to which access is not barred. As water must be manually pumped into the individual header tanks, a common practice is to "bring the bucket to the tank" with obvious results.

Excess water from these tanks is pumped through a highly complex network of underground holding tanks totalling 47 in all, destined eventually for any of the 11 main reservoirs and will be used for "outside location" domestic, hospital and individual supplies. It may also be recirculated "inside location" through many different routes to any point necessary.

Obviously should a major contamination occur at any point within location, the effect would be far reaching, and if a dry spell should follow, would ultimately affect the entire island community.

No single tank of the 47 underground tank system through which all the water passes can be isolated, thus eliminating the possibility of continual chlorination at that point, nor is manual chlorination of all tanks practical. Complete and adequate treatment would seem to be impossible until a fully reticulated water supply is provided. However, having considered all factors inherent in the present system, the following scheme has been devised to reduce the risk factor to a manageable level.

Eight of the underground tanks have been isolated, through which all water movement routes are channelled either "inside" or "outside" location. These key tanks are kept to a very high level of residual chlorine (8-10 ppm). The frequency of dosage necessary to maintain this level is still under evaluation and bacteriological control is strictly maintained. Excess water from this system destined for "outside" location is pumped to one specific reservoir which again is strictly controlled by bacteriological checks, further chlorinated if necessary before pumping to the general reservoirs which are filled sequentially and cleared before release via tanker transport to the domestic tanks.

All "non-key" tanks within location are at present chlorinated twice monthly. Gilbertese and Chinese personnel who have been trained to estimate tank volumes are provided with the appropriate amounts of chlorine slurry (Nichlon-70). They manually chlorinate and perform residual chlorine estimation using Wallace and Tiernan field kits. Spot checks are run in the laboratory on their results and it is hoped to use a Wallace and Tiernan Amperometric titrator to enable more accurate and complete data to be compiled.

Bacteriological samples are taken for analysis by standard techniques. MPN index and faecal *E. coli* colony counts[3] are performed.

Domestic-Industrial refuse.

Thrice weekly collections (in some areas daily) are transported in open trucks to an industrial incinerator. Once burnt the remains are dumped, bulldozed and compacted but not sealed with earth. The burning of all rubbish prior to dumping is a recent practice instituted to help overcome the fly problem associated with unsealed dumps.

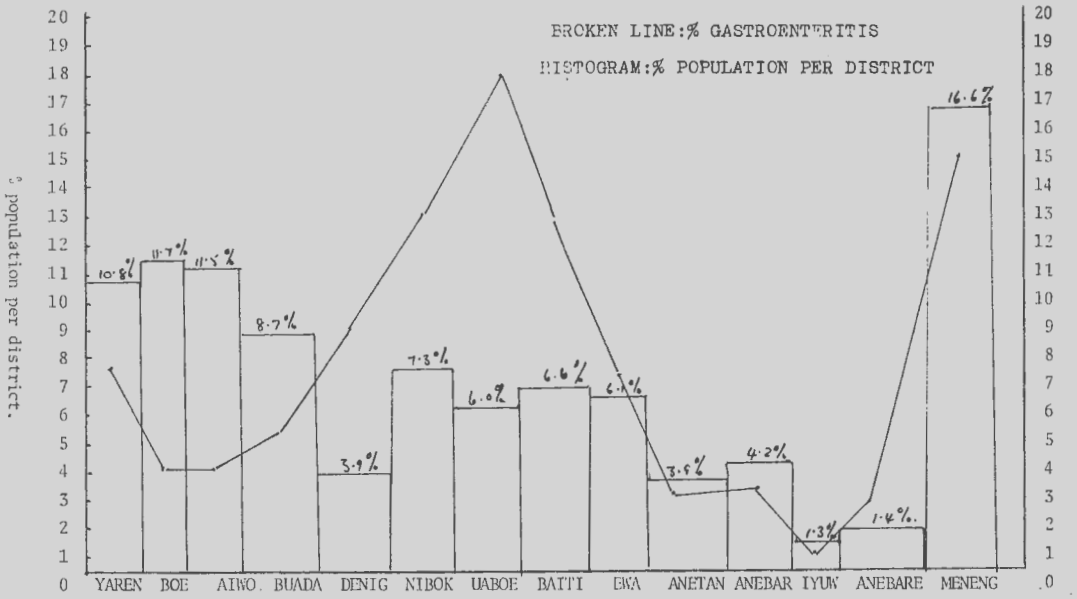
Sewage Disposal.

(1) *Raw waste.* Effluents from both hospitals, some schools and from the entire location area are pumped in the raw state directly over the reef discharging approximately 100 yards offshore but not into the deep water beyond the reef edge. Contamination of the reef and shoreline around the discharge areas does occur although not to a severe degree. Beach latrines are not used.

(2) *Cesspits.* The vast majority of Nauruan houses have cesspit facilities adequate for the normal use of a family of six to eight, but where households extend to 15-20 persons sheer volume of sewage is both too great and the flow too rapid to allow proper bacterial action before passing into the drainage pit. Overuse, poor soil drainage and maintenance result in badly contaminated seepages and surface water, especially in the densely populated areas. Many overcrowded households also employ additional pit latrines of variable standards.

FIGURE 2.

GASTROENTERITIS BY DISTRICT.



(3) *Septic tanks.* Under the housing reconstruction programme begun in 1970 all new houses are being provided with standard septic tanks rather than cesspits and of a far greater capacity.

The need for improved sewerage systems is fully recognised and ultimately it is hoped to provide both a fully reticulated water and sewerage system.

High Density Areas

The problem of overcrowding referred to in connection with sewage disposal can be shown to be directly linked to the incidence of gastroenteritis in those areas.

Figure 2. Illustrates the percentage of the total Nauruan population in each of the 14 districts against the incidence of gastroenteritis admission for that district covering the period of this survey. In general, the incidence follows the population density with the notable exception of four neighbouring districts, Denigomodu, Nibok, Uaboe and Baiti. Only non-phosphate bearing land (coconut land) is used for housing purposes. These four districts, not only smaller in overall size than most other districts, also have a smaller proportional area of available coconut land. Hence similar population numbers are more densely housed with the resulting incidence of gastroenteritis almost double that of other districts.

Summary

Evidence has been presented to link the incidence of gastroenteritis on Nauru directly to the joint problems of overcrowding, poor housing and sanitary facilities. A scheme is presented aimed at reducing the risk of a major waterborne epidemic, although this is felt to be an unlikely occurrence owing to the peculiar nature of the island water supply system. Current conditions have been evaluated and future measures outlined.

Acknowledgments

Dr V. B. Malhotra, G.M.O., R.O.N., Director of Public Works and Community Services. R.O.N. Director of Lands and Survey. R.O.N. All for verbal communications.

REFERENCES

1. Census Report 1977. R.O.N. Department of Island Development and Industry.
2. World Health Organisation "News Release". March 1977.
3. "WHO" International Standard for Drinking Water. Second Edition. 1963. World Health Organization, Geneva, Switzerland.

A Comparison of the Predictive Value of the Pregnanediol/Creatinine Ratio and the Human Chorionic Gonadatrophin Titre in Threatened Miscarriage

Necia France
Pathology Department, Waikato Hospital, Hamilton

Received for publication, March 1978

Summary

Two biochemical methods for assessing pregnancy viability in patients presenting with a diagnosis of threatened miscarriage in early pregnancy were compared. Using early morning urines, a level of the pregnanediol/creatinine ratio could be distinguished below which a high proportion of non-viable pregnancies and no continuing pregnancies fell. No such level could be distinguished for the human chorionic gonadatrophin titre. The place of both methods in the assessment of threatened miscarriage is discussed.

Introduction

A common diagnostic problem in patients presenting with threatened miscarriage in early pregnancy is to distinguish the non-viable pregnancy as soon as possible, with certainty, so that the uterus can be evacuated as an elective rather than an emergency procedure and the patient spared needless hospitalisation and stress. To this end any test regime should be aimed at the early diagnosis of non-viability without false negative results.

Various biochemical products of the ovary, foetus and placenta have been used to monitor early pregnancies. In addition, ultrasound equipment is now available in many hospitals which enables trained operators to estimate the size, growth rate and gestational age of the foetus and to recognise certain abnormalities.

The relative usefulness of these various approaches in distinguishing the non-viable pregnancy in threatened miscarriage has been compared by several workers. Brown *et al* (1970)[2] found the 24-hour urine pregnanediol (PD) or total oestrogen to be a better index of pregnancy viability than the urine human chorionic gonadatrophin (HCG) pregnancy test, at first assessment; the HCG often becoming negative (less than 2,500 IU/1) only with serial testing in patients who later miscarried. Either steroid test could distinguish without false negative results 40 percent of non-viable pregnancies at first assessment, the remaining patients having steroid levels above the first percentile of the normal range. The comparable figure for HCG was 25 percent.

A serum progesterone or oestradiol level lower than the mean $\pm$ 1 SD was found to predict miscarriage more accurately than either the HCG, placental lactogen or α foetoprotein levels, by Kunz *et al* (1976)[5]. Use of two parameters in combination greatly improved the predictive value of the initial assessment. However, a high proportion of false negative results occurred with all parameters tested in this study, possibly owing to the diurnal variations of the hormones in serum.

Duff (1975)[3], in comparing urinary hormone tests with ultrasound assessment, found that all the hormone tests, especially the steroids, predicted miscarriage with great accuracy. Ultrasound gave more false negative results, but it also gave more information about the gestational age and type of pregnancy failure. More recently Hunter *et al* (1977)[4] have reported greatly increased accuracy in diagnosing all forms of pregnancy failure by ultrasound.

This study is a retrospective comparison of the PD/creatinine ratio and the HCG titre performed on early morning urines (EMU's) at first assessment, as indices of pregnancy viability in patients presenting over the last six months of 1977 with threatened miscarriage in early pregnancy.

Material and Methods

Specimens: EMU's included in this series were collected from patients presenting with both a positive pregnancy screening test and a diagnosis of threatened miscarriage. (This eliminated any possibility that a negative pregnancy test was influencing management.) Specimens with a creatinine level of <9 mmol/l were arbitrarily excluded since the dilution extracted by the method of Metcalf (1973)[6].

factor would have prejudiced the comparison in favour of the PD/creatinine ratio. Frequently a series of EMU's was analysed for any one patient but only the first was included in this study. The subsequent course of the patient's pregnancy, together with an estimate of its duration at the time of sampling, were obtained from the medical records. Patients whose miscarriage had become clinically inevitable at the time of sampling were not included in this study.

Pregnanediol: Urine was hydrolysed and extracted by the method of Metcalf (1973)[6] Following trimethylsilyl derivatisation (BSTFA 50 μl dichloroethane 50 μl, 50°C overnight) 1 μl was chromatographed on 1 percent OV 1 in a 2 m, 2 mm ID glass column using a Hewlett Packard 5710A gas chromatograph and epicoprostanol as internal standard.

Creatinine: This was estimated by the standard Technicon method on an SMA 6.

HCG: The HCG titre was estimated by the UCG Quicktube quantitative procedure (Denver Laboratories, Australia). The detection limit of this test is 1000 IU/l.

Precision of PD assay: 20 consecutive singlicate analyses of an early pregnancy urine deep frozen in aliquots yielded the following (mean $\pm$ 95% limits):

PD: 15 $\pm$ 3.9 nmoles/l

Predictive value of PD/creatinine ratio compared with HCG/titre: This is summarised in Figure 1. Many of the patients discharged with a continuing pregnancy had not delivered at the time the records were consulted. Duration of pregnancy had in most cases been confirmed or estimated by ultrasound examination.

Of a total of 40 pregnancies, nine patients subsequenty miscarried, or had the uterus evacuated following a later diagnosis, on clinical grounds (other than knowledge of the PD/creatinine ratio) of inevitable miscarriage or missed abortion. Eight of these had a PD/creatinine ratio below 0.1. No patient with a continuing pregnancy had a value for the PD/creatinine ratio in this range. The nine patients whose pregnancies proved to be non-viable had HCG levels varying from 1000 to 10,000 IU/l. Nine continuing pregnancies also had HCG levels in this range.

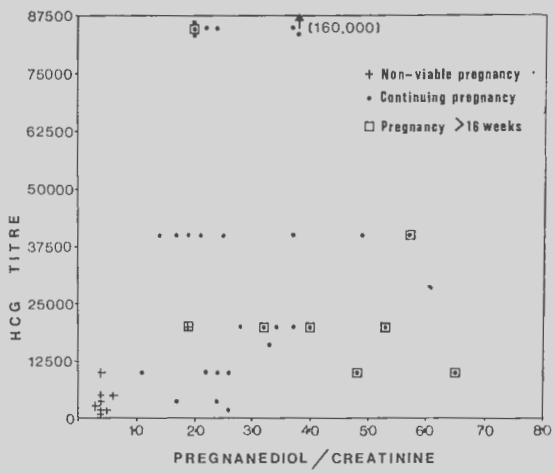


Figure 1. Pregnanediol/creatinine ratio v/s human chorionic gonadatrophin titre performed on early morning urines from 40 patients presenting with threatened miscarriage in the first 20 weeks of pregnancy.

Discussion

These results are similar to those of other workers in suggesting that the urine PD frequently falls into a range which is incompatible with continuing pregnancy before the HCG titre becomes negative in a non-viable pregnancy.

While the method used here for PD estimation involves derivatisation this is unnecessary if one uses NGA as a stationary phase (Barrett *et al* 1969)[1]. However, under these conditions a single PD estimation would take a minimum of two hours' working time, which makes the test uneconomic unless batched. This comment also applies to other biochemical tests of pregnancy viability with the exception of the HCG titre which can be performed in a few minutes and read two hours later. Unless the throughput justifies daily batches, the discriminatory advantage of the PD assay over the HCG titre will often be lost. In these circumstances, serial assessment of threatened and habitual miscarriage patients using urinary HCG titres as an adjunct to ultrasound examination would seem the most rational approach pending the development of fast steroid assays.

Acknowledgments

Pregnanediol and creatinine estimations

NEW:
slide test for detection of antibodies to streptococcal exoenzymes

(an aid in detection of rheumatic fever and acute glomerulonephritis).

STREPTOZYME

Rapid : results in two minutes.
Easy : for titration simply dilute sample serially prior to test.
Self-contained : kit includes Reagent, Positive and Negative controls, glass slide and capillary tubes.
Sensitive : detects more specimens with elevated titers than any other single test. (1)
Specific : detects five related streptococcal enzyme antibodies* and is unaffected by nonspecific enzyme inhibitors. (2)
Stable : may be stored for over 1 year at refrigerator temperature.

Streptozyme TM Kits for 15 tests, including positive and negative controls

* ASO, AH, ASK, ADNase, ANADase

(1) Klein, G. C. and Jones, W. L. : Applied Microbiol. 21 : 257, 1971.
(2) Janeff, J., Janeff, D., Taranta, A., & Cohen, H. : Lab. Med., 1971 (in press).

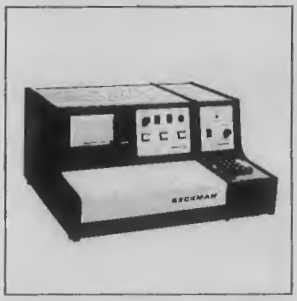
SMITH BIOLAB
SCIENTIFIC DIVISION
P.O. Box 36007,
Auckland 9, New Zealand

Auckland Ph. 483-039
Wellington Ph. 683-453
Christchurch Ph. 63-661

ENZYME ANALYSIS

Enzyme Activity Analyzer, System TR: The System TR is a totally automated, push-button operated and electronically calibrated *True Rate* enzyme activity analysis system. It is designed to perform both batch enzyme samples and stat enzyme determinations of: AP, LDH, SGOT, SGPT, CPK, GGTP, HBDH and other enzyme activity measurements.

ELECTROPHORESIS



Microzone* Computing Densitometer: The CDS-100 features fluorescent scanning capability for CPK isoenzymes along with unsurpassed ease of calibration and operation. Automatic gain and zero adjusting circuitry—eliminates manual instrument adjustments to compensate for sample-to-sample variations, minimizes instrument set-up time and preparatory pattern scanning.
*Microzone is synonymous with excellence in complete electrophoresis systems and supplies.

ELECTROLYTE ANALYSIS

Cl/CO_2 Analyzer: The Cl/CO_2 Analyzer features small sample size (10μl), stat speed, and extremely easy operation.

Chloride determinations can easily be run on sweat samples, as well as plasma, serum, or spinal fluid.

ELECTROLYTE ANALYSIS

KLiNa Flame System: A fully automated system that's designed especially for the clinical laboratory's minimum workspace requirements, high volume workloads and need for exceptional stability. For K, Li & Na determinations.

AUTOMATED GLUCOSE/BUN ANALYSIS

Beckman System I: A fully automated Glucose/BUN Analyzer, for routine or STAT samples. Results are digitally displayed and printed 64 seconds after sample introduction. When either glucose or BUN is required, the unused channel can be flipped off.

GLUCOSE ANALYSIS

Glucose Analyzer-2: Rapid, accurate glucose, cholesterol and uric acid analysis when you need it fast. The Beckman Oxygen Rate method virtually eliminates interference and tedious procedures common to other glucose, cholesterol and uric acid techniques. Runs up to 60 samples per hour.

BUN ANALYSIS

BUN Analyzer-2: Now, blood urea nitrogen can be done fast and easy with the Beckman BUN Analyzer—a bench companion to the Beckman Glucose Analyzer. Runs up to 60 samples per hour.

CREATININE ANALYSIS

Creatinine Analyzer-2: This new Beckman instrument features the same operational ease and speed as the Glucose and BUN Analyzers, with Creatinine analysis performed in 60 seconds by the colorimetric rate Jaffe method. 25μl of sample is all that's required to get fast, accurate creatinine measurements.

CALCIUM/MAGNESIUM ANALYSIS

Calcium/Magnesium Analyzer: This low-cost, compact analyzer is designed especially for the clinical determination of calcium and magnesium. It combines the accuracy of the atomic absorption spectroscopy with the operating ease of the KLiNa "Flame Photometer. Auto calibration and Auto-zero features help give you stat determination in just 60 seconds on 24μl samples.

PROTEIN ANALYSIS

ICS Immunochemistry Analyzer: A revolutionary concept in protein analysis, the ICS is a microprocessor-controlled rate nephelometer that performs specific protein assays in less than 60 seconds and displays direct readout in concentration units. Methods are currently available for Alpha-Antitrypsin, C3 Complement, IgG, IgA and IgM.

WATSON VICTOR LTD

were performed by staff of the Biochemistry steroid and automated sections, and HCG estimations by staff of Immunology, Pathology Department, Waikato Hospital. Assistance from the Medical Artist, Waikato Hospital, is also gratefully acknowledged.

REFERENCES

1. Barrett, S. J. and Brown, J. B. (1970), *J. Endocr.* **47**, 471.
2. Brown, J. B., Evans, J. H., Beischer, N. A., Campbell, D. G. and Fortune, D. W. (1970), *J. Obstet. Gynaec. Br. Commonw.* **77**, 690.
3. Duff, G. B. (1975), *Br. J. Obstet. Gynaec.* **82**, 858.
4. Hunter, C. and Picker, R. H. (1977), *Aust. N.Z. J. Obstet. Gynaec.* **17**, 192.
5. Kunz, J. and Keller, P. J. (1976), *Br. J. Obstet. Gynaec.* **83**, 640.
6. Metcalf, M. G. (1973), *Steroids* **21**, 193.

A Case of Platelet Satellitism?

T. J. Lowe and Lois Jones
Pathology Department, Taranaki Base Hospital, New Plymouth

Received for publication, April 1978

Summary

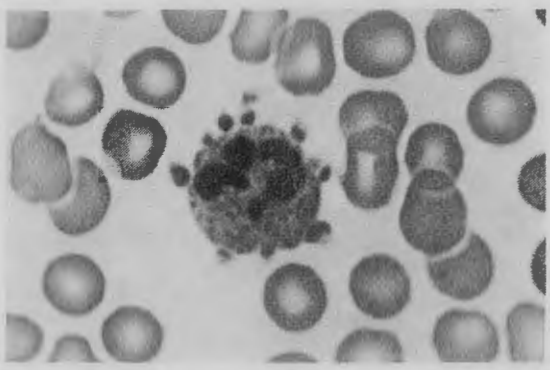
A case of platelets satelliting neutrophils is reported. Investigations into this phenomenon and results obtained, are described along with a discussion into the possible aetiology of this finding.

Introduction

The finding of platelets adhering to neutrophils has aroused interest in the workers reporting it since 1963[1, 2, 3, 4, 8, 9, 10, 12, 13, 14]. It is a rarely reported finding, with no apparent clinical significance. It has been implicated in various thrombotic problems but this is based on experimental data only. To date no conclusive answers as to the aetiology, or nature, have been established.

Case Report

In October, 1977, a self-reliant, 75-year-old lady was admitted to Taranaki Base Hospital with a suspected myocardial infarction. At the time of her admission, "Mrs P.", a non-smoker and non-drinker, was shown on examination to clinically have had a myocardial infarction. The serum myocardial enzymes and E.C.G. also supported this. Her routine haematology screen was normal except for an ESR of 100 mm/h, and the platelet count being elevated on one occasion. Her long-term drug therapy had included digoxin and bendrofluazide, and during her stay in hospital she had been given anti-hypertensive and pain relieving drugs. She had previously been in hospital in 1974 with a similar complaint, at which time it was felt that her chest pain was not cardiac but rather muscular or skeletal.



Investigation

During this previous admission to hospital, platelets satelliting neutrophils was noted (Fig. 1) for which a limited investigation had been carried out. Previous reports[1, 2, 4, 8, 13, 14] indicated that time involved in mixing the sample was not important. We were unable to confirm this. In fact, 60 minutes appeared to be the optimum time required to achieve satellitism in a continuously *mixed* sample, whilst an unmixed sample showed no satellitism over a similar length of time.

Investigations as to the effect, if any, of the various anticoagulants were performed. Blood specimens were collected into vacuum tubes, (a) Venoject™ (Jintan Terumo), (b) Vacutainer™ (Becton Dickinson) containing EDTA citrate, and heparin as anticoagulants. Films made on each specimen after mixing at room temperature for one hour showed EDTA to have the most striking result. Films made from the other anticoagulants, from unanti-

coagulated venous blood, and from a capillary sample showed no satellitism. From these results it would appear that EDTA potentiated the satellitism effect.

We now felt that this platelet neutrophil phenomenon was not an artifact as other bloods treated in a similar manner did not show any satellitism. If a similar effect could be induced on normal bloods by the patient's serum or plasma this would help confirm our feelings. The patient's serum, along with an unknown normal serum and normal saline, were mixed with ABO compatible, EDTA bloods in a random manner. Films made before and after mixing at room temperature for one hour indicated that the patient's serum was able to induce a similar effect on normal bloods. Neither the normal serum nor saline had any effect.

Investigation of Mrs P.'s blood was carried out, the following negative or normal results being obtained.

Quantitative Direct Coombs: Negative. Cold agglutinins: Negative 4°C, 20°C, 37°C. Cell panel: Negative. Donath-Landsteiner: Negative H L-A Antibodies (Lymphocytoxicity test): Negative. Auto Antibodies: Thyroglobulin, Thyroid, Microsomal, Parietal Cell, Mitochondrial, A.I.C.F., and A.N.F. all negative. Antibodies to Smooth Muscle were detected to a titre of 32.

Complement CH_{50} titre of 85 (Normal). Anticomplementary activity: Normal. Serum protein electrophoresis: Normal. Immunoglobulins: Normal. Cryoglobulins: Suspected on one occasion but not confirmed. LE Cells: Negative.

The white cells were checked, by firstly looking at their enzyme status, using cytochemical techniques. The N.A.P. and peroxidase stains both gave normal reactions, as did the N.B.T. reaction. The P.A.S. stain, although normal, showed a curious finding; the more intensely staining neutrophils appeared to have more platelets satelliting them than the less intensely staining cells. It was also noted that those platelets that were satelliting tended to be PAS negative, whilst some that were free showed variable PAS positivity.

A washed, buffy coat suspension, from the patient, was mixed with platelet rich plasma from normal donors. After mixing at room temperature for one hour, no satellitism could be seen in the stained films. It was concluded from the results that there probably was no functional abnormality of the white cells.

Platelet function was studied in the following tests: Template Bleeding Time, Whole Blood Clotting Time, Clot Retraction, Prothrombin Consumption, Platelet Factor 3 availability, and a simple Platelet Aggregation test. The results of all these tests were within normal ranges. A check of the plasma coagulation factors was also carried out, these being within normal limits. A washed, platelet rich suspension was tested in a similar manner to the white cells as above. After mixing with normal bloods, stained films showed no satellitism. From this it was concluded that there was no abnormality in the coagulation process and that the platelets were probably functioning normally.

Acetylsalicylic acid, known to have an adverse effect on platelet function by inhibiting intrinsic release of ADP, was mixed with Mrs P.'s blood along with a random normal. Films were made before and after mixing, and examined, the normal blood showing no satellitism, whilst the test blood continued to show satelliting. The patient was given two Aspirins and blood samples collected two and five days after taking the Aspirin showed the satelliting phenomenon after suitable mixing. Thus it would appear that acetylsalicylic acid had no direct or indirect effect on platelet satellitism.

No satellitism could be demonstrated in bloods collected from Mrs P.'s daughters. Although this neither confirms nor refutes a heredity basis for this phenomenon, we feel that this is probably unlikely.

Discussion

We have been able to establish that the *in vitro* demonstration of platelet satellitism is dependent on time and mixing. We have also been able to show that the platelets and white cells appear to function normally and that a serum factor, which is stable at 56°C and apparently not complement dependent is present. Although we were unable to demonstrate any specific white cell or platelet antibodies, either bound to the cells or present in the serum, this does not exclude there being one present.

The detection of smooth muscle antibodies (SMA) to a titre of 32 would appear to have no clinical significance in this case. Of the 180 requests for autoantibodies from our hospital in the last two years only 11 (6 percent) have had S.M.A. titres of 16 or greater. The only common factor amongst these cases was an elevated E.S.R. No other link between S.M.A. levels and clinical condition was noted.

Of the reported cases[1, 2, 3, 4, 8, 12, 13, 14] of platelet satellitism totalling at least 22 (as at July, 1977), we have been able to review 14, finding no common factors. Of the reported cases three appear to be dissimilar to the others, in that the findings either could be related to the clinical condition, or were of a transient nature. Five of the 14 cases reported were surgical cases or normal persons, two were hypertensive, three had shown alcohol involvement, and three had malignancies of various types. The ages of patients in which satellitism had been seen ranged from 14-60, with the majority being in the 50-60 age group.

The phenomenon of platelet satellitism has interested many workers, and several suggestions as to the mechanisms have been put forward. The report of Bauer (1975)[1] suggests the answer could lie in one of three areas; changes in the cell membrane of the neutrophils conferring on them a foreign surface character, the presence of a new factor in the serum, or a change in the platelets that in some way makes them suitable for neutrophilic phagocytosis. We feel that the answer probably is a combination of the latter two suggestions.

The report of Reisman *et al.* (1974)[13] includes an electron photomicrograph of a neutrophil apparently phagocytosing a platelet. Other workers[9, 15] have reported similarly. Careful re-examination of several slides of our patient showed in fact that some of the neutrophils and at least one monocyte could be regarded as being in the process of engulfing platelets. If this is so, it raises an interesting question. Why are the platelets being phagocytosed?

It is known and reported[15] that when bacteria and other particles are coated with sufficient amounts of specific antibody, they are ingested by phagocytes, with great avidity. A similar effect involving phagocytosis of antibody-coated platelets by neutrophils, has been shown in an article by Handin and Stossel (1974)[5]. Using ^{51}Cr labelled platelets, N.B.T. reduction testing, and direct microscopy of platelets, they were able to show that antibody mediated phagocytosis of platelets may be important in the pathogenesis of idiopathic thrombocytopenia (I.T.P.).

In a review of antiplatelet antibodies and their detection, Karpatkin *et al.* (1972)[7] found antibodies to platelets in 65 percent of patients with I.T.P. and in 78 percent of patients with S.L.E., of whom only 14 percent were thrombocytopenic. An earlier report[6] suggests that platelet counts can be normal in patients with antiplatelet antibodies and that this could represent a compensatory thrombocytolytic state.

Yankee *et al.* (1969)[17] reported that several recognised HL-A antigens, as well as other antigens found on lymphocytes, are present on platelets. Svejgaard *et al.* (1970)[15] have reported complement fixing platelet isoantibodies active against HL-A, A1, A2, A3, A9, HL-A B5, B7 and B15. Nymand *et al.* (1971)[11] were able to demonstrate platelet antibodies that reacted positively with all platelets possessing HL-A 5 or HL-A 7 antigens as established by the lymphocytotoxicity test. The HL-A type of our patient, as recorded, as A1, —, B7, B15, all three having been previously associated with platelet antibodies.

It has also been shown that certain HL-A antigens have increased frequency in patients with various disease states, e.g., HL-A B_{27} and ankylosing spondylitis. HL-A antigens A_1 and B_{w15} have been shown to have an increased frequency in patients with S.L.E. Mrs P., interestingly enough, had both the A_1 and B_{15} antigens. Although no HL-A antibodies were detected, and no evidence to support a diagnosis of S.L.E. was found, an interesting hypothesis could be advanced. Platelets satelliting neutrophils, or as evidence would strongly suggest, neutrophils phagocytosing platelets, could be the result of an autoimmune process, similar to, but not necessarily identical with S.L.E. involving a platelet autoantibody.

Conclusion

Association between HL-A typings, platelet antibodies and disease states, have already been established. By reviewing the HL-A typing neutrophlis conferring on them a foreign sur-

recognised H.L.A. antigens, as well as other active against H.L.A. A1, A2, A3, A9, H.L.A. H.L.A. 5 or H.L.A. 7 antigens as established by the lymphocytotoxicity test. The H.L.A.

It has also been shown that certain H.L.A. with various disease states, e.g., H.L.A. B_{27} and ankylosing spondylitis. H.L.A. antigens A_1 antigens. Although no H.L.A. antibodies were

Association between H.L.A. typings, platelet of our patient, in the light of these points it would appear that there is strong evidence, if somewhat circumstantial, to suggest the presence of a platelet autoantibody. It would also appear that this antibody, by a process of opsonisation, is responsible for the phagocytosis of the platelets.

Because of the few cases, and lack of adequate data, this remains conjecture at this stage. Many questions still need to be answered regarding this finding. Perhaps by more careful examination of those bloods showing "satellitism", or by routinely screening all patients with suspected autoimmune diseases, such as S.L.E., for the satelliting phenomenon more evidence may be found to add weight to the proposals presented here.

REFERENCES

1. Bauer, H. M. (1975), *Am. J. Clin. Path.* **63,** 824.
2. Bolton, F. G. and Boyd, J. (1963), *Brit. Med. J.* **2,** 747.
3. Crome, Patricia E. and Barkan, P. (1963), *Brit. Med. J.* **2,** 871.
4. Field, E. J. and MacLeod, I. (1963), *Brit. Med. J.* **2,** 388.
5. Handin, R., Hanndin, S. and Stossel, T. P. (1974), *New Eng. J. Med.* **290,** 989.
6. Karpatkin, S., Garg, S. K. and Siskind, G. W. (1971), *Amer. J. Med.* **51,** 1.
7. Karpatkin, S., Strick, N., Karpatkin, Margaret and Siskind, G. W. (1972), *Amer. J. Med.* **52,** 776.
8. Kjeldsberg, C. R. (1974), *New Eng. J. Med.* **290,** 165.
9. MacDonald, G. A., Dodds, T. G. and Cruickshank, Bruce. (1970), *Atlas of Haematology* 3rd Edition, 140. E. and S. Livingstone. Edinburgh and London.
10. Miale, J. B. (1972), *Laboratory Medicine-Haematology* 4th Ed. 1074. C. V. Mosby. St Louis.
11. Nymand, G., Heron, I. and Jenson, K. G. (1971), *Vox Sang* **20,** 85.
12. Prchal, J. T. and Blakeley, J. (1973), *New Eng. J. Med.* **289,** 1146.
13. Reisman, L. E. and Sabesin, S. S. (1974), *New Eng. J. Med.* **290,** 691.
14. Signy, A. G. and Green, A. E. (1963), *Brit. Med. J.* **2,** 624.
15. Stossel, T. P. (1974), *New Eng. J. Med.* **290,** 717, 744-780, 833-839.
16. Svejgaard, A. and Kissmeyer-Nielson, F. (1970), *Vox Sang,* **18,** 12.
17. Yankee, R. A., Grumet, F. G. and Rogentine, G. N. (1969), *New Eng. J. Med.* **281,** 1208.

Experience with Curve Regeneration in Continuous Flow Analysis

J. B. Kitto, ANZIMLT
Medical Laboratory, Plunket House, Dunedin

Received for publication, April 1978

Summary

(1) A brief outline of the principles of curve regeneration is given, a full investigation of the practical and theoretical considerations being the subject of previous publications[1, 2].

(2) A schedule of the workload of a diagnostic laboratory dependent on two single channels of Technicon AAI and two channels of Technicon AAII autonalyser for the handling of 15-16 routine chemistries daily is described. The latter equipment being linked to a dual channel data printer.

(3) Although the primary reason for consideration of curve regeneration in our laboratory was the capacity to utilise high cost equipment to greater advantage, other major advantages readily became apparent and these are discussed.

Introduction

Continuous flow autoanalysers such as those marketed by Technicon have been part of the routine chemistry laboratory for a number of years and most will be familiar with their mode of operation. For a time it seemed inevitable that this mode of automative analysis would supersede all other alternatives in the handling of increasing workloads. How-

ever, almost in response to such a challenge other modular systems began to appear, some to remain only temporarily, others to make their appeal through either increased precision and efficiency or decreased reagent and sample consumption or a combination of factors. The only response of the continuous flow developers to this challenge seemed to be the production of multichannel systems, which admittedly provided one answer to the demand of the large laboratory where significant "profile" requisitioning might justify such systems, but to the medium size and smaller laboratories where requisitioning of tests might be termed as "selective", such multichannel systems seemed hardly a viable proposition.

Principle

One of the limiting factors of continuous flow systems is the relatively slow speed at which they may be operated. Some of the more robust methodologies tolerate a sampling rate of 60 per hour while others require to be reduced to as few as 30 per hour, the problems being carryover from one specimen to another and the swamping of small peaks which follow excessively high peaks.

It has been shown that ultimate peak height for a given channel and chemistry can be expressed by the equation:

$$E = h + b\frac{dh}{dr} \qquad (1.2)$$

where E = ultimate peak heights
h is the position of the pen at any time, T.
b is a constant for the channel and the chemistry
$\frac{dh}{dr}$ is the rate of rise (or fall) of the peak at T

The Curve Regenerator* is an analogue computer which continuously performs this mathematical transformation on the imput signal and recalculates the new corrected signal which then goes to the recorder, the result being that peaks are much better differentiated and sampling rates can be increased by at least 50 percent without any loss of peak resolution or more importantly accuracy.

* The Curve Regenerator was originally developed by Weir Electronics Ltd and is now available from MSE dealers.

Curve regeneration needs to be performed on a linear absorbance signal, hence a logarithmic amplifier is required between the colorimeter and curve regenerator. Colorimeters which already have a linear output do not require the logarithmic amplifier.

Both the curve regenerator and log amplifier modules may be switched out of the measuring circuit independently if the system needs to be checked in its unregenerated form. Because of the greatly increased sampling times attainable with curve regeneration it is felt that improved performance is attained by the use of electronic timers to control the sample rather than relying on the conventional mechanical cam.

Workload

Our chemistry laboratory is required to process up to 650 test requests per day, 90 percent of the workload being handled by two channels of AAI Technicon Autoanalyser and two channels of AAII Autoanalyser to which is attached a dual channel data printer. This workload is distributed unevenly between 17 chemistries, with between 13-16 of these being run on a given day.

Each method was set up individually with the curve regenerator to ascertain the optimum degree of regeneration, a time constant being determined empirically for each test by successive approximation on a series of high standards. Sampling rates were then able to be increased progressively to rates which would still produce 95 percent peaking. It was found that curve regeneration enable the more robust chemistries to have their sampling rates increased by at least 50 percent and the more "labile" method by a lesser degree. Methods on the Autoanalyser II were able to be increased to the maximum sampling rate of 120 samples per hour; presumably because of the better wash characteristics of the flow cell in the AAII colorimeter. Towards the end of 1977 our workload was at the point where we were having to consider either extending the hours of the working day at present, 7.30 a.m.-5.30 p.m., or the purchase of further equipment. It was at this point that it was decided to purchase two curve regenerators incorporating logarithmic amplifiers and have electronic timers installed in both sampler II's on our Autoanalyser I channels.

TABLE I.—Autoanalyser I.

	Unregenerated		Regenerated	
	Sampling Rate/Hour	Sampling Volume	Sampling Rate/Hour	Sampling Volume
Protein	50	0.185	80	0.115
Alkaline Phosphate	50	0.185	80	0.115
Cholesterol (Solvent Ext)	40	—	60	—
Triglycerides (Solvent Ext)	40	- -	55	—
Uric Acid	50	0.26	80	0.16
Iron	40	0.9	60	0.6
Creatinine	50	0.65	70	0.4
Oestriol (Urine Diln)	40	—	70	—
Chloride	60	0.21	80	0.16
Calcium	50	0.13	80	0.08
Phosphate	50	0.18	80	0.115

TABLE II.—Autoanalyser II.

	Unregenerated		Regenerated	
	Sampling Rate/Hour	Sampling Volume	Sampling Rate/Hour	Sampling Volume
(SGPT) + Blank	80	0.214	120	0.144
(SGOT)	80	0.28	120	0.190
(Bilirubin) + Blank	80	0.134	120	0.090
(GTP)	80	0.067	120	0.045
(Urea)	80	0.067	120	0.045
(Glucose)	80	0.067	120	0.045

Table I shows the improved sampling rates obtained with curve regeneration and the associated reduction in sample volume.

The effect of curve regeneration of AAII methodologies was studied and sampling rates achieved are shown in Table II.

Discussion

With the aid of curve regeneration sampling rates on a standard Technicon AAI system have been increased from an average of 47-72 samples per hour, and on AAII equipment from 80-120 samples per hour.

The cost of curve regeneration and electronic timers is approximately $1,000 per channel for AAI systems, and less than $500 per channel for AAII systems, the difference being that the output from AAII colorimeters is linear, and no logarithmic amplifier is required.

In addition to the obvious advantages of increased sampling rates with the accompanying reduction in sample volume, there are several other advantages which may not be immediately apparent and these are listed:

(1) Analysis is increased by at least 50 percent, allowing often much needed time for preventative maintenance or method investigation.

(2) Reagent consumption for test is reduced. This is particularly significant in enzyme analysis where expensive co-enzyme reagents are used.

(3) Less sample is required. Liver function tests, including 4 enzymes, bilirubin and total protein, can be assayed on 0.7 ml compared with 1.065 ml previously. This applies equally to the volume of calibration sera used for standardisation.

(4) Precision is improved. Recorder tracings are now all linear and straight line calibration is obtained, thereby reducing the need for as many calibration points, and eliminating errors which can be intro-

duced when drawing calibration curves.

(5) Effective life of pump tubes is extended by reducing the operating time for each method. With the cost of manifold pump tubes assuming increasing proportions this factor can represent a considerable saving when changes of manifold pump tubes are recorded and preventative maintenance attended to.

(6) Capital expenditure on expensive new automative equipment can at least be deferred.

One always has hopes that the one instrument which will process every routine request using the smallest aliquot of reagent and infinitely small volume of sample without producing vast quantities of non-requested test results, may be about to appear on the market, but with the advent of curve regeneration at modest cost we have a further tool to enable us to at least produce more efficiently and precisely those routine parameters requested.

It is hoped that these observations may be of some assistance to those who have combinations of single channel continuous flow systems operating in their laboratories and who have a cautious cost conscious attitude towards the purchase of expensive new equipment.

REFERENCES

1. Carlyle, J. E., McLelland, A. S. and Fleck, A. (1973), *Clin. chim. Acta,* **46,** 235.
2. Walker, W. H. C., Townsend, J. and Keane, P. M. (1972), *Clin. chim. Acta,* **36,** 119.

The Performance of Cholesterol and Triglyceride Analyses in New Zealand

M. Lever and D. J. Munster

Department of Clinical Biochemistry, Christchurch Hospital

Received for publication, May 1978

Summary

A new design for interlaboratory surveys was used to evaluate the performance of cholesterol and triglyceride analyses in New Zealand. A majority of New Zealand clinical laboratories may need to improve analytical and control systems to consistently meet minimal clinical requirements. Medical practitioners expect a higher standard of performance than the minimal standards, and hence a much higher standard than is achieved. Despite considerable changes in the analytical methods in use, New Zealand laboratories have not significantly altered their standard of performance between 1974 and 1976 except for a possible improvement in triglyceride precision in 1974-1975.

Introduction

Serum lipid concentrations have a positive correlation with atherosclerosis[3], and quantitative levels have been quoted for given risk factors[1]. However, cholesterol and triglycerides are not easy to estimate in blood, and there is reason to doubt the ability of laboratories to meet the clinical requirements for assessing this risk factor[9]. The National Heart Foundation of New Zealand supported a survey of New Zealand clinical laboratories between late 1974 and the end of 1976 to evaluate the seriousness of this problem in New Zealand[6, 7].

In this work it was initially shown that existing survey designs were not satisfactory for evaluating blood lipid estimations[7, 4] and a new design was developed[5]. Using this design it was shown[6] that few laboratories in New Zealand achieved a precision as good as that expected by clinicians; though about 60 percent of cholesterol analyses, and 40 percent of triglyceride analyses, are performed with precision which should[1,2] be adequate for clinical use. During the course of this survey work laboratories were questioned about their lipid analyses, and this report discusses some of the technical findings which extend those reported by Siebers[8] and which illustrates changes since the earlier survey was carried out. Further, some of the areas are identified which laboratory workers could investigate in an effort to improve the service they provide to the clinician and hence to the patient.

Methods

The mechanics of the survey are described in detail elsewhere[6, 7, 5]. In brief, two different

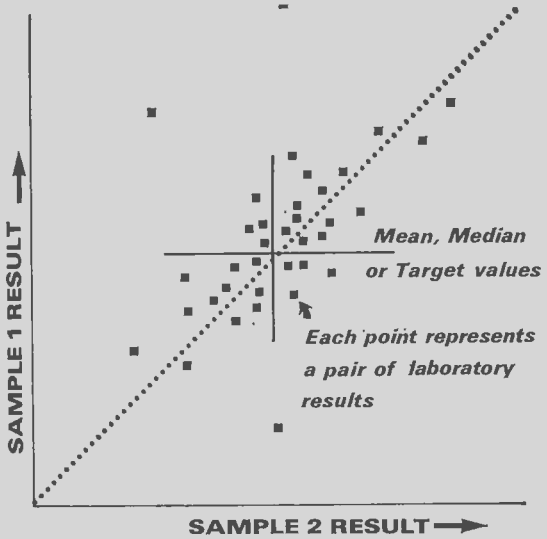


Figure 1. — Youden diagram, original form. If all errors are purely in standardisation the points will all lie on a diagonal. Points well away from this diagonal are visually shown to be grossly in error.

serum specimens were sent each month to each of the 53 participating laboratories. The results returned were reported back in the form of a Youden diagram (Fig. 1), which provides an easily understood visual presentation of the place of each laboratory with respect to its peers, and does not require a knowledge of statistics before it can be interpreted. Statistical data were also calculated.

At the end of each six-month period the 12 results from each laboratory were compared with reference results using linear regression. The slope and intercept of the line of best fit are used as measures of accuracy in that they show how the results reported by the laboratory vary as the concentration of the component varies. The portion of variance unexplained by the line of best fit (the coefficient of nondetermination or CND) is used as a precision measure: this latter can be approximately thought of as a measure of "proportion of random rubbish" in results, so that a CND of 0.05 implies that 5 percent of the variation in the laboratory results are unrelated to concentration differences.

Before and during the survey period, questionnaires were distributed to laboratories asking about techniques used for cholesterol

TABLE I
PERFORMANCE EXPECTED BY PROFESSIONAL GROUPS

	EQUAL OR BETTER THAN...(mmol/L)	MANZ RESPONDERS	NZACB RESPONDERS
A. Within laboratory precision (long-term)			
Cholesterol	± 0.2	11	5
	± 0.5	40	16
	± 1.0	46	21
	Total quoting limits	48	21
Triglycerides	± 0.2	42	17
	± 0.5	48	20
	Total quoting limits	50	20
B. Between laboratory agreement			
Cholesterol	± 0.2	12	0
	± 0.5	34	13
	± 1.0	44	17
	Total quoting limits	46	20
Triglycerides	± 0.2	32	12
	± 0.5	44	17
	Total quoting limits	45	20
C. Precision clinicians wish to interpret			
Cholesterol	± 0.2	1	0
	± 0.5	21	11
	± 1.0	48	20
	Total quoting limits	52	21
Triglycerides	± 0.2	39	8
	± 0.5	50	17
	Total quoting limits	52	20

and triglyceride measurement, control procedures, frequency of analyses and other details. Questionnaires were also sent to members of the Canterbury Division of the Medical Association of New Zealand asking about their expectation of inter- and intra-laboratory variation in serum lipid estimations.

Results

Clinical Expectations

The return rate for the questionnaire sent to MANZ members was only 13 percent. Added to some returns were comments which are worth bringing to the attention of laboratory workers; a sample of these is given in Appendix I. The questionnaire was subsequently sent to members of the New Zealand Association of Clinical Biochemists, a diverse group which includes medically qualified personnel (pathologists, registrars and some phy-

TABLE II

PERFORMANCE ACHIEVED COMPARED WITH REQUIRED PERFORMANCE

SPECIMENS (set of 12)	TOTAL VARIANCE (mmol/l)²	MEAN mmol/l[a]	MEDIAN ASSUMED CMD[b]	MEDIAN REQUIRED CMD[c]	ACCEPTABLE CMD[d]	PROPORTION OF LABS. ACCEPTABLE
Cholesterol:						
12/75- 5/76	1.56	6.12	0.03	0.04	0.13	27/50
6/75-11/75	1.79	6.10	0.02	0.03	0.11	25/50
1/76- 6/76	3.23	6.06	0.01	0.02	0.06	27/46
7/76-12/76	3.19	6.05	0.01	0.02	0.06	32/51
Triglycerides:						
12/74- 5/75	0.86	0.20	0.007	0.013	0.05	3/38
6/75-11/75	0.55	0.12	0.010	0.005	0.07	12/40
1/76- 6/76	0.95	0.06	0.006	0.013	0.04	13/33
7/76-12/76	1.03	0.08	0.005	0.002	0.04	12/40

[a]Calculated after conversion to corresponding Fisher's z value.

[b]CMD calculated from precision assumed by 50% or more of MANZ respondents (table I), that is, precision expected by 50% of clinicians.

[c]CMD calculated from precision required to allow clinicians to interpret the differences which 50% or more expect to interpret (table I).

[d]Criteria of Cotlove et al. (ref. 8).

Note that CMD values from one six-month period cannot be directly compared with those from another unless first corrected for the total variance.

TABLE III

REPLICATION OF RESULTS

CONCENTRATION DIFFERENCES (mmol/l)[a]	NUMBER OF REPLICATES	
	Cholesterol[a]	Triglycerides
>+1.0	4	6
+0.5 to +0.99	12	15
+0.2 to +0.49	47	39
+0.0 to +0.19	86	55
-0.2 to -0.01	76	57
-0.5 to -0.21	36	39
-1.0 to -0.51	7	13
<-1.0	6	7

[a]For cholesterol, multiply concentration differences by 2.5.

Six (out of possible twelve) pairs of results used in analysis.

sicians), scientists working in the area of medical biochemistry, and graduate technologists fulfilling a paramedical function. The return rate in this case was almost identical (14 percent). The low return rates suggest that the results given below may be biased because the 86 percent to 87 percent who did not return the questionnaire are likely to have less interest in the subject than those that replied. In consequence, the expectations here could represent the views of better informed groups rather than of the entire professional groups.

More than three-quarters of responders from each professional group expected the between-batch precision in one laboratory to be better than ± 0.5 mmol/l for cholesterol analyses and better than ± 0.2 mmol/l for triglycerides (Table I). There is fairly widespread awareness of interlaboratory variability, though this is still underestimated. In the case of cholesterol, less than half the MANZ responders expected to take physiological interpretations from differences in cholesterol concentration smaller than 0.5 mmol/l, though over half would assume significance in triglyceride differences of only 0.2 mmol/l.

Laboratory Achievements

The essential features of laboratory precision performance are summarised in Table II, along with (for comparison) data recalculated from the results given in Table I, and from Cotlove's[2] estimates of clinical requirements. Taking into account the changes in variance, it can be seen that the overall cholesterol performance (precision only) remained approximately constant over the two-year period, whereas triglyceride performance improved significantly, almost all this improvement occurring during the first year.

For cholesterol, the average performance (precision) was close to that regarded as meeting minimum clinical requirements; in fact, almost half the laboratories in New Zealand probably do not meet these requirements. As many (probably most) clinicians expect (and base their interpretations on the assumption of) a considerably higher standard of performance, it is obvious that patient management in cases of suspected hyperlipidaemia must be commonly affected by misleading laboratory data. For triglycerides, the situation is much worse; only a minority of laboratories are meeting minimal clinical requirements, and in this case the expectations of clinicians are probably unrealistic in terms of what can be achieved or what is needed.

Precision was also examined by sending out specimens from the same pools in different orders in two successive six-month periods. Table III shows the distribution of the differences between pairs of laboratory results on the same specimens when analysed two to 12 months apart. These results confirm the

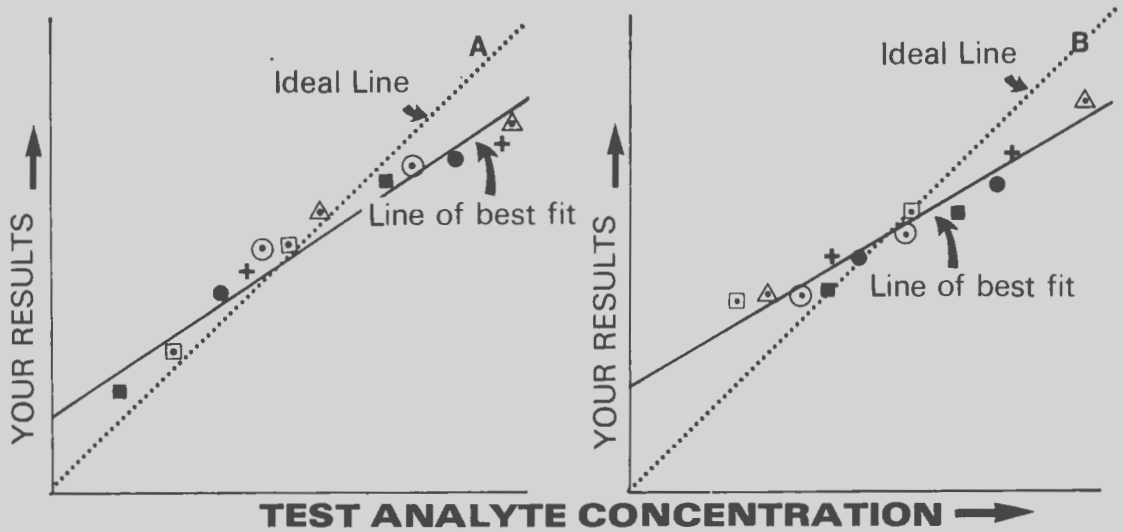


Figure 2. — Linear regression plots, with pairs of specimens indicated by different symbols. Two model cases, (A) with supposed non-linearity, (B) with erroneous blank and standard calibration with between batch variability.

prevalence of unsatisfactory performance, and that triglycerides (relative to clinical requirements) are performed less adequately. As reported elsewhere[7], there are strong correlations between the differences and the concentration of cholesterol and triglyceride, showing that for these tests the absolute error increases with concentration.

Accuracy assessments were also made from the survey data (reported elsewhere[6, 7]). The design[5] used in this work makes it possible to give some insight into possible forms of error[4], and in Appendix II is given the protocol which was supplied to laboratories to assess error identification. It is worth noting here that, for both cholesterol and triglyceride analyses, it was common to find reasonably precise laboratories with the intercepts of their lines of best fit which were significantly greater than zero, combined with slopes significantly less than one. This combination means that results may be biased high at low concentrations and low at high concentrations, the error increasing with distance from a central point (usually the calibration point), at which target values and laboratory results agree (Fig. 2). Two explanations for this pattern have been described[4], both illustrated in Figure 2: first, serum calibration of a non-specific method (e.g., direct acid-colour cholesterol methods or enzymatic triglycerides), and secondly, non-linear analytical systems. In practical terms the two can rarely be distinguished on survey specimens (a few examples of gross non-linearity were observed), and both potential problems were suggested for consideration to the laboratories that obtained this combination of statistics (Appendix II). From correspondence and unpublished experimental data, it would appear that non-linearity is common, especially with the ferric-chloride acid-colour cholesterol methods and with enzymatic triglycerides.

Finally, it was found[6] that only three New Zealand laboratories maintained a fully satisfactory standard for cholesterol analyses over a two-period period, and only one for triglyceride analyses. "Satisfactory" in this context is based on the minimal standards of Cotlove *et al.*[2], taking into account systematic errors as well.

Standardisation and Quality Control Procedures

Information on standards was not obtained from all laboratories. However, some general trends were apparent. For example, at least 16 laboratories used only one standard for cholesterol; this was a serum standard in nine cases. Another five laboratories simply multi-

TABLE IV

NUMBER OF CONTROLS USED BY LABORATORIES

	CHOLESTEROL	TRIGLYCERIDES
One control	4	5
Two controls	18	17
Three controls	25	16
Four controls	0	1
No abnormal[a] control	20	15
One abnormal control	22	21
Two abnormal controls	5	3

[a]Abnormal: for cholesterol, above 6.7 mmol/l; triglycerides above 2 mmol/l

TABLE V

ANALYTICAL METHODS USED BY LABORATORIES

METHOD CATEGORY	NUMBER USING METHODS	
	SIEBERS 1974[5]	OCT. 1976
a. Cholesterol:		
Manual Acid Colour - with Fe salt	23	11
" Acid Colour - no Fe salt	17	12
" Enzymatic	0	4
Automated Acid Colour - with Fe salt	4	8
" Acid Colour - no Fe salt	7	3
" Enzymatic	0	9
b. Triglycerides:		
Manual [illegible]	24	[illegible]
" Chromotrope acid	0	2
" Enzymatic	2	[illegible]
Automated [illegible]	6	[illegible]
" Enzymatic	[illegible]	[illegible]

plied absorbance readings by a pre-determined factor. Thus at least 21 laboratories assume a linear assay when calculating the results for each batch of cholesterol analyses. Only 12 laboratories used three or more standards. In addition to this there was considerable variation in the number of steps in the analytical procedure that the standards were carried through, at least 12 laboratories introducing the standards part way through.

A similar pattern was observed with triglyceride analyses. Nine laboratories are known to have used only one standard, four of these being serum standards; at least another 15 laboratories calculated triglyceride results from instrument response using a conversion factor. Nine laboratories stated that they used three or more standards.

The chemical nature of the standard varied also. Cholesterol is present in serum lipoproteins as predominantly cholesteryl esters, with 20 percent to 40 percent unesterified cholesterol, and this pattern applies in most, but not all, control sera used for standardisation (Munster, unpublished data). Laboratories used unesterified cholesterol as standard unless using serum standards or a conversion factor. Triglycerides were standardised against a mixture of esters (control sera), tripalmitin, triolein (most common) and glycerol.

These variations in standardisation procedures could be a major factor in interlaboratory variability, and this factor has been estimated[7] to be of the order of 30 percent of interlaboratory variability for cholesterol estimates and 39 percent for triglyceride estimates. These figures were obtained from a study of the tendency of the paired reported results to be high or low together.

Single point serum standardisation can lead to systematic errors[4] which are characterised by low slopes with positive intercepts in the end-of-period reports. Reported results become less accurate with distance from the serum standard. This form of error was observed in this survey[7] and in consequence it would seem desirable that laboratories which are obliged to use a serum standard should choose one close to the clinical decision levels. This appears to be done with triglyceride determinations, but at least three laboratories use serum standards with cholesterol concentrations below 5 mmol/l.

An interlaboratory survey audits the effectiveness of internal control procedures, and the unsatisfactory performances found are consistent with inadequate control procedures used in many laboratories (Table IV). A feature not made clear in Table IV is that 11 laboratories which ran two controls per batch, and five which ran three, did not use an abnormal control. An example of the consequences of this was seen in one laboratory's results for cholesterol determinations. These (though reasonably precise) were grossly non-linear, so that concentrations approaching

TABLE VI

LIPID TESTS CARRIED OUT IN NEW ZEALAND LABORATORIES

TEST	NUMBER OF LABORATORIES	
	LATE 1973[a]	NOV. 1974
Total Lipids	15	12
Cholesterol	51	55
Triglycerides	43	44
Phospholipids	1	2
Free Fatty Acids	-	4
Lipoproteins - Ultracentrifugation	2	1
- Electrophoresis	35	32

[a]Siebers (1974): (Ref. 9)

the textbook upper limit of normal (ca 6.7 mmol/l) would never be reported. They used two control sera, with their target values of 145 mg/dl (3.8 mmol/l) and 75 mg/dl (1.9 mmol/l): levels at which they reported accurate results, which have little diagnostic value.

The data reported here on standardisation and control procedures cannot be quantitatively related to performance, since the choice of the materials is only part of the control process. Nevertheless, the surveys showed that (i) many laboratories are in fact not controlling their lipid analyses adequately, and (ii) the questionnaire showed cases of laboratories using calibration and control materials which were incompatible with good control. It is not the number of standards and controls which is important, but the appropriate choice of them for the methods used and clinical decision levels; and the responsiveness of the laboratory to unsatisfactory control results.

Analytical Methods in Use

The analytical methods used for cholesterol and triglyceride analyses were surveyed by Siebers[8] in late 1973. In October, 1976, a questionnaire was circulated which allows a direct comparison to be made with the earlier survey (Table V), and in the approximately three-year period there had been a large increase in the number of laboratories using

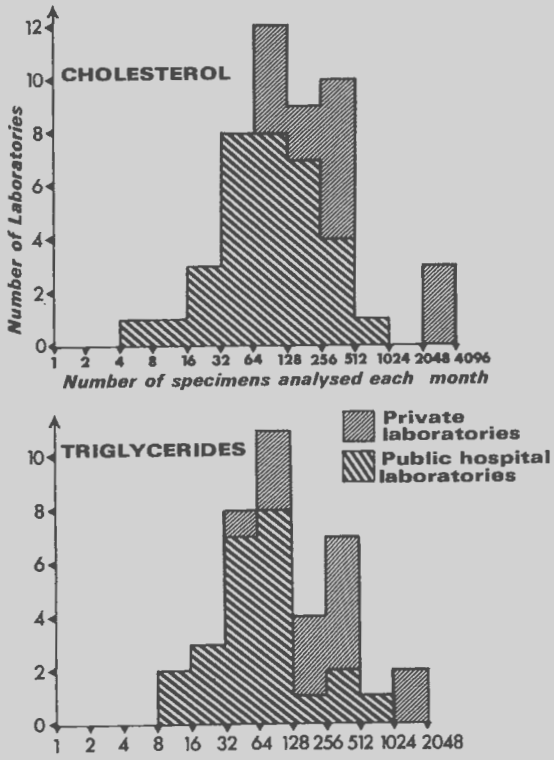


Figure 3. — Numbers of specimens analysed for cholesterol and triglycerides by survey participants each month.

enzymatic methods. The change occurred mainly at the expense of manual non-enzymatic colorimetric and fluorometric methods. At the same time there has been an overall increase in the application of automation to lipid analyses. An attempt was made to assess performance differences between method categories, and the only convincing difference found[7] was a highly significant difference between enzymatic and non-enzymatic laboratory results. For cholesterol and triglycerides, laboratories using enzymatic methods appeared to perform less well overall than other laboratories, possibly because many of these laboratories had less experience with the newer methods or had changed methods because they had never been able to obtain satisfactory lipid results.

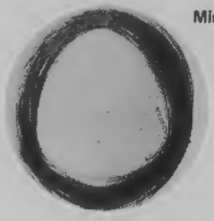
Laboratories in the Survey

The population of laboratories in the survey was essentially that surveyed by Siebers, and

NORWOOD

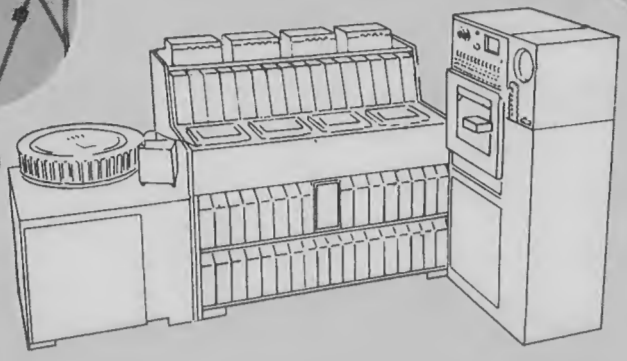
"One source for all your auto analysis needs"


Glassware


Miscellaneous Tubings

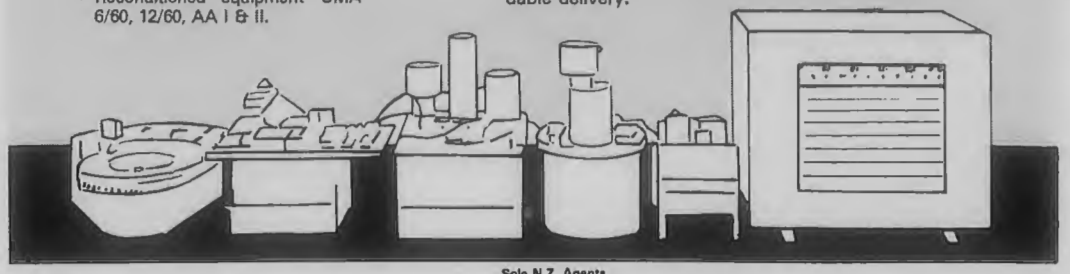

Recorder Paper


Manifold Pump Tubing



- Manifold Tubing Standard, Solvaflex & Flow-rated.
- Glassware (all types)
- Dialyzer plates & blocks
- Membranes • Stream Dividers
- Motor Stirrers • Nipples
- Pen Holders and Fiber tip pens
- Labels & tapes
- Chart paper • Connectors
- Reconditioned equipment SMA 6/60, 12/60, AA I & II.

Throughout the world, wherever there are hospitals and laboratories using Auto-analysis, NORWOOD laboratory products are used. NORWOOD has earned a reputation for quality and dependability at realistic prices. That's why more and more hospitals and laboratories are specifying NORWOOD. They want quality, dependability and reasonable cost. They get it from NORWOOD. NORWOOD distributors offer fast, dependable delivery.



NORWOOD SCIENTIFIC ASSOCIATES INC., New Jersey, USA.

Sole N.Z. Agents

GENERAL DIAGNOSTICS (NEW ZEALAND) LTD.

206 THE PARADE, ISLAND BAY, WELLINGTON, 2. P.O.BOX 7170 WELLINGTON SOUTH. CABLES & TELEGRAMS: DIAGNOSTIC. TELEX: GENDIAG NZ 3859. TELEPHONE 836-255

the previously reported[8] spectrum of tests offered was confirmed (Table VI). Of the laboratories which are known to estimate lipids in New Zealand, only one small private laboratory and two very small hospital laboratories carried out cholesterol analyses but declined to participate in the survey. Thus, though the New Zealand population of methods has changed, the population of laboratories performing lipid analyses has remained stable. There is some correlation between performance of cholesterol assays and performance of triglyceride assays; taking Hotelling's z values corresponding to the coefficient of nondetermination of each laboratory for cholesterol versus those for triglycerides, correlation coefficients of +0.21, +0.20, +0.40 and +0.20 were obtained, indicating that a common factor accounted for a small part (less than 10 percent) of the variation in performance. At the moment it is not possible to say whether this factor is more general in that there is a tendency for laboratories performing poor lipid analyses to perform other tests poorly.

Figure 3 shows the lipid test workloads of participating laboratories. Of the 15,500 cholesterol and 9,500 triglyceride analyses performed in New Zealand each month, approximately two-thirds are performed in 16 private pathology laboratories. Three private laboratories account for half of the cholesterol analyses. Correlation between number of tests performed (log of monthly figure used in calculation) and precision performance (Hotelling's z) was statistically quite insignificant, r = +0.14 for cholesterol and +0.01 for triglycerides; and there was no significant difference detected between the performances of public hospital and private pathology laboratories.

Discussion

The work described here is part of a study of blood lipid analyses as carried out in clinical laboratories. The questions asked concerned the reliability and accuracy of patient results reported to clinicians, the nature and sources of errors; and possible remedial action to improve the service to the clinician and hence to the patient. These are not the usual questions which interlaboratory surveys have been designed to answer: the first surveys were simple "round-robins" designed to see how results varied between laboratories. Thus it was no surprise that conventional survey designs proved to be inadequate for the purpose of this work. However, as outlined elsewhere[7, 4, 5], the design developed to study cholesterol and triglyceride estimations was found to be able to meet all functions of interlaboratory surveys as well as or better than do conventional designs.

The main function of an interlaboratory survey is to externally audit the ability of the laboratory to maintain an analytical standard necessary for patient diagnosis and management. There are two variables involved in the assessment process; one is the variation in the concentration of the test analyte in health and disease, in particular in patients' specimens referred to the laboratory, and the second is the variation in results reported by the laboratory on these specimens. *The real task of the external audit process is the study of the co-variance of these two variables.* In this respect, the present study shows that half the laboratories in New Zealand do not meet the requirements for cholesterol analysis, and the majority fail for triglycerides, when assessed over the range used for diagnosis and patient management. Most surveys do not cover that range.

A survey can be a powerful research tool to provide information about laboratory performance. This information should be available to clinicians as well as laboratory staff, and above all it should be made familiar to the educators who teach both groups. The results of the questionnaire cited here show that there is a very unsatisfactory communications gap, together with (to judge by the low return rate) unjustified complacency or apathy. Generally speaking, it was found that lipid analyses were performed well or badly in some laboratories, large or small, public hospital or private pathology. Even the choice of methods has relatively little effect, as was shown by the most and least precise laboratories for triglyceride assays who used (in two successive six-month periods) the same kitset method. A likely explanation for this is that the experience and ability of senior staff is the main factor in determining laboratory performance.

There are some specific suggestions which can be made on the basis of both this work

and conversations with the technologists and biochemists in participating laboratories:

1. Laboratories should more fully evaluate the performance of analytical methods in their hands, and not introduce apparently trivial modifications to published procedures without careful study. Linearity over the range of concentrations used in diagnosis and patient management is crucial.

2. Quality control procedures should be examined to ensure that the variation of reported results is an adequate reflection of physiological variation, over the range used in diagnosis and patient management. This means that values established in the laboratory (especially at higher levels) should be externally checked, and that the range of control sera should straddle clinical decision levels.

3. Standardisation of methods should be critically examined. The chemical nature of standard material and the standards matrices should be considered in the light of their effect on the chemistry of the methods used. The number of standards and method of calculating results from standards, should be considered carefully.

4. The interpretation of external survey data is not as simple as some surveys make it appear. Assessments of accuracy and precision must be considered in the light of the range of concentrations used for that assessment, the method of calculating the assessment statistics (e.g., repeatability or covariance for precision; mean bias or bias at different levels for accuracy).

Although the work reported here is concerned with blood lipid analyses, the conclusions should be applicable to many other tests. There is a great temptation to consider laboratory proficiency assessments too narrowly, without regard to the two questions of what is clinically necessary, and what the clinician (without laboratory experience) intuitively expects.

Acknowledgments

The authors appreciate the co-operation and tolerance of all laboratories that participated in the lipid survey. Analysis of data would not have been possible without computing aid from J. Brown, H. W. Taylor and T. A. Walmsley. We also acknowledge financial support from the National Heart Foundation and the Medical Research Council, and helpful comments and criticisms from M. H. Abernethy, C. M. André and other colleagues.

REFERENCES

1. Barnett, R. N. (1968), *Amer. J. clin. Pathol.* **50,** 671.
2. Cotlove, E., Harris, E. K. and Williams, G. Z. (1970), *Clin. Chem.* **16,** 1028.
3. Editorial (1977), *Br. med. J.* **1,** 789.
4. Lever, M. and Munster, D. J. (1977), *Clin. Biochem.* **10,** 56.
5. Lever, M. and Munster, D. J. (1977), *Clin. Biochem.* **10,** 65.
6. Munster, D. J., Lever, M., André, C. M. and Carrell, R. W. (1978), *N.Z. med. J.* **88,** 93.
7. Munster, D. J., Lever, M. and Walmsley, T. A. (1978), *Clin. Biochem.* (in press).
8. Siebers, R. W. L. (1974), *N.Z.J. med. lab. Technol.* **28,** 81.
9. Wenk, R. E. (1971), *Amer. J. clin. Pathol.* **55,** 311.

APPENDIX I
COMMENTS ON QUESTIONNAIRE RETURNS

(i) Don't know.
(ii) Would have no idea.
(iii) I am in no position to evaluate these findings nor is any other G.P.
(iv) These are situations where we expect guidance from colleagues such as yourselves — from the experts.
(v) I expect the laboratory to know what is the validity of their results.
(vi) The sky is the limit.
(vii) I would like to see results quoted with ± (such and such) or ± (so and so) %.
(viii) One would hope a laboratory measures as accurately what they think they are measuring as is possible within the bounds of cost and current technology.

APPENDIX II
A KEY TO FAULTS

The following key is simplified, but hopefully will be useful in the more straightforward cases.

Question	Next Question or Reply
Q1. Is your CND less than or equal to 0.05?	Yes — Q 2 No — Q 7
Q2. Are your slope and intercept statistics both close to the target values, with t-values less than 1.5 in each case?	Yes — R 1 No — Q 3

Q3. Is the t-value associated with your slope statistic (B) less than 1.5? Yes — R 2; No — Q 4

Q4. Is your slope (B) less than 1.0? — Q 5
Is your slope (B) more than 1.0? — Q 6

Q5. Is the t-value associated with your intercept statistic (A) more than 1.5? Yes — R 3; No — R 4

Q6. Is the t-value associated with your intercept statistic (A) more than 1.5? Yes — R 5; No — R 6

Q7. Draw graph of your results against reference results. Does one result or *one pair* of results deviate markedly more from the ideal line than the others? Yes — R 7; No — Q 8

Q8. Are specimens displaced in the regression diagram in pairs? Yes — R 8; No — Q 9

Q9. Do your higher results all fall below the ideal line, deviating more as the reference results increase? Yes — R 9; No — R10

Replies:

R 1. Your precision and accuracy are probably adequate for clinical purposes.

R 2. Possible errors are (1) a non-specific method or (2) incorrect blank (or baseline) settings.

R 3. Possible errors are (1) a non-linear assay in which your results are increasingly in error as the concentration increases; (2) inappropriate standardisation, e.g., a serum standard in a non-specific assay, or an erroneous blank used in two-point standardisation; (3) concentration dependent errors; check the precision of your assay at higher levels.

R 4. (1) Check the concentration and purity of your standards. (2) Does your method of standardisation correct for losses in the procedure? (3) Look for concentration dependent random errors by checking the precision of your assay at higher levels.

R 5. Possible causes are (1) faulty blank setting, or (2) the precision of your assay decreases at higher levels.

R 6. Possible causes are (1) incorrect standards (check concentration and purity), and (2) concentration dependent random errors; check the precision of your assay at higher levels.

R 7. Check whether a clerical error was made with the discrepant results. Examine your quality control procedure to discover why the erroneous results were not rejected. Ask us to recalculate your statistics omitting the erroneous results.

R 8. You appear to have between-batch imprecison. Check quality control procedures, stability of standards, and the reliability of instruments and techniques.

R 9. Your assay appears to have a serious non-linearity problem. In enzymatic methods this can be caused by depletion of substrate (e.g., a coenzyme in an aged kitset preparation). Incomplete hydrolysis of esters, insufficient dilution, or reagent exhaustion are other possible causes.

R10. Your within-batch precision is not adequate. Starting with the final step, work stepwise back through the procedure until the imprecise step is located.

The Design of an On-line Data Acquisition System from the Coulter Model S

H. W. Taylor, B.Sc., ANZIMLT, J. D. Brown, B.Sc. (Hons.).
Pathology Services, Christchurch Hospital

Received for publication, March 1978

Summary

The design of an on-line, real time data acquisition system for the Coulter Counter Model S is described. The performance of this design after implementation is reviewed.

Introduction

In the five-year period to 1976 the number of tests in the routine laboratory of the

Haematology Department, Christchurch Hospital, increased by over 100 percent, while stable staff numbers were retained. This was achieved by increasing automation, including the installation of a Coulter Counter Model S*. A consequence of this was that an increasing proportion of the laboratory staff's time was spent in manual transcription of results. In particular, the transcription of seven parameters from the Coulter result card into a format acceptable to the clinicians, and compatible with the current reporting system, placed a considerable clerical load on the laboratory.

Proposals were prepared to interface the Coulter S to the pathology computer used at that time for data acquisition in biochemistry as previously described by Abernethy and Brown (1973)[1].

Although computer interfacing of this equipment is not new, the apparent scarcity of literature here prevented us from using the experience of others in the design.

The purpose of this article is not to describe the overall function of laboratory operation under a computer system, but to show design concepts, and their development in the real laboratory situation.

It was felt that the laboratory must control the computer, rather than the reverse situation which has been seen as a frequent fault of some laboratory computer systems. The computer is just another piece of laboratory equipment, and should aid, and be run by laboratory staff.

The objectives in this case, then, were to provide an easily used, cost beneficial reporting system from the Coulter Model S, improving the performance of tests through closer control on the equipment, elimination of transcription, early detection of errors and rapid reporting in an acceptable format, without degrading the laboratory operation.

Design

OUTPUT REPORTS

Three types of output reports were considered according to function:

1. The Coulter results.
2. An immediate monitor of performance for control by a feedback loop involving the operator.
3. Management and statistical information for longer term control.

COULTER RESULTS

Unlike others, such as Barnard *et al.* (1974)[2] it was felt that Coulter result cards were not generally suitable for direct reporting to the wards. The format of these cards could be much improved and they were difficult to integrate into the reporting system. We required a result form well laid out that would fit in with the existing workflow and reporting mechanism. Transcription should be eliminated to save time and reduce errors. The results should be available to the Coulter operator as soon as possible. Incorrect results such as the result of 99.9 produced by the Coulter for very high white counts should not be printed on a report for issue to the wards. Unique specimen identification on each result form was a requirement. A copy of the results which could be subjected to the same workflow as the original through the laboratory was needed for filing.

MONITOR REPORT

The concept of a monitor report is to give messages to the Coulter operator so that immediate action can be taken. There are four basic types of information necessary here:

1. The unique specimen identifier including specimen type.
2. Indications of computer interface or line malfunction.
3. Indications of Coulter malfunction or result unacceptibility.
4. Identification of specimens requiring further tests as dictated by the Coulter results.

Because of the similar timing requirements of the result and monitor report, these were combined on a single form, the monitor messages occurring on a tear-off section on the right side. A two-part form was selected to meet the filing requirement. Because a matrix type printer was used as the output device, it was initially decided that the carbon copy, generally having a superior image from this type of printer, would be used for the report to be sent to the wards. A self-adhesive strip on the back of this copy allowed for easy attachment to the requisition form to produce a result form suitable for dispatch to the wards.

* Coulter Electronics Limited, Hertfordshire, England.

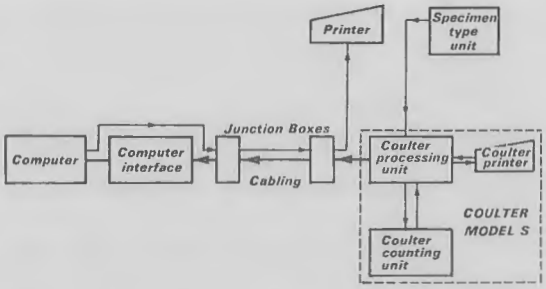


Figure 1. The hardware configuration of the Coulter data acquisition system.

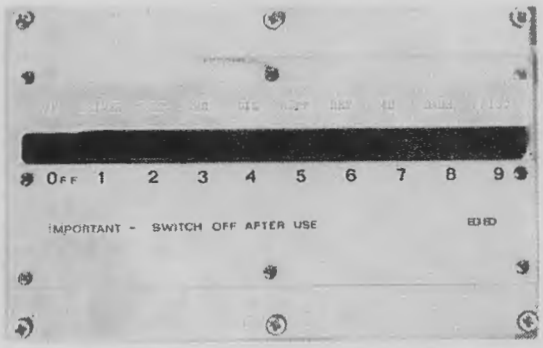


Figure 2. The specimen type unit which is used to indicate the type of specimen being analysed.

However, experience with the system showed that this copy was prone to smudging during handling in the laboratory. In future the carbon copy will become the filed report.

MANAGEMENT REPORTS

Workload information on the number of each type of specimen analysed, and workload data based on the Canadian Schedule (1977)[4] aid management in the planning function.

It was felt that we had insufficient experience with computerised quality control in haematology to perform any immediate on-line quality control function. The system involving frequent analysis of secondary accuracy and other control specimens, and manually checking the tolerance of these results was retained. However, the capturing of control specimen and patient data by the computer was initiated to give long-term quality control information, provide an initial basis for experience, and to enable study of population parameters.

Having similar timing requirements, the statistical and quality control reports were combined on a single management report. This report is capable of being produced when required and covers results captured since the last printing. Currently this is performed daily in a batch mode.

INPUT

There are three types of information that must be entered into the computer to obtain the reports described:

1. The Coulter results, including test name
2. The specimen type
3. The unique specimen identity.

The Coulter results are entered automatically into the computer as they become available via junction boxes, some 100 metres of shielded cable, and a locally built special interface. This configuration is shown in Figure 1.

The entry of specimen information could conceivably be through a teletype input, in a predetermined order as defined by a worklist, or by more simple means.

Most previous systems such as those described by Nelson and Elder (1972)[4], and Cavill *et al.* (1974)[5], require manual entry of specimen identity information and often involve the use of special specimen numbers to identify controls. The use of previously printed worklists often found in biochemistry systems do not lend themselves to the Coulter situation as the flexibility to rapidly change specimen order is often required, particularly for repeats. An extension of the idea previously suggested by Lewis and Puariea (1974)[6] gives specimen type and number identity through the Coulter circuitry.

A fairly simple method was devised. A specimen type unit was locally built to indicate to the computer the type of specimen being analysed (Fig. 2). This is a simple push-button box distinguishing patient specimens from controls, references, etc. As the computer maintains the date, this facility has been removed from the Coulter and the numerals previously used to indicate date now reflect the setting on the specimen type unit.

Currently a 10-button unit is used, although this could be extended if required. The function of each button is shown in Table 1.

Patient specimens received in the laboratory are registered with a three-digit number. This is a cyclic system running from zero to 999 and back to zero. With the addition of the

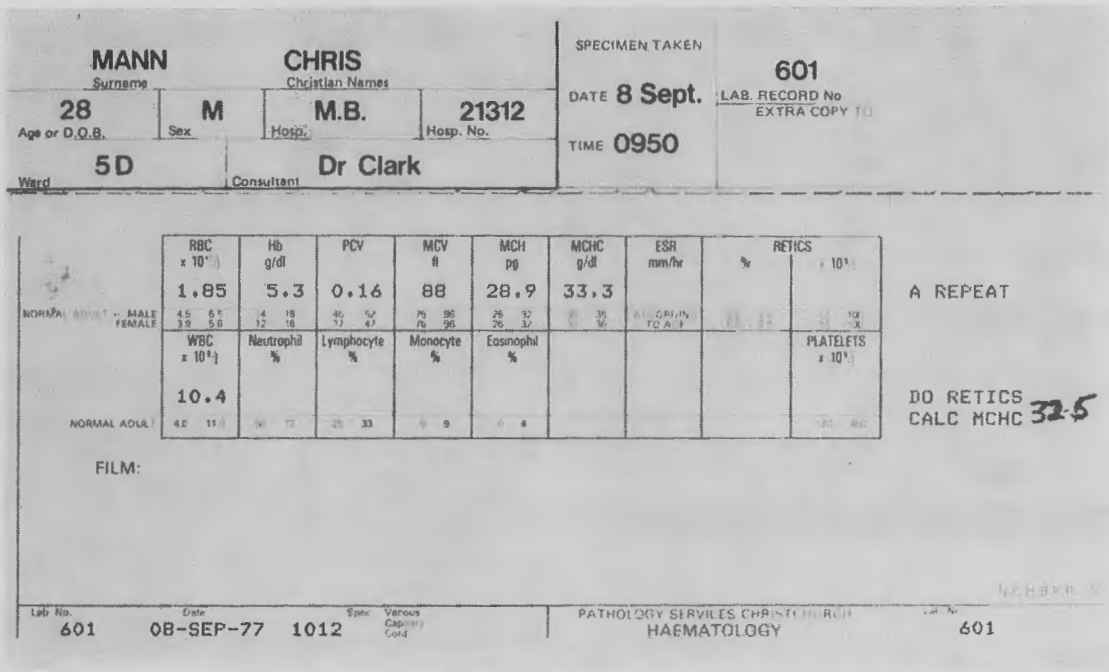


Figure 3. a. The result form as it leaves the Coulter workstation.

Table 1. The function of the buttons on the Specimen Type Unit.

Button	Name	Function
0	OFF	Computer operation off
1	PRIMER	For priming blood specimen
2	TEST	For patient specimen
3	RBC	For red cell screens
4	DIL	This specimen is a 1:9 dilution
5	REPT	Indicates a repeated specimen
6	REF	Reference blood or secondary standard
7	4C	Calibration or primary standard
8	DADE	Accuracy Control
9	MISC	Other specimens.

date, this forms a unique identifier for patient specimens. This is the specimen number used on the Coulter. A remote display of this number has been extended to the specimen type unit for ease of use.

OPERATIONAL CONCEPTS

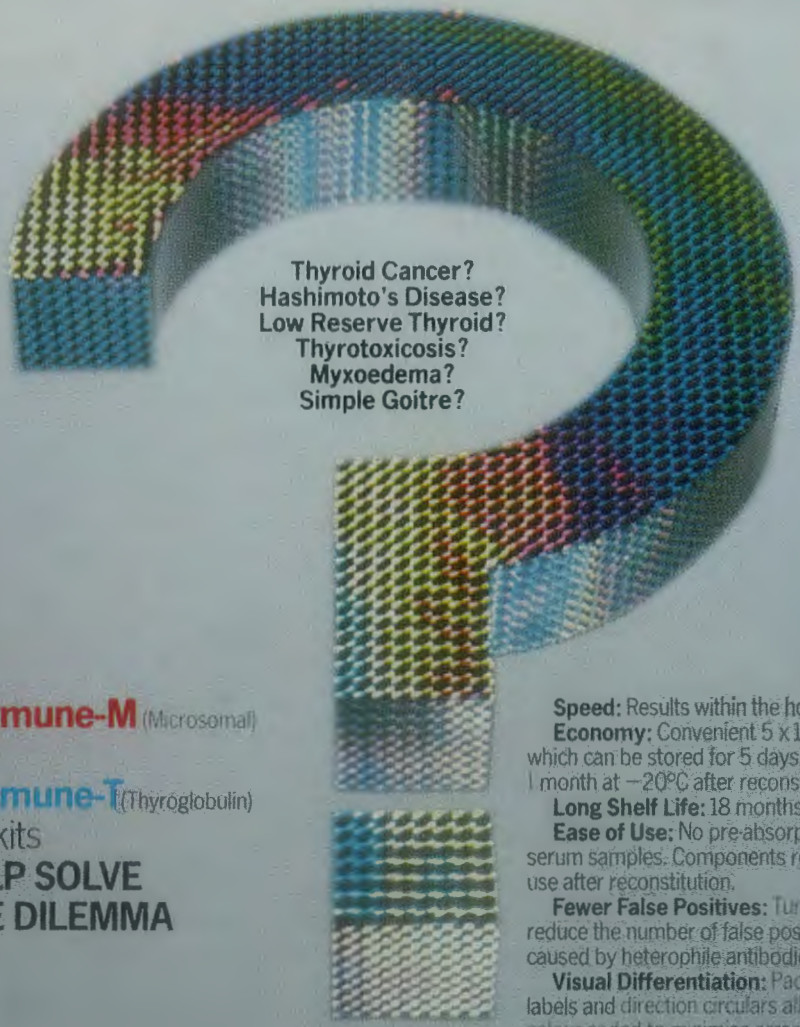
The system is designed for ease of operation, transparency of the computer, no time delays, improvement of Coulter operation, and performing many checks that were previously undertaken manually.

To the Coulter operator the computer itself is transparent, only the specimen type unit, which simplifies some operation steps, and the output teletype, appear in any way different from a non-computerised system. The operator merely checks the specimen number, sets the appropriate specimen type button, samples the specimen, removes the result slip from the printer, and if no immediate action is indicated, attaches the slip to the result form checking the specimen number (Fig. 3a).

As previously mentioned it was felt that worklists are not applicable to the Coulter situation as rapid order changes are often necessary and batching is not required or desirable. Hence the system is designed so that specimens may be analysed immediately without batching or special treatment of urgent specimens. Sequential order is not necessary but speeds operation as it becomes unnecessary to reset the specimen number.

The Coulter is designed so that the specimen number is automatically advanced after each operation. If non-patient specimens such as controls, standards, are analysed, the number must be reset. The specimen type unit takes over control of this feature, providing automatic increment only when required. The specimen type set on this unit appears on the result

Microsomal and Thyroglobulin Auto-Antibody Testing–both belong in your thyroid panel



Thyroid Cancer?
Hashimoto's Disease?
Low Reserve Thyroid?
Thyrotoxicosis?
Myxoedema?
Simple Goitre?

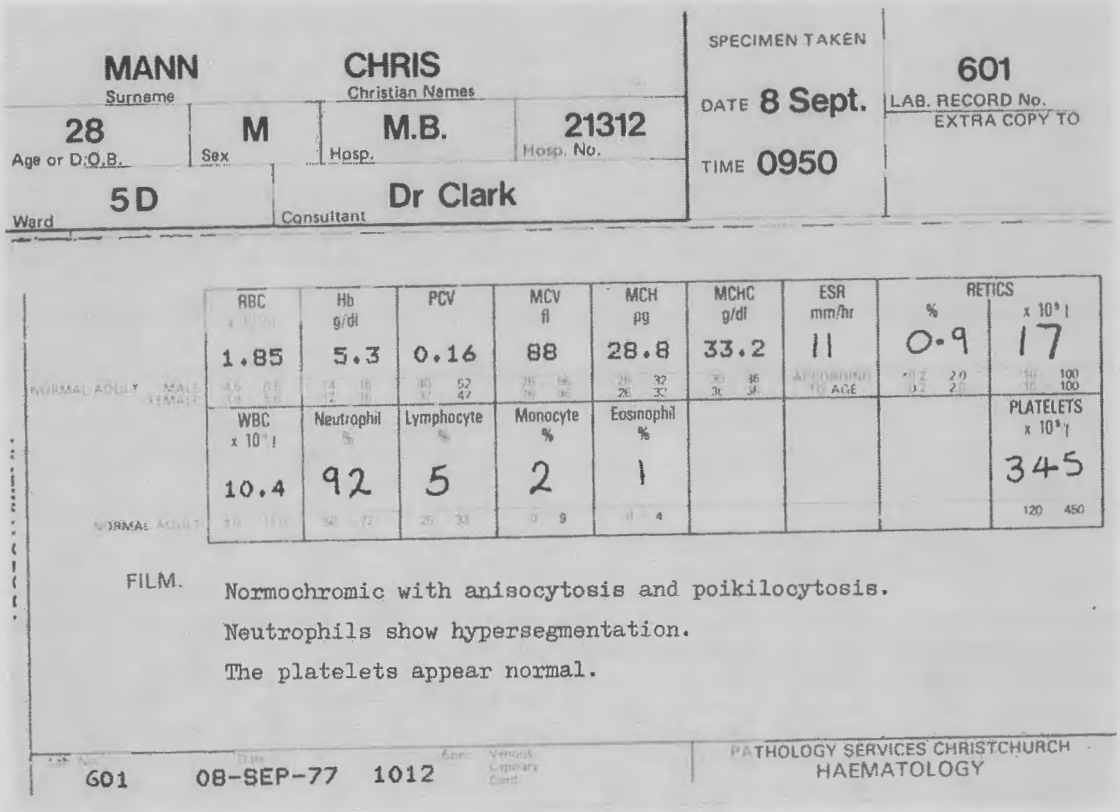
Thymune-M (Microsomal)
and
Thymune-T (Thyroglobulin)
HA kits
HELP SOLVE THE DILEMMA

Speed: Results within the hour.
Economy: Convenient 5 x 10 test pack which can be stored for 5 days at 4°C or 1 month at −20°C after reconstitution.
Long Shelf Life: 18 months at 4°C.
Ease of Use: No pre-absorption of serum samples. Components ready for use after reconstitution.
Fewer False Positives: Turkey cells reduce the number of false positives caused by heterophile antibodies.
Visual Differentiation: Packaging, labels and direction circulars all colour-coded to minimise error.
Reproducibility: Test materials freeze dried for stability.

Wellcome

For a copy of our comprehensive brochure please write to:

Wellcome New Zealand Limited, P.O. Box 22-258, Otahuhu, Auckland 6.



MANN (Surname) CHRIS (Christian Names)
28 (Age or D.O.B.) M (Sex) M.B. (Hosp.) 21312 (Hosp. No.)
5D (Ward) Dr Clark (Consultant)
SPECIMEN TAKEN DATE 8 Sept. TIME 0950
601 LAB. RECORD No. EXTRA COPY TO

RBC x 10¹² l	Hb g/dl	PCV	MCV fl	MCH pg	MCHC g/dl	ESR mm/hr	RETICS %	RETICS x 10⁹ l
1.85	5.3	0.16	88	28.8	33.2	11	0.9	17
NORMAL ADULT MALE 4.5 6.5 FEMALE 3.9 5.9	14 18 12 16	40 52 37 47	76 96	26 32 28 32	30 36 31 34	ACCORDING TO AGE	0.2 2.0 0.2 2.0	30 100 30 100

WBC x 10⁹ l	Neutrophil %	Lymphocyte %	Monocyte %	Eosinophil %	PLATELETS x 10⁹ l
10.4	92	5	2	1	345
NORMAL ADULT 3.0 11.0	50 72	25 33	0 9	0 4	120 450

FILM. Normochromic with anisocytosis and poikilocytosis.
Neutrophils show hypersegmentation.
The platelets appear normal.

601 08-SEP-77 1012
PATHOLOGY SERVICES CHRISTCHURCH
HAEMATOLOGY

b. The final report as issued to the wards.

form, and is also used in management and quality control reports. The display of the specimen number on the specimen type unit, in a much more convenient location than the display on the Coulter itself, is an additional improvement. A further improvement to the Coulter operation which we did not include but should be considered would be to insert a time delay into the specimen number and specimen type circuitry. Currently the specimen number indicated on the Coulter is the specimen about to be printed, not that being sampled.

The computer performs a number of checks, giving an appropriate message when error conditions are detected. For conditions requiring immediate action by the operator, a bell on the printer is rung. When a result is unacceptable, an appropriate error message, and the result if available, are written on the message section of the result form. In most cases the relevant parameter is left blank on the results section.

Results from the Coulter are checked for correct sequence and for problems on the line to the computer.

The computer compares the Coulter calculated values for MCH, HCT and MCHC with its own calculated values allowing small preset tolerances.

The Coulter performs the MCV, red and white counts each in a number of counting chambers. If the results in these chambers are not within close agreement a rejection is indicated. The computer system detects this and along with haemoglobin levels incompatible with life, will give a reject message for the appropriate parameter.

Brittin *et al.* (1969)[3] showed that specimen interaction occurs on the Coulter. Counts that may be effected by a previous specimen are indicated for repeat. Moderately elevated

white counts that may be diluted and very elevated counts requiring manual analysis are marked accordingly.

An appropriate message is generated where a test result indicates that further work is warranted, such as a low haemoglobin requiring a reticulocyte analysis.

COMPUTER PROGRAMME DESIGN CONCEPTS

The modular approach used in the biochemistry system is used throughout. The Coulter programme, and the programme used for production of statistical reports are independent of any other programme running concurrently. Hence there are no time delays while other pieces of laboratory equipment, such as autoanalysers, are running.

Conclusions

COSTS

The total development and installation cost was N.Z.$8,900. $4,750 of this was for development and the substantial documentation required for possible national implementation. The remaining $4,150 includes $936 for the interface, as well as installation, wiring and the full cost of the printer which is in fact on loan from the Department of Health. Other computing costs have not been included as existing hardware was used and no other additions were necessary.

FINANCIAL BENEFITS

A benefit of $9,800 was realised in the first year of operation.

A technologist previously responsible for the transcription of results from the Coulter cards to patient result forms and checking them, has been moved to another section of the laboratory. The employment of a senior technologist had been necessary as it was felt that a junior or a clerical person could not appreciate the consequences of transcription errors or Coulter malfunction.

The relatively expensive Coulter cards are now only used for back-up purposes. The computer slips are less than one-third of the cost of these cards and the previous preprinted result slips.

Secretarial saving in the collection of workload statistics has been shown.

In final result checking, a considerable proportion of a senior technologist's time was spent in retrospective study for transcription error, checking if other tests had been performed, and ordering further work they considered necessary. This task has been greatly reduced.

The manual calculation of daily quality control parameters is a laborious procedure that is readily handled by the computer, as are distribution studies for normal range preparation.

OTHER BENEFITS

After installation of this system the time to process a specimen dropped by 10 percent as transcription was eliminated, checking time and the number of repeat analyses was reduced. Faster turn-around time resulted. The errors associated with manual transcription no longer occur.

The quality control report is also run on calibration data, which considerably aids the calibration procedure.

Tighter control on the calculated parameters enforced by the system gives rise to improved result quality.

The modification to the automatic specimen advance feature has lead to easier operation of the Coulter.

The system performs certain operations depending on the specimen type, performing the necessary calculations on dilutions, and suppressing normal white counts on a red cell screen request. Operator time is also saved here.

Acknowledgments

The assistance with this project of the Departments of Medical Physics, Works, Engineering and Haematology of the North Canterbury Hospital Board is acknowledged.

The output printer was loaned by the Data Processing Division of the New Zealand Department of Health.

REFERENCES

1. Abernethy, M. H. and Brown, J. D. *Proc. N.Z. med. Information Processing Conference.* University of Otago (1973).
2. Barnard, D. F., Carter, A. B., Crosland-Taylor, P. J. and Stewart, J. W. (1974). *J. clin. Path.* **22**, suppl. (Coll. Path.), **3**, 26-33.
3. Brittin, G. M., Brecher, G. and Johnson, C. A. (1969), *Amer. J. clin. Path.* **52**, 679.
4. Canadian Schedule of Unit Values for clinical laboratory procedures. (1977), Statistics Canada.
5. Cavill, I., Ricketts, C., Moulding, T., Jacobs, A. and Page, M. ,1974), *J. clin. Path.* **27**, 330.
6. Lewis, J. W. and Puariea, B. S. (1974), Letter entitled, Entry of specimen accession numbers to a clinical laboratory computer system from an on-line Coulter S. *Amer. J. clin. Path.* **62**, 872.
7. Nelson, M. G. and Elder, E. (1972), *J. clin. Path.* **25**, 594.

Technical Notes

A Rapid, Simple Method for Plasma (Serum) Paraquat Determination

The purpose of this note is to confirm the value of a method for paraquat determination[1] in plasma or serum that has been used in our laboratory since October, 1977. The procedure involves precipitation of protein and other macromolecules by organic solvents and ammonium sulphate followed by the addition of alkaline dithionite to the clear supernatant. The absorbance at 396nm is then determined. The absorbance must be read within 15 minutes as the colour is unstable in light and decreases with time. The time required for an assay is about 30 minutes. The test is sensitive to 0.5 μmol/l and the absorbance follows Beer's Law over a range of 0-27 μmol/l. (Figure 1).

In two recent cases of paraquat poisoning the following results were obtained:

In case 1, non-fatal, the patient swallowed an unknown amount of granular paraquat. A screening test showed trace amount of paraquat in the urine and the serum level was less than 5 μmol/l.

In case 2, fatal, the patient swallowed a quantity of a 20 percent solution of paraquat. The screening test showed a large amount of paraquat in the gastric aspirate and urine. Serum levels were 292 μmol/l three hours after ingestion and 167 μmol/l $7\frac{3}{4}$ hours after ingestion.

In our hands, this method of paraquat determination in plasma or serum has proved to be rapid, simple and reliable.

REFERENCE

1. Janusz Knepil, a Short, Simple Method for the Determination of paraquat in Plasma. Climica Chimica Acta. **79** (1977), 387-390.

Meow-Keng Choe, B.Sc., Laboratory Services,
Wellington Hospital.

January, 1978.

Evaluation of a Domestic Electric Cook Pot as a Constant Temperature Heat Source for Laboratory Purposes

A Ralta Cook Pot was evaluated with respect to its ability to hold temperature constant at a number of intervals over its usable range.

The pot (10 x 26cm) was half filled with laboratory grade sand and an aluminium block (10 x 7 x 5cm) suitable for holding tubes and provided with a thermometer hole, was placed in this bed. Temperatures approximately 10°C apart were selected from an arbitrary scale on the thermostat and, after an initial stabilising period of one hour, each temperature point was monitored using a mercury thermometer (1°C division) at 10-minute intervals over a period of three hours.

Approximate Temp. point selected (°C)	Mean (N = 19)	Coefficient Variation
30	28.10	1.42
40	40.2	0.49
50	52.26	0.78
60	60.00	0.46
70	70.21	0.54
80	79.44	0.71
90	89.95	0.25
100	100.07	0.18
110	109.97	0.28
120	119.94	0.12
200	198.9	0.13
225 (T. Max.)	225.3	0.15

Within the reading accuracy of the thermometer, temperature intervals from 30°C to 225°C were extremely stable (C.V. >1.42) when the apparatus was used in the manner described. The small order of variance must be equivalent to any specialised apparatus and as such, satisfactory for procedures requiring highly uniform temperatures. In addition the temperature range of this stability makes the Ralta electric hot pot equally suitable for physiological reaction (incubations and enzyme

reactions) carried out at lower temperatures of 37-42°C and analytical or clinico-chemical procedures requiring higher temperatures such as derivatisations of compounds prior to GLC. Heat sources as purchased for laboratory purposes are extremely expensive and in addition have limitations imposed on capacity by their physical form and on range of temperatures by limitations of their thermostats. The cost of the cook pot ($42 trade) is of the order of three magnitudes less than more specialised equipment which in addition are obtainable only in restricted ranges of temperature.

H. Potter, Steroid Unit, Pathology Services,
The Princess Margaret Hospital,
Christchurch.

June, 1978.

N.Z. Register of Cell Lines

The N.Z. Ministry of Agriculture and Fisheries has assumed responsibility for the maintenance and annual upgrading of a New Zealand register of animal and insect cell lines, with the undersigned as registrar. The Ministry has legal responsibility for the control of imported cell lines, with regard to both the original importation, and to subsequent usage. The purpose of the register is to facilitate the interchange of cell lines within New Zealand, so as to minimise the need for further importation of cell lines, with the attendant risks of introducing infectious disease.

Requests for import permits for animal and insect cell lines should be submitted to the Director, Animal Health Division, N.Z. Ministry of Agriculture and Fisheries, P.O. Box 2298, Wellington. Any requests for transfer of cell lines must be referred to the above director, consequent to conditions imposed by the original MAF import permit. Application forms for importation and transfer are available from the Director.

It is intended that the register would be upgraded in April/May of each year. It would be helpful if anybody importing cell lines would notify the undersigned of this fact, giving details of the cell designation, its origin, source institution and any other relevant data.

P. J. K. Durham, Registrar, Animal Health
Reference Laboratory, Private Bag,
Upper Hutt.

July, 1978.

Correspondence

Sir,—In the July, 1978, N.Z.J. med. Lab. Technol., M. Legge discusses "a potential error in screening for galactosaemia". He refers to the failure of his laboratory to recognise the galactosaemic patient by urine examination. In addition, because of the error inherent in the blood glucose (autoanalyser) method, hyperglycaemia was indicated rather than the severe hypoglycaemia which actually existed. Problems with metabolite studies in galactosaemia have been well documented. A child must receive sufficient milk to accumulate the substrate for the deficient enzyme before either illness occurs or elevated metabolite levels can be detected in body fluids. In many children self-preservation will lead to a failure to assimilate the offending diet. Mr Legge suggested the lack of milk feeding approximately for six hours was the reason why no urinary galactose was detected. Unfortunately he does not indicate the time of collection of the blood sample containing an extremely high level of galactose but one must conclude this was at/or near the same time as the urine collection. If this is true, one cannot explain the failure to excrete the excessively high level of blood galactose. In 1969, Dahlqvist *et al.* described a case of galactosaemia in which the patient still had detectable urine galactose (22 mmol/l) at 11 days, yet three exchange transfusions had been performed between the seventh and ninth day and a lactose free diet introduced on the ninth day. The blood galactose before this change was 7.6 mmol/l but 24 hours later was hardly detectable.

Mass screening for galactosaemia was introduced in New Zealand in July, 1970, by expansion of the phenylketonuria programme to include the Beutler test. This test involves the measurement of enzyme-galactose-l-phosphate uridyl transferase (GALT) in the dried blood spot sample collected from each child at approximately five days of age. In the case referred to by Mr Legge the blood sample was collected at five days and received and tested in Auckland on day 10 when the positive result was reported by airmail. The next day a microbiological assay for blood galactose was also positive, with a level of 1.6 mmol/l (normal <3 mmol/l). The result was available to Mr Legge by 13 days but the patient was

dead. The problem with this method of screening is clearly the delay in obtaining results. As the enzyme defect is present at birth a cord blood sample could be collected from all children and sent to Auckland, where the result would be available before the fifth day.

It is extremely rare for children to die of galactosaemia within five days of birth, as the child, relatively normal at birth, is only seriously affected by the consumption of milk products containing lactose. The duplication of blood sampling (day 1 and day 5) of newborns would be too expensive, but we have always advocated the collection of additional cards from "sick babies" provided the sample is so marked and sent "urgently" to Auckland. The routine sample collected at five days for Guthrie testing must follow. Increased blood galactose, urine galactose or galactitol are not sufficient to confirm a diagnosis of galactosaemia as suggested by Mr Legge. Both are also present in galacto-kinase deficiency. Only the quantitative enzyme study of GALT will satisfy that requirement.

Unfortunately we did not receive either a liquid blood sample or skin culture from this child, but the history, the positive Beutler test, the parents' RBC GALT levels and finally the dried blood spot RBC galactose-1-phosphate level of 1.2 mmol/l (normal undetectable) do indicate the child had galactosaemia.

If a physician considers galactosaemia may exist in his patient he should take appropriate blood samples for enzyme studies, stop all lactose containing foods and as bacteraemia causes death in one-third of cases, put up blood cultures and start antibiotics particularly for *E. coli*. The blood sample for enzyme studies must be taken before any exchange transfusion to exclude the errors due to presence of donor cells.

Only when the enzyme result is available can the diagnosis be made. Galactose is not the substrate for the enzyme but a precursor of galactose-l-phosphate. This metabolite is retained in the RBC until the cell's death and so is a good indicator of the disease and also of dietary management.

Of the eight cases of galactosaemia detected among 476,916 New Zealand babies tested only two, the first and most recent case, have died. Six survive on treatment. The apparent incidence of galactosaemia for New Zealand is 1 : 60,000.

Yours faithfully

I. C. T. LYON,
Director, National Testing Centre, University of Auckland Medical School, Private Bag, Auckland, New Zealand.

August, 1978.

REFERENCE

Dahlqvist, A., Jagenberg, R., Mark, A. (1969). Acta Paed. Scand. **58**, 237.

Book Reviews

Introductory Exercises for Medical Technologists. Shauna C. Anderson. Published by the C. V. Mosby Company and obtained from N. M. Peryer Ltd., Christchurch. 121 pages illustrated. $NZ9.10.

This little book is derived from an introductory course provided by Brigham Young University, Utah, and is written by the medical technologist programme director. It is an elementary introduction for people considering a career in medical laboratory technology. The actual text consists of some 70 pages, the rest being work sheets related to a practical course. It touches on a rather arbitrary selection of manual procedures including cytogenetics, radioimmunoassay and a rather disproportionate amount of toxicology. The selection of tests does not reflect current trends or practice. There is no mention of automation. This book might find a place here in a high school library to provide an inkling of medical laboratory work.

There are quite a number of illustrations and a nice picture on the cover.

R. D. A., B. W. M., A. E.K., H. C. W. S. and A. G. W.

Introduction to Research in Medical Sciences. A. Cuschieri and P. R. Baker. Published by Churchill Livingstone 1977; 216 pp., illustrated. Obtained from Penguin Books Ltd., Auckland.

The authors have written a general text aimed primarily at the medical graduate who wishes to improve his career prospects by

acquiring a higher degree. For this audience it appears admirable. There are short, clear introductions to a wide variety of subjects ranging from the care of laboratory animals to the principles and practice of analytical techniques commonly used in medical research. Reading lists are provided at the end of each chapter and advice given on the use of a library and the importance of undertaking a critical review of the literature before starting new research projects.

There are sections on experimental design with a reminder that " the advice of a statistician is essential in all but the simplest analysis and should be sought at the onset of the research project "; and a further reminder that " statistical analysis does not *prove* a hypothesis, but only suggests the likelihood of it being correct or not." Other sections deal with *in vivo* measurements, clinical trials and animal experimentation; and in a final chapter there is an impassioned plea for clarity and simplicity in the presentation of scientific data.

" Thou shalt remember thy readers all the days of thy life . . .
Thou shalt not cloud thy message with a miasma of technical jargon . . .
Thou shalt not hide the fruits of thy research beneath excess verbiage . . .
Thou shalt write and rewrite without tiring . . ."

Despite a few comments which have regrettable implications as to the attitudes of medical graduates both to hospital laboratory staff and to the basic measurements on which their investigations depend, the book provides useful introductory information of a general nature on research in the medical sciences. It can be recommended to all who are involved with, or interested in, medical research. M. G. Metcalf.

Elementary Principles of Laboratory Instruments. 4th Ed. Leslie W. Lee. Published by C. V. Mosby Company, Saint Louis, 1978. 323 pages with 223 illustrations. Obtainable from N. M. Peryer Ltd., Christchurch. Price NZ$18.95.

The first edition of this book was published in 1967 and its popularity is shown by that in only 11 years it is up to its fourth edition. This book is dedicated to explaining the principles of laboratory instruments without the need of a deep background knowledge in physics, mathematics and electronics. No detailed operation of any equipment is described nor the chemistry employed by the equipment.

The first three chapters deal with the basics of matter and energy, simple electrical components and circuits, and light and its measurement. This is followed by a chapter on spectrophotometry which covers the basic principles and laws of spectrophotometry. Simple colorimeters, calibration, care and operation and selection of photometric instruments described in this chapter are ones mainly manufactured in America, but some of them have found a place in New Zealand laboratories. Some common instruments discussed include the various Coleman, Hitachi, Bausch and Lomb, Gilford, Beckman and Turner spectrophotometers.

The chapter on light emission and absorption measurement deals with the theoretical and practical aspects of flame and atomic absorption photometers and discusses various instruments such as the Coleman, IL 143 and IL 433, Radiometer FLM 2 and FLM 3 and the Beckman Klina. With regards to the latter the author states that Beckman has had bad luck with clinical flame photometers in the past but this model seems very promising. Common atomic absorption spectrophotometers discussed include the Perkin Elmer and IL models.

The chapter on fluorescence and fluorometry describes the principles of fluorescence and deals with such instruments as the Turner, American Instruments, Farrand and Baird range. Some instruments utilising fluorescence such as the American Optical Instruments' morphine analyser and the Corning calcium analyser are also briefly described.

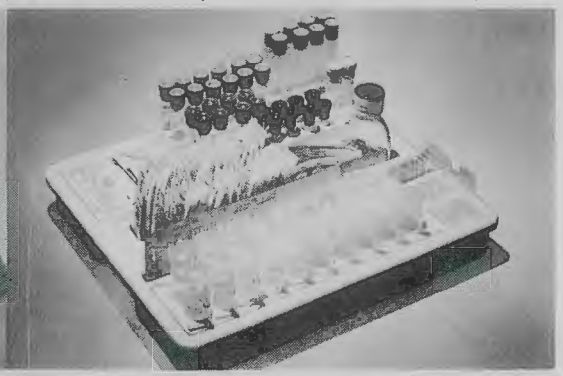
The next two chapters are devoted to pH measurement and chromatography and electrophoresis. The chapter on pH measurements is up to date and includes description of instruments such as the Radiometer ABL 2, Beckman glucose, urea and Cl/CO_2 analysers, the Orion Ionised calcium analyser and spacestat sodium/potassium analysers. The next chapter after discussing principles of electrophoresis and chromatographs briefly describes systems such as the Beckman, Corning, Gelman and IL company's produce. No chromato-

Less blood
More information

Introducing the

B-D UNOPETTE™ Disposable Diluting Pipette

a complete micro-collecting dilution and reagent system, for blood samples in the Clinical Laboratory.



The **UNOPETTE** system utilizes a precision prefilled reagent/diluent reservoir and a precision capillary pipette with an overflow chamber. By semi-automating specimen collection and dilution, the **B-D UNOPETTE** system provides simple, accurate and reproducible micro procedures for New Zealand Medical Technologists in Biochemistry, Haematology and Veterinary Laboratories.

The **B-D UNOPETTE** system has particular application for paediatric and other difficult to sample patients.

A wide range of UNOPETTE tests are available

Micro Chemistry systems include Sodium and Potassium Determinations with a flame photometer.

UNOPETTE Haematology systems are available for manual and automated blood cell determinations and Erythrocyte Fragility Tests.

UNOPETTES for use with Coulter TM Counter automated haematology equipment are available.

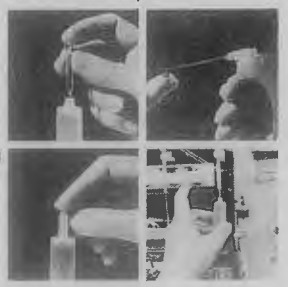
The **UNOPETTE** system is another part of the total blood collection system from Becton, Dickinson & Company. Your Smith-Biolab Representative will be happy to supply full details.

B-D UNOPETTE

B-D and **UNOPETTE** are trademarks of Becton, Dickinson & Company.
COULTER COUNTER is a trademark of Coulter Electronics Incorporated, Hialeah, Florida, 39010, U.S.A.

"A laboratory test is no better than the specimen and the specimen no better than the manner in which it was collected."

B-D UNOPETTES are manufactured to exacting standards for the New Zealand Laboratory.



Instructions: 1. Puncture reservoir diaphragm with pointed polystyrene shield. 2. Make finger puncture. Allow blood to fill UNOPETTE capillary pipette. Carefully wipe excess blood from outside of pipette. 3. Seat pipette securely in reservoir. Gently squeeze reservoir several times to rinse all blood from pipette. Mix by inversion. 4. Insert aspirator tubing for pre-diluted samples in reservoir.

SB 11982

SMITH BIOLAB

SCIENTIFIC DIVISION

P.O. Box 36007,
Auckland 9, New Zealand

Auckland	Ph. 483-039
Wellington	Ph. 683-453
Christchurch	Ph. 63-661

graphy systems available of any sort are described.

The next two chapters dwell on automation in haematology and chemistry. The chapter on haematology automation describes adequately the principles of particle counting and devotes most of its machine descriptions to the Coulter cell-counting devices, including the latest Model Ssr. Several other makes of cell-counting devices are also described, including the Ortho laser counter and the Technicon series. Also described in this chapter are the various models concerned with automated differentials by pattern recognition, various automated coagulation devices and miscellaneous instruments such as the IL haemoglobinometer, Radiometer Hemoximeter, Fibrinogen analyser and the Coulter Zetafuge. The chapter on automated chemistry very briefly describes Technicon's moving stream principle and describes some of their systems, including the SMAC. Various discrete systems, such as the Hycel Mark X 4 M, Monitor KDA, Beckman DSA, Du Pont ACA, Clinicard, Coulter ACS, GEMSAEC, Centrifichem, Gilford 3500, Beckman TR, ABA-100 and Rotochem.

The next chapter deals with computerisation and briefly describes its principles and uses in the medical laboratory. The chapter following this deals with nuclear medicine instrumentation and after a simple introduction to radiant energy principles discusses various systems for measurements *in vivo* and *vitro*.

Miscellaneous instruments such as heating and cooling baths, centrifuges, recorders, osmometers and automation for bacteriology are described in the last to one chapter. In the final chapter some basic rules for the care, maintenance and repair of instruments are given.

Overall this book lives up to its title in that the elementary principles of laboratory instruments are taught in a simple manner. This book is easy to read, has many informative illustrations and is very much up-to-date with the instruments it describes. This book can be recommended for any laboratory interested in the principles and teaching of principles of laboratory instruments.

R. W. L. Siebers.

Atlas of Haematology, 4th Ed., 1978. George A. Mcdonald, T. C. Dodds and Bruce Cruickshank. Published by Churchill Livingstone and obtained from N. M. Peryer Ltd. Christchurch. 309 pages. Price $NZ41.

The new edition of this popular atlas contains 309 pages compared to 225 pages in the third edition, the major portion of this increase in size being devoted to electron microscope studies. These include studies of all the normal leucocyte and platelet elements, together with abnormal cells in leukaemia, secondary tumour, Gaucher's disease, "Hairy cell leukaemia," etc.

The printing of colour plates throughout is generally excellent, though comparison with the previous edition shows a deeper colouration enhancing basophilia but tending to give red cells an even more unnatural hue in some illustrations.

Some new illustrations include fig. 41 showing a beautiful example of basophilic stippling, fig. 99 Chediak-Steinbrink-Higashi anomaly, figs. 176-77 leukaemic reticuloendotheliosis, all of which are excellent photomicrographs.

The one disappointing new illustration is fig. 40, which purports to be β thalassaemia minor but shows no target cells, which is always a feature of this condition.

An atlas such as this is an essential part of any haematology department library and this new edition confirms its place.

B. W. Main.

Review of Medical Microbiology, 13th edition 1978. By Ernest Jawetz, Joseph L. Melnick and Edward A. Adelberg. Published by Lange Medical Publications. 550 pages, illustrated. Price $19.60. from N. M. Peryer Ltd.

This book is familiar to all who read in the broad microbiological sense and the appearance of a 13th edition is no surprise. Relatively, the price is right.

This publication is ideally suited for those studying for the part 3 NZIMLT examinations and is very helpful from the point of revision.

The extraordinary expansion of the section of virology is understandable, perhaps too much emphasis on theoretical aspects. Previous criticisms about the lack of technical detail remain valid but read in conjunction with laboratory standard methods it is ideal for

basic preparations covering all aspects of the broad field.

The authors would have done well to have brought together information to cover more properly sexually transmitted diseases and the short reference set out under epidemiology. prevention and control are dismissed in a matter of eight sentences. After all this a global problem.

Disinfectants are occupying an equally brief space despite chapter seven.

The chapter relating to antimicrobial therapy is much the same and would have been improved with a wider coverage of the Cephalosporins. Considering the world distribution of leprosy patients the appropriate use of Rifampicin may well have been discussed at some depth.

Parasitology is again concise with good diagrams.

I would not be without this book, both as a teaching aid and bench reference.

H. C. W. Shott.

Bailey and Scott's Diagnostic Microbiology. Sydney M. Finegold, M.D., William J. Martin, Ph.D., Elvyn G. Scott, M.S., M.T. (ASCP). Fifth edition, 1978. Published by C. V. Mosby Company and obtained from N. M. Peryer Ltd., Christchurch. 514 pages illustrated. Cost $22.55.

Elvyn Scott has been joined by Doctors Finegold and Martin in the production of this Fifth Edition of Diagnostic Microbiology. The general structure of the book remains in the same readable form but there is much new information and rearrangement of material to make the book useful to a wider group of health workers.

The first two parts discuss laboratory methods and recommended procedures. A short new chapter has been added on the general approach to clinical specimens with discussion on the rejection of specimens, how far to go in definitive identification, quantitation of results and expeditious reporting of results.

The third part of the book again deals with the micro-organisms found in clinical material such as blood, cerebrospinal fluid and from sites such as the respiratory tract, gastrointestinal tract, urinary tract, genital tract and wounds. Each of these sections has a general introduction followed by a list of both normal flora and common infecting organisms. The section continues with methods of collecting specimens, culture procedures and concludes with general discussion and a list of references.

The fourth part is devoted to the methods for identification of pathogenic micro-organisms. It is in this part of the book in which the greatest changes are seen. A complete chapter is now devoted to the anaerobic cocci. Usually each section introduces the species of organism, followed by the methods of isolation, identification and general clinical information and antimicrobial sensitivities. In the larger groups of organisms such as Enterobacteriaceae miniaturised and rapid methods of identification are discussed. Again each section is concluded by an up-to-date list of references. Laboratory diagnosis of viral and rickettsial diseases is limited to the provision of guidelines for the collection and transport of specimens, together with some brief discussion on isolation and serological methods available for the diagnosis of viral and rickettsial infections. These guidelines are followed by a list of 11 references, each are recent books on medical virology, and it is appropriate that the present edition is limited to this basic information.

Laboratory diagnosis of mycotic infections gives definitions of fungal structures, then general laboratory methods, followed by discussion on dermatophytes, yeast-like fungi and the systemic mycoses. The treatment of mycoses, the use of hyper-sensitivity tests and serological tests rounds off the section on mycology.

Laboratory diagnosis of parasitic infections is rewritten by Lynne Shore Garcia and includes useful information on the collection, transport and preservation of specimens. This section is extremely well done with details of practical procedures for concentration, staining and the obtaining of relevant specimens. There are many clear illustrations and instructive line drawings.

Part five is on antimicrobial susceptibility tests and assays and contains concise information on methods, along with details on disc concentrations, zone sizes and preparation of stock solutions of antibiotics.

Part six deals with serological methods in

diagnosis which includes a brief section on fluorescent antibody techniques.

Part seven covers quality control in the microbiology laboratory, serving as a good introduction to this aspect of microbiology.

Lastly, part eight includes formulae and methods for preparation and use of media, stains, reagents and tests.

A Glossary forms a useful ending to the book.

This fifth edition of Bailey and Scott can be recommended to medical technologists. It is in a readable form, contains useful up-to-date information and is supported all through with current and relevant references. At the cost of $22.55 it is an excellent book for trainee technologists. G. R. Rose.

Recent Advances in Clinical Immunology. No. 1. R. A. Thompson. Published by Churchill Livingstone and obtained from Penguin Books Ltd., C.P.O. Box 4019, Auckland 1. 299 pages, some illustrations. $NZ27.40.

This is the first volume of what one can assume will be a regular series. The nineteen authors are of international repute and represent many countries.

The preface states that the book covers some of the areas of immunopathology and applied technology and examines some of the problems associated with the institution of therapy based on immunological concepts. A further observation is that rational prophylaxis and therapy of those conditions in which immunological factors play a role should be the natural outcome of progress in this subject.

The 12 chapters are unrelated and should be assessed separately. If the reader is unversed in the subject of immunology there is a competent introduction. This is followed by chapters on protein calorie malnutrition, amyloidosis and amyloid protein, ageing and immune function and the immunopathology of schistosomiasis.

The treatment of those topics is thorough, if not exciting, and very well referenced, and details the consequences and implications of the not unexpected findings that immunological reactions are weak and antibodies decreased in malnutrition, the situation improving with proper feeding, or that immunological reactions are defective in old people. Amyloidosis is a generic term for several products not only associated with disorders of the immune system. Hope for alleviation of this dread disease is raised by the discovery that colchicine can prevent its formation. There are nine pages of references following this particular chapter.

Immune complexes in clinical investigation tells of the physiological function and fate of complexes in infectious diseases, their pathological action in chronic infections such as T.B., leprosy, chronic hepatitis and (in a separate chapter), schistosomiasis and even more detrimental effect in rheumatoid arthritis and S.L.E. The usual techniques for the identification of immune complexes are described. One of particular interest is the correlation of C3d breakdown product of C3 with the level of immune complexes and the clinical activity of the disease process. Radial immunodiffusion is carried out on the supernatant after precipitation of native C3 and its products C3b and C3c with polyethylene glycol.

Three chapters entitled human T and B Lymphocyte populations in blood, abnormalities of circulating phagocyte function and the clinical use of antilymphocyte globulin follow. The first deals with tests which identify different population of cells involved in immune response and their application in diagnosis and treatment. T and B cells can be separated and subsets of T distinguished. This aids the categorisation of lymphoid neoplasms.

The second reviews the techniques available for investigating defects such as neutropenia, locomotive, phagocytic and killing defects.

The third evaluates the benefits of antilymphocyte globulin, a very expensive product, and concludes that more stringently controlled experiments are required to determine its true value.

The final three chapters are replacement therapy in immunodeficiency, immunotherapy of human leukaemia and the treatment of allergic disease. The first two evaluate the pros and cons of those treatments and the last is clinically orientated. It includes a discussion on the use of the drug disodium cromoglycate in several conditions.

This is a book for the specialist dealing with a series of somewhat arbitrary contemporary topics in the field of immunology. The

calibre of the authors ensures its worth as a source of reference. It is not unduly expensive for a book of this nature.

R. D. Allan.

Serodiagnosis of Mycotic Diseases. Dan F. Palmer, Leo Kaufman, William Kaplan, Joseph J. Cavallaro. Charles C. Thomas, Springfield, Illinois, U.S.A. 1977. 191 pages, 56 figures. Price $US21.50.

The latest addition to the monographs in the American Lecture Series in Clinical Microbiology carries the highest recommendation in authorship, for all four are members of the Immunology or Mycology Divisions at the Centre for Disease Control, Atlanta. Another four members of the divisions assisted in the development of the manual and Dr Libero Ajello, director of the Mycology Division, has contributed the foreword.

In the series foreword by the editor, Dr Albert Balows, it is stated that this book is the first to have been published which is devoted exclusively to the serodiagnosis of the systemic mycoses. It must be recorded that this is not completely correct. Although less impressive in size and format and understandably less concerned with histoplasmosis, coccidioidomycosis and blastomycosis, the laboratory manual, "Serology of Fungal Infection and Farmer's Lung Disease" was published by a working party of the British Society of Mycopathology under the editorship of Dr E. G. V. Evans of Leeds University in 1976. This slim little manual of 36 pages is equally devoted to the serodiagnosis of systemic mycoses and any laboratory with a need for development in this field would be wise to purchase both books. The book here reviewed is intended as a manual of instruction and not as a textbook for reading but there are brief descriptions of the fungal diseases at the beginning of each section of tests. It is logically divided into five parts. Part One is concerned with the serodiagnosis of diseases caused by dimorphic fungi, namely *Coccidioides immitis, Histoplasma capsulatum* and *Blastomyces dermatitidis.* Part Two deals with diseases caused by the yeast-like fungi, *Candida albicans* and *Cryptococcus neoformans.* In Part Three under the heading of "Miscellaneous Fungi", the serodiagnosis of aspergillosis and sporotrichosis is detailed. The relegation of the dimorphic fungus, *Sporothrix schenckii,* to the status of miscellaneous fungi is convenient but curious. Part Four describes the direct fluorescent antibody technique and Part Five complement fixation.

For New Zealand laboratories the sections on the yeast-like fungi and aspergillosis are those that will be of more immediate practical interest. In these sections, as in others, there is a meticulous step-by-step description of the materials, equipment, preparation of reagents, method of dilution, the performance of the test and finally the interpretation of the results. Important notes are accented by printing in bold type. Figures comprising charts, diagrams, tables and photographs are used generously throughout the text. References are given at the end of each chapter, with a separate author and subject index. The format, paper, printing and binding are of the highest standards and it is a pleasure to report the absence of typographical errors.

This manual (and its small British predecessor) can be recommended for larger laboratories where the demand for these investigations may be matched by the enthusiasm of a laboratory worker.

F. M. Rush-Munro.

Book Received

Textbook of Immunology, by James T. Barret. Third edition. Published by C. V. Moseby Co., 1978. Obtained from N. M. Peryer Ltd.

Obituaries

MR M. FLACK

It is with great regret that we record the death of Murray Flack at the early age of 35 years. He died of a heart attack after a short illness. Murray trained in Hastings and completed his COP in Dunedin. He was in charge of Immunohaematology at the Tauranga Hospital Laboratory at the time of his death. He served on Council for three years as the Central North Island representative. One of his principal hobbies was golf, and he was prominent in the development of the Omanu Golf Club and was currently club captain. He was a very popular member of staff and will be sadly missed. Murray leaves a widow (Elaine) and two young daughters.

J. H.

Now just this one name

TOWNSON LABORATORY SUPPLIES

Formerly Townson and Mercer (NZ) Ltd. and just one telephone call brings you top quality Chemicals, Glassware and Laboratory equipment ex stock!

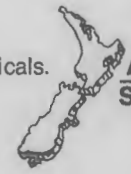
Townson Laboratory supplies is just a phone call away from all the top quality chemicals, glassware and laboratory apparatus you require.
We specialise in Bulk Chemicals, Glassware and Laboratory Equipment for all Industries.

Agencies include:
Biochemicals
– Sigma, ICN

Laboratory Chemicals
– Baker, B.D.H., Merck, Bulk Chemicals.

Glassware
– Kimble, Volac, Jobling, Zeal.

Plastic ware
– Vitri Labor, Azlon, Kartell.
Whatman filter paper and Laboratory Hardware



Telephone any office

Auckland	Wellington	Christchurch
483039	683453	63661

Another first class service from
Smith-Biolab Ltd Scientific Products Division

SMITH BIOLAB SB

P.O. Box 36007,
Auckland 9, New Zealand.

Auckland	Ph. 483-039
Wellington	Ph. 683-453
Christchurch	Ph. 63-661

14142

Be up to date with all we offer. Send now for latest catalogues and price lists, or telephone our Auckland office.

NAME .....
COMPANY .....
.....
ADDRESS .....
.....
TITLE .....
PHONE .....

SCI MED

Instrumentation & Technology
Science-Environment-Health

SCI-MED (N.Z.) LTD.

PRODUCT INFORMATION

SCI-MED N.Z. LTD. is a technical marketing organisation distributing to the science based customer in New Zealand and South Pacific Islands INSTRUMENTATION and TECHNOLOGY products

for – MED-LAB — Bio Chemical Instrumentation
BIO-MED — Physiological bioengineering
ANAL-IND — Chemical Analysis equipment
PHYS-LAB — Physics and Nuclear Instruments

Head Office:
P.O. BOX 321
DUNEDIN
Telephone 69-482

Regional Offices:
P.O. BOX 77043
AUCKLAND 3
Telephone 863-980

P.O. BOX 5221
CHRISTCHURCH
Telephone 799-050

MED - LAB

Bio-chemical Instrumentation for Prethology and Research Laboratories

DISCRETE ANALYSERS

I.L. MULTISTAT III micro-centrifugal analyser for drug screening, fluorescence and light scattering measurements. From "Instrumentation Laboratory". The well-proven "Giford" 300 series Med-Lab spectrophotometer which can be expanded into the system 3, 4, 5 or 3500 computer directed analyser and now used in more than 80 percent of New Zealand hospitals.

ELECTROLYTE ANALYSERS

From Instrumentation Laboratory Feature: IL443 or 643 Flame Photometers. IL446 Chloride/CO^2 analyser. IL919 Glucose Bun Creatinine. These can be expanded into the Multistat I, 4, 5 or 7 channel analyser by addition of the IL463 printer/sampler with interface to labs own data processor unit or I.L. D/P equipment

BLOOD GAS ANALYSERS

From Instrumentation Laboratory Feature: Micro-13 semi-automated 6 parameter system. To the IL813 automated analyser which can be part of the I.L. Blood Gas Laboratory when fitted with the IL282 co-oximeter. For THb, %O2, Hb, %Hb and Met. Hb, a new range of Blood Gas controls are available ex stock.

CONTINUOUS FLOW

$7,000 can purchase a complete two channel system. All modules are interfaceable with existing flow system from pumps, colorimeters, manifolds, samplers to eight channel Data Processors from CHEMLAB. All flow supplies available.

HAEMATOLOGY ANALYSERS

Fisher Scientific have introduced a new line of cell counters, automated coagulation timers, haemoglobinometers. I.E.C. — Plasma Analyser. Ortho Instruments introduce a new range of flow cytometry cell sorting equipment — cytofluorografs.

MICROBIOLOGICAL ANALYSERS

Rapid, automated, high sensitivity systems utilising Impedance measurements for detection of microbial activity. Data processing also available for large scale systems.

MED-LAB General

Please refer to chemical analysis section (ANAL-IND) for description of UV-VIS, AA, fluorescent spectrophotometers and HPLC-GC systems and other related equipment. Also refer (BIO-MED) for details of gamma counters, R.I.A, etc.

REAGENTS AND BIO-CHEMICALS

Fisher Scientific offer an extensive range of specialist reagents, buffers and now introduce the LEDERLE range of controls, standards for Bio-chem, Haematology, R.I.A. and Toxicology units. Gilford Worthington—Enzyme kits for your Gilford system ex stock New Zealand.

MR W. JOYCE

It is with sincere regret that the Institute records the untimely death of Walter Joyce, at the age of 57 years, at Waipukurau.

Walter commenced his career in laboratory technology at the Royal Hospital for Sick Children in Glasgow, and after spending the war years as a petty officer in the Royal Navy, joined the Victoria Infirmary, Glasgow, obtaining his Fellowship of the IMLT in 1948. He and his family spent 10 years in Northern Rhodesia, now Zambia, before emigrating to New Zealand. His first position was with the diagnostic section at Wallaceville. He then spent a couple of years in a private laboratory before joining the Waipukurau Veterinary Club in 1961, where he was employed until his illness earlier this year.

He was a meticulous, methodical worker, the orderliness of his laboratory being a testimony to his training and ability as a technologist.

He was a very active member of the local RSA Club and enjoyed a game of golf, besides being a fanatic of scrabble.

Mae, has wife, accompanied him to many of the Institute's conferences, which afforded them many memorable moments, whilst Linda, the eldest of his three daughters, is a qualified technologist in her own right.

His amiable, polite manner, together with his rather dry sense of humour, caused him to be one of those personalities never to be forgotten. B. S. C.

Dr P. P. LYNCH, CBE.

Dr Philip Patrick Lynch, an honorary member of the NZIMLT, died in Wellington on July 25, 1978, in his 84th year.

Born in Oamaru, Dr Lynch was educated at Marist Brothers School, Timaru, Victoria University of Wellington and Otago University, where he graduated M.B., Ch.B. in 1923 and M.D. in 1925.

After several years as pathologist at Wellington Hospital he commenced pathology in private practice in 1932, at the same time continuing as part-time pathologist at Wellington Hospital. The late Mr Norman Ellison, the second president of our Institute, joined Dr Lynch six years later, and with the addition of one clerk the private laboratory now known as Medical Laboratory, Wellington, was established.

Through three decades Dr Lynch was consultant pathologist to the N.Z. Police and gained an international reputation in forensic medicine.

Dr Lynch was a Foundation Fellow of the Royal Australasian College of Physicians, and president in 1951 of the N.Z. branch of the BMA. He was awarded the CBE in 1954. However, Dr Lynch also made his mark outside medicine. He was Chancellor of Victoria University from 1966 to 1968 and a Victoria University Council member for 20 years. In 1971 he received an honorary LLB in recognition of his long and valuable service. Dr Lynch had a considerable interest in the sporting field, particularly rugby union and cricket. His many interests and long lists of achievements are all the more remarkable in a man who had fought considerable disability in his early youth, with its continuing handicap through all his career and public life.

Dr Lynch had been in retirement for a number of years, and while many members of the Institute would have known him by name only, a number of the present staff of Medical Laboratory, Wellington, were privileged to know and work with him. Older members of the Institute would remember him well as an examiner in the days when all our examinations were held at the Otago Medical School.

Throughout his career Dr Lynch had the affairs of the Institute at heart and in him we always had a staunch friend and supporter.

Mr M. O. EKDAHL, M.A.

Miles Oscar Ekdahl served in the army during the last war and then started laboratory work at Wellington Hospital.

He had previously graduated M.A. and obviously had rather different intentions to start with.

After qualifying in medical laboratory technology he worked in various medical laboratories, including Cook Hospital, Gisborne. He finally settled down as a microbiologist at Wallaceville.

From conversations with people who knew him one gets the impression of a quiet, intelligent and likeable man.

I am indebted to Hugh Bloore for most of this information. Editor.

INDEX TO ADVERTISERS

Index to Volume 32

Directions for Contributors

These instructions are provided with the object of ensuring uniformity of presentation. Manuscripts should be typed double spaced, on one side only of good quality paper with one inch margins. Carbon copies are not acceptable. Give the author's name with initials if male, or one christian name if female, and the address of the laboratory where the work was carried out. Use capitals only where indicated and do not underline except 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

Illustrations are costly and should be used sparingly. Graphs, line drawings and photographs are all referred to as 'Figures' and should be numbered in the order of their appearance in the text using arabic numerals. Drawings (in indian ink on stout white paper) and photographs, should be about twice the size of the actual reproduction. The position of figures in relation to the text should be noted in the typescript. Legends typed on separate sheets are numbered to correspond with the illustrations. Tables should be typed separately and numbered in roman numerals.

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: kg/litre, g/litre, mg/litre, μg/litre. For the present concentrations per 100 ml also accepted as are daily outputs in urine and faeces.
Molar concentrations: mol/litre, mmol/litre, μmol/litre, nmol/litre. (For the present mequiv/litre may also be used.)
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 'specific gravity')
Clearance: litre/s, ml/s (for the present ml/min may also be used).

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 abbreviations 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

References should be listed alphabetically at the end of the article and numbered to correspond with the numbers used in superscript within the text. Citations in the text should give the author's name using *et al.* if more than one author, and the year, thus: Walker *et al.* (1972)[1]. All authors' names should be listed with initials; year of publication in brackets; journal title abbreviated and underlined to indicate italics; volume number in arabic numerals underlined with a wavy line to indicate bold type and the first page number. The reference for abbreviations is the World List of Scientific Periodicals. In general nouns have capitals, adjectives do not and conjunctions are omitted. Authors are referred to previous journals for examples.

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.

Reprints

Reprints are available to authors at their own expense on a cost basis. Orders for reprints (minimum 50), must be given when returning the proofs.

Contents