DRY CHEMISTRY PATHOLOGY TRIAL

PART 1

PRE-TRIAL INSTRUMENT EVALUATIONS

A REPORT BY THE

NON-LABORATORY PATHOLOGY TESTING WORKING PARTY

OF THE

NATIONAL HEALTH TECHNOLOGY ADVISORY PANEL

SEPTEMBER 1987

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EXECUTIVE SUMMARY

- Following a recommendation in a report to Health Ministers on dry chemistry pathology testing, a trial was carried out on the use in general practice and hospital wards of biochemistry analysers intended for 'office pathology' applications. This report summarises the pre trial assessment of the instruments.

- Four types of multipurpose analysers (Ames Seralyzer, Kodak Ektachem DT60, Abbott Vision, Boehringer Reflotron) and one haemoglobinometer (Leo HemoCue) were evaluated by the Institute of Medical and Veterinary Science, Adelaide. All except the Vision are dry chemistry analysers.

- Tests were carried out on the levels of imprecision, inaccuracy and linearity achievable with each instrument for a number of analytes, using protocols recommended by the Australian Association of Clinical Biochemists.

- Most methods achieved acceptable levels of analytical imprecision and inaccuracy and showed linear responses within the ranges cited by the manufacturers.

- The levels of inaccuracy obtained for some methods were just outside the criteria selected for acceptable performance. However, these methods were considered suitable for use by non laboratory operators, provided appropriate warning was given of necessary precautions.

- The Working Party notes that the manufacturers concerned have subsequently taken steps to improve the analytical performance of these tests.

- As a result of the evaluations, all instruments were recommended as suitable for use during the trial by operators in general practices and hospital wards provided that the requirements of the protocol were followed.

- While quality control issues were not addressed in these preliminary studies, results from the evaluations indicated that all the instruments had significant potential for use in decentralised pathology services.

DRY CHEMISTRY PATHOLOGY TRIAL

INTRODUCTION

Microprocessor controlled reflectance photometry is a technology which has been in existence for some time. Recent developments in instrumentation and dry chemistry (carrier bound) technology now offer the potential for several simple blood analytes to be analysed reliably and accurately by relatively unskilled personnel. Testing of such analytes in hospital ward side-rooms and doctors' consulting rooms has become a real possibility. Hospital ward staff and general practitioners can now perform those tests required urgently within a few minutes.

Following the introduction, in Australia, of the first multipurpose instrument of this type, the Ames Seralyzer, Health Ministers decided in May 1983 that their Standing Committee (SCOHM) should establish a working party to investigate the introduction of advances in dry chemistry technology and to propose guidelines or requirements prior to inclusion of appropriate items in the Medicare Benefits Schedule. The working party included representatives from both the National Pathology Accreditation Advisory Council and the National Health Technology Advisory Panel. Input on the subject of dry chemistry pathology testing was also obtained from the Australian Association of Clinical Biochemists.

In its report to SCOHM (1), the Working Party recommended that there should be a trial involving hospital wards and general practices to obtain information on the performance and utilisation of dry chemistry pathology testing under non-laboratory conditions. This recommendation was accepted and funding for the trial provided in the 1984 Federal Budget.

The Working Party was given the task of planning and supervising a study to assess the utilisation, reliability and effectiveness of dry chemistry pathology testing. Membership was expanded to include representation from the Royal Australian College of General Practitioners and a consultant to advise on the study design.

It was proposed that the study would be conducted in two parts:

1. An assessment of the analytical reliability of dry chemistry pathology systems (pre-trial instrument evaluations)

2. An assessment of the utilisation and cost-effectiveness of dry chemistry pathology in two settings - hospital ward side-rooms and general practitioners' consulting rooms.

This report describes the first part of the study which was designed to assess imprecision, inaccuracy and general operating conditions of the instruments, primarily in a laboratory setting. It was considered important to demonstrate that all instruments gave acceptable analytical performance before including them in the second part of the study - when test results would be available as part of patient management. The analytical robustness of these systems in the hands of non-expert users in non-laboratory settings was assessed as a component of the second part of the study, details of which will be presented in later reports.

The Principal Investigator for this part of the study was Dr David W Thomas of the Division of Clinical Chemistry at the Institute of Medical and Veterinary Science, with the assistance of Mr T D Geary and Mr T D O'Leary.

Instruments

The Working Party was aware that, in addition to the Seralyzer, other multi-purpose instruments intended for non laboratory use had been developed including the Kodak Ektachem DT60, the Boehringer-Mannheim Reflotron and the Abbott Vision. These instruments, and the Seralyzer, accept specimens of either plasma or serum, and the Reflotron and Vision can also accept whole blood. In addition, the Leo HemoCue, a specific analyser for haemoglobin which makes use of dry chemistry technology, was distributed in Australia by Medipac Pty Ltd.

Following discussion with the Working Party, the manufacturers/distributors provided generous support through making instruments available on loan and assisting with training of users.

The instruments evaluated were:

SERALYZER	- Ames Division, Miles Laboratories (Elkhart, Indiana, USA) Dry chemistry system
EKTACHEM DT60	- Eastman Kodak Co (Rochester, New York, USA) Dry chemistry system
VISION	- Abbott Laboratories (North Chicago, Illinois, USA) Wet chemistry system (centrifugal analyser)
REFLOTRON	- Boehringer Mannheim GmbH (Mannheim, West Germany) Dry chemistry system
HEMOCUE	- Aktiebolaget Leo Diagnostics (Helsingborg, Sweden) Dry chemistry system

At the time of evaluation, methods were available on all of the multipurpose instruments for measurements of plasma or serum cholesterol, triglycerides, urea and glucose. Measurements available on only some of the instruments at that time included uric acid, creatinine, haemoglobin, γ-glutamyl transferase (GGT), lactate dehydrogenase (LD), aspartate and alanine aminotransferases (AST and ALT), creatine kinase (CK) and theophylline.

METHODS

Protocols recommended by the Scientific and Technical Committee of the Australian Association of Clinical Biochemists, (2,3), which in turn are based on recommendations of the National Committee for Clinical Laboratory Standards in the USA, were used for the assessment of imprecision, inaccuracy, linearity and certain other specific features.

Analytical reliability was assessed by comparing analytical results from the instruments under evaluation with results from established routine methods ("comparative methods") used in the Division of Clinical Chemistry at the Institute of Medical and Veterinary Science, Adelaide. Results were analysed using the method of simple linear regression, with calculation of the correlation coefficient, slope, intercept and the standard error of the estimate, Syx(4).

Analytical "imprecision" (the distribution of results when repeated analyses are performed on the same specimen) was considered acceptable when the coefficient of variation (CV) was less than the calculated CV based on twice the median Standard Deviation (SD) obtained for the corresponding analyte by laboratories participating in the RCPA-AACB Quality Assurance Programmes in Chemical Pathology and the RCPA Quality Assurance Programme in Haematology. These calculated CV values are listed in Appendix I. Interbatch imprecision was assessed using analyses of two lyophilised quality control materials, usually at different concentrations, in separate batches.

Analytical "inaccuracy" (the deviation or bias of the result from that obtained by the comparative method on the same specimen) was assessed by comparing the test results obtained on patient specimens from the instrument being evaluated with those obtained using established routine methods. As wide a spread of results as possible over the linear range was sought. Inaccuracy was considered acceptable when the correlation coefficient was greater than 0.950, the slope was between 0.90 and 1.10 and the intercept was less than Syx. Plots of individual results on which the regression analyses were based are shown in Appendix II.

Linearity was assessed using "high" and "low" pools of quality control material mixed in varying proportions to cover the linear range of each analyte as specified by the instrument manufacturer. Linearity was assessed by inspection of the plots of obtained values against predicted values, and was considered acceptable when a straight line relationship was observed.

RESULTS

SERALYZER

The Ames Seralyzer (5) was available for assessment over the period June to July, 1985.

The analytes which could be determined by the Seralyzer at the time of this assessment and the analytical methods are listed in Table 1. Since this instrument had been available for some time, most of the various methods available had been documented in the literature as reliable (6 - 16). Only the most recent tests, triglyceride and theophylline, were assessed on this occasion. Comparative methods were lipase/glycerol kinase (Abbott ABA 100) for triglyceride and an EMIT method (Syva) for theophylline.

Results for interbatch imprecision studies are shown in Table 2 and those for inaccuracy in Table 3. Plots of individual results on which the linear regression analyses are based are shown in Figures 1 and 2.

Analysis of triglyceride and theophylline using the Seralyzer gave levels of imprecision which were acceptable according to criteria established for these evaluations. Coefficients of variation for the interbatch measurements of theophylline gave values which were considerably better than the median performance of laboratories participating in the RCPA-AACB Chemical Pathology Quality Assurance Programmes. Analysis of triglyceride and theophylline also gave levels of inaccuracy which were acceptable according to the criteria set for the evaluations. Linearity for both analytes was acceptable.

TABLE 1 - TESTS and METHODS AVAILABLE ON THE SERALYZER*

TEST	METHOD
Glucose	Colorimetric glucose oxidase (kinetic)
Urea	O-phthalaldehyde (kinetic)
Urate	Colorimetric uricase (endpoint)
Bilirubin	Van den Bergh (endpoint)
Triglyceride	Colorimetric enzymatic (endpoint)
Cholesterol	Colorimetric enzymatic (endpoint)
Haemoglobin	Methaemoglobin (endpoint)
Theophylline	Colorimetric apoenzyme reactivation immunoassay system with monoclonal antibody
Creatinine	Benedict-Behre (kinetic)
AST	Colorimetric enzymatic (kinetic)
LD	Pyruvate-lactate UV (kinetic)
CK	Modified Oliver Rosalki UV (kinetic)

* At time of assessment, June-July 1985

TABLE 2 - INTERBATCH IMPRECISION STUDIES ON THE SERALYZER

ANALYTE	MEAN	S.D.	C.V.%
		(n = 10)	
Triglyceride (mmol/L)	(a) 3.25	0.25	7.69
	(b) 3.23	0.18	5.57
Theophylline (µmol/L)	(c) 29.3	0.84	2.87
	(d) 74.0	1.10	1.49

(a) Single dilution repeated ten times
(b) Ten separate dilutions
(c) Stated value of 27.0 µmol/L
(d) Stated value of 79.0 µmol/L

TABLE 3 - INACCURACY STUDIES ON THE SERALYZER

ANALYTE	NUMBER OF PAIRS	CORRELATION COEFFICIENT	Syx	SLOPE	INTERCEPT
Triglyceride (mmol/L)	47	0.954	0.310	1.047	0.005
Theophylline (µmol/L)	37	0.971	6.555	1.099	0.545

EKTACHEM DT60

The Kodak Ektachem DT60 analyser and the optional Ektachem DTE Module (17, 18) were available for assessment over the period March to July, 1985. The analytes which could be measured by the Ektachem DT60 at that time and descriptions of the analytical methods used are listed in Table 4. The methods/instruments against which these measurements were compared are also listed in Table 4 under "comparative method".

Results for intra- and interbatch imprecision are shown in Table 5, and those for inaccuracy in Table 6. Plots of individual results on which the linear regression analyses are based are shown in Figures 3-10.

The level of imprecision obtained on this instrument was most acceptable. Analysis of all analytes except urea (interbatch), exhibited imprecision better than the median performance of laboratories participating in the RCPA-AACB Chemical Pathology Quality Assurance Programmes.

Measurements of all analytes except sodium and potassium gave acceptable levels of inaccuracy as defined by the criteria established for these evaluations. The measurement of sodium exhibited excessive and variable bias, usually positive, with sporadic specimens. The measurement of potassium met all criteria except that the intercept was marginally greater than Syx.

This problem with sodium measurements using the Ektachem DT60 Electrolyte Module has been observed by other groups and recognised by the manufacturer. The effect does not apply to most specimens, and is considered to arise as a result of certain matrix interactions. Modifications to the electrolyte reference fluid have been made, the most recent of which is currently undergoing evaluation. It appears that this problem has now been largely overcome (19).

Linearity for all analytes was acceptable.

TABLE 4 - TESTS and METHODS ON EKTACHEM DT60 and COMPARATIVE METHODS USED IN ASSESSMENT*

TEST	EKTACHEM DT60	COMPARATIVE METHOD
Glucose	Glucose oxidase/peroxidase	Hexokinase (SMAC II)
Urea	Urease	Diacetyl monoxime (SMAC II)
Urate	Uricase	Uricase (SMAC II)
Bilirubin	Diphylline	Jendrassik and Grof (SMAC II)
Triglyceride	Lipase/glycerol kinase	Lipase/glycerol kinase (Abbott ABA 100)
Cholesterol	Cholesterol oxidase	Cholesterol oxidase (Abbott ABA 100)
Sodium	Direct ISE	Indirect ISE (SMAC II)
Potassium	Direct ISE	Indirect ISE (SMAC II)

* At time of assessment, March-July 1985.

TABLE 5 - INTRABATCH and INTERBATCH IMPRECISION STUDIES ON THE EKTACHEM DT60

	INTRABATCH			INTERBATCH		
	(n = 10)			(n = 10)		
ANALYTE*	MEAN	SD	CV%	MEAN	SD	CV%
Sodium	124.2	0.59	0.48	124.74	1.13	0.91
	140.8	0.91	0.65	140.58	1.36	0.97
Potassium	3.09	0.020	0.65	3.08	0.045	1.46
	5.75	0.053	0.92	5.61	0.077	1.37
Glucose	4.96	0.052	1.05	4.98	0.116	2.33
	14.70	0.067	0.46	14.55	0.224	1.54
Urea	4.48	0.103	2.30	4.71	0.212	4.50
	16.20	0.228	1.41	16.31	0.475	2.91
Urate	0.272	0.003	1.10	0.273	0.004	1.47
	0.494	0.005	1.01	0.496	0.010	2.02
Triglyceride	1.60	0	0	1.63	0.011	0.67
	3.0	0.047	1.57	3.13	0.062	1.98
Cholesterol	2.99	0.059	1.97	3.0	0.057	1.90
	6.64	0.097	1.46	6.31	0.110	1.74
Total Bilirubin	39.4	1.65	4.19	38.8	1.73	4.46
	84.8	5.05	5.96	85.3	3.58	4.20

* All mmol/L except bilirubin which is μmol/L

TABLE 6 - SUMMARY OF INACCURACY STUDIES ON THE EKTACHEM DT60

ANALYTE *	NUMBER OF PAIRS	CORRELATION COEFFICIENT	Syx	SLOPE	INTERCEPT
Glucose	103	0.998	0.298	1.064	-0.227
Urea	99	0.994	0.678	0.950	0.201
Urate	61	0.994	0.017	1.067	-0.003
Bilirubin	59	0.986	5.744	1.035	3.196
Triglyceride	55	0.988	0.174	1.015	0.062
Cholesterol	57	0.992	0.211	0.947	-0.041
Sodium	99	0.680	2.630	0.688	42.283
Potassium	99	0.977	0.178	0.951	0.214

* All mmol/L except bilirubin which is µmol/L

VISION

The Abbott Vision (20) was available for assessment during March, 1986. The tests which were assessed and the methods used on the Abbott Vision for their measurement are listed in Table 7. The methods/instruments against which these measurements were compared are also listed in Table 7 under "comparative method".

Results of imprecision studies are shown in Table 8. (Insufficient specimens were analysed for urate for an assessment of imprecision of this test.) Studies of inaccuracy of methods are summarized in Table 9, with individual regressions illustrated in Figures 11-15.

Analyses of glucose, urea, triglyceride and cholesterol performed on the Vision gave very acceptable imprecision which was better than the median performance of participants in the RCPA-AACB Chemical Pathology Quality Assurance Programmes.

Measurements of glucose, urea, urate and cholesterol gave acceptable levels of inaccuracy as assessed by comparative studies. The value of the slope for triglycerides was marginally greater than the criterion established for this study and the value of the intercept was greater than Syx. Linearity was acceptable for all methods.

If certain measurement parameters (such as baseline absorbance and rate of change of absorbance) are outside preset limits an "error" code is given by this instrument. "Error" rates on cartridges were less than 5% and probably resulted from mildly haemolysed specimens in the majority of cases. Calibration remained stable during the assessment period.

TABLE 7 - TESTS AND METHODS AVAILABLE ON THE VISION AND COMPARATIVE METHODS USED IN ASSESSMENT*

TEST	METHOD	COMPARATIVE METHOD
Glucose	Hexokinase	Hexokinase (SMAC II)
Urea	Urease	Diacetyl monoxime (SMAC II)
Urate	Uricase	Uricase (SMAC II)
Triglyceride	Lipase/glycerol kinase	Lipase/glycerol kinase (Abbott ABA 100)
Cholesterol	Cholesterol oxidase	Cholesterol oxidase (Abbott ABA 100)

* At time of assessment, March, 1986

TABLE 8 - INTERBATCH IMPRECISION STUDIES ON THE VISION

ANALYTE *		n	MEAN	SD	CV%
Glucose	A	17	4.28	0.077	1.80
	B	17	15.89	0.127	0.79
Urea	A	19	6.14	0.160	2.61
	A	19	17.76	0.373	2.10
Triglyceride	A	16	1.47	0.057	3.87
	B	16	2.77	0.069	2.49
Cholesterol	A	17	2.50	0.050	2.00
	B	17	6.45	0.103	1.60

* mmol/L

TABLE 9 - INACCURACY STUDIES ON THE VISION

ANALYTE *	NUMBER OF PAIRS	CORRELATION COEFFICIENT	Syx	SLOPE	INTERCEPT
Glucose	100	0.996	0.279	0.985	-0.107
Urea	55	0.985	0.648	0.954	0.418
Urate	35	0.989	0.018	1.020	0.005
Triglyceride	99	0.994	0.091	1.110	-0.273
Cholesterol	97	0.979	0.189	0.999	0.014

* (mmol/L)

REFLOTRON

The Boehringer Reflotron (21) was available for assessment during January 1986.

The tests which were assessed and the methods used on the Reflotron are listed in Table 10. The methods/instruments against which these measurements were compared are also listed in Table 10 under "comparative method".

Results of imprecision studies are shown in Table 11. (Only one concentration was used for the assessment of haemoglobin). Inaccuracy studies are summarised in Table 12 and individual regressions are shown in Figures 16-22.

Analyses of glucose, γ-glutamyl transferase and triglyceride gave acceptable results for imprecision. Analyses of glucose (low concentration), triglyceride (low concentration) and γ-glutamyl transferase exhibited levels of imprecision better than the median performance of laboratories participating in the RCPA-AACB Chemical Pathology Quality Assurance Programmes. The coefficients of variation for haemoglobin and cholesterol (both concentrations) were slightly larger than the specified criteria.

Analyses for glucose (except for plasma on Reflotron compared with plasma on SMAC II, which gave an unacceptable slope) and γ-glutamyl transferase gave acceptable results for inaccuracy. Linearity was acceptable for all tests.

Slopes for cholesterol, triglyceride and haemoglobin, intercepts for cholesterol and haemoglobin and the correlation coefficient for cholesterol did not meet the required criteria. These analyses were performed using pre-production batches of reagent strips. The company has subsequently made appropriate adjustments to these tests, which have resulted in improved reliability of analytical performance. A recent evaluation of cholesterol measurements using the Reflotron indicated acceptable levels of inaccuracy (22).

TABLE 10 - TESTS AND METHODS AVAILABLE ON THE REFLOTRON AND COMPARATIVE METHODS USED IN ASSESSMENT*

ANALYTE	REFLOTRON	COMPARATIVE METHOD
Glucose	Glucose oxidase/ tetramethylbenzidine	Hexokinase (SMAC II) (plasma)
GGT	Phenylenediamine-carboxylate/methylan-thranilic acid-potassium ferricyanide	γ-glutamyl para-nitroanilide (SMAC II) (plasma)
Cholesterol	Cholesterol oxidase/ tetramethylbenzidine	Cholesterol oxidase (Abbott ABA 100) (plasma)
Triglyceride	Lipase/glycerol kinase	Lipase/glycerol kinase (Abbott ABA 100) (plasma)
Haemoglobin	Cyanmethaemoglobin	Cyanmethaemoglobin (Coulter S+VI) (whole blood)

* At time of assessment, January 1986

TABLE 11 - INTERBATCH IMPRECISION STUDIES ON THE REFLOTRON

ANALYTE		MEAN	SD	CV (%)
Glucose (mmol/L)	A	5.38	0.17	3.16
	B	13.86	0.63	4.55
Haemoglobin (g/L)		131.4	3.9	2.96
Cholesterol (mmol/L)	A	3.14	0.15	4.77
	B	5.48	0.25	4.56
Triglyceride (mmol/L)	A	1.49	0.05	3.35
	B *	2.15	0.10	4.65
GGT (U/L)	A	47	1.6	3.40
	B	148	5.9	3.99

(n = 30, except for * where n = 41)

TABLE 12 - INACCURACY STUDIES ON THE REFLOTRON

ANALYTE		NUMBER OF PAIRS	CORRELATION COEFFICIENT	Syx	SLOPE	INTERCEPT
Glucose	P	32	0.983	0.519	0.955	-0.139
	P	28**	0.991	0.504	0.879	-0.436
	*	28	0.986	0.620	0.952	-0.126
Haemoglobin	B	31	0.980	0.556	1.150	-1.32
Cholesterol	B	22	0.933	0.458	0.877	0.615
Triglyceride	P	27	0.984	0.135	0.826	0.040
GGT	P	31	0.995	9.08	1.004	6.24

P = plasma, B = whole blood for comparative method. All Reflotron measurements on whole blood except ** where plasma was used and * which was a comparison of blood (y) and plasma (x) on the Reflotron.

HEMOCUE

The HemoCue system (23) was available for assessment during July, 1985. It provides a fast, simple method to measure haemoglobin in whole blood. No sample preparation is required and a control cuvette is supplied. This control is read prior to the patient analyses to see if calibration is necessary. There was no need for calibration during the evaluation as the control cuvette read within the required range.

Results from assessments of intrabatch imprecision are shown in Table 13 and those for inaccuracy in Table 14. Linear regression for assessment of inaccuracy is shown in Figure 23.

Levels of intra and interbatch imprecision were acceptable according to the criteria set for this evaluation. Coefficients of variation were better than the median performance of laboratories participating in the RCPA Haematology Quality Assurance Programme.

In the assessment of inaccuracy the intercept was larger than Syx, but otherwise an acceptable level of inaccuracy according to the criteria established for this study was obtained. Linearity was also acceptable.

TABLE 13 - IMPRECISION STUDIES ON THE HEMOCUE

HAEMOGLOBIN (g/L)

	MEAN	SD	CV(%)
INTRABATCH (n=9)	160	1.97	1.23
INTERBATCH (n=5)	159	1.87	1.18
(n=4)	114	(1.25)	(1.10)

TABLE 14 - INACCURACY STUDIES ON THE HEMOCUE

HAEMOGLOBIN (g/L)

NUMBER OF PAIRS	CORRELATION COEFFICIENT	Syx	SLOPE	INTERCEPT
76	0.987	3.92	0.940	8.39

(Comparative method - Cyanmethaemoglobin, Coulter S +VI, whole blood)

ADDITIONAL STUDIES ON INSTRUMENT PERFORMANCE

In addition to the assessments of inaccuracy and imprecision described above, the opportunity was taken to carry out the following additional studies on some of the instruments to obtain data on their robustness.

EKTACHEM DT60

A study to assess interoperator performance was undertaken with this instrument. Staff with varying technical skills, ranging from minimal to extensive training, performed selected tests. Triplicate analyses of lyophilised quality control materials were performed on two separate occasions by each operator. Performance was limited to one colorimetric method (triglyceride) and one potentiometric method (sodium). Results are shown in Part A of Table 15. Imprecision of analysis by groups of staff was also assessed, and results are shown in Part B of the same Table. There were no significant differences in the levels of analytical performance with different operators. These results agree with those obtained in a similar assessment (24).

TABLE 15 - INTEROPERATOR PERFORMANCE ASSESSMENT OF EKTACHEM DT60

A - RELATIVE ACCURACY[1]

STAFF	SODIUM (mmol/L)	TRIGLYCERIDE (mmol/L)
Laboratory Staff		
1	140.3	2.96
2	139.9	2.95
3	140.2	3.01
4	139.3	2.97
Ancilliary Staff		
1	139.5	2.85
2	140.2	2.90
3	139.8	2.95
4	140.0	1.98

B - INTERBATCH IMPRECISION (CV%)[2]

	SODIUM	POTASSIUM	GLUCOSE	UREA
Laboratory Staff	1.06	0.86	1.35	1.88
Multidisciplinary Staff	0.96	1.72	1.36	1.85

(1) Mean value of triplicate determinations on two separate occasions

(2) CV% calculated from multiple analyses of quality control material

VISION

Specimen volume requirements were assessed by using a range of volumes of whole blood at two concentrations. Results are shown in Table 16.

In the measurement of glucose, specimen volumes less than 40 µL gave 'low', 'incorrect' or 'insufficient' results. Specimen volumes above this amount were not critical.

TABLE 16 - EFFECT OF SPECIMEN VOLUME ON GLUCOSE MEASUREMENTS BY THE VISION

SPECIMEN VOLUME (µL)	LOW GLUCOSE (mmol/L)		HIGH GLUCOSE (mmol/L)	
	Run 1	Run 2	Run 1	Run 2
20	-	-	'Low'	'Low'
30	3.6	5.2	3.7	3.2
40	5.3	5.4	14.4	14.4
60	5.5	5.2	14.3	14.4
80	5.3	5.2	14.3	14.3
100	5.3	5.2	14.4	14.3
120	5.3	5.2	14.4	14.4
140	5.1	5.0	14.2	14.5
160	5.0	5.1	14.5	14.3

REFLOTRON

The effect of various anti-coagulants was assessed by collecting a specimen of whole blood into containers with lithium heparin, sodium citrate, potassium ethylene diamine tetraacetic acid (EDTA), and sodium fluoride with EDTA as anti-coagulant - preservatives. Plasma prepared from blood anti-coagulated with lithium heparin was also used in the assessment. Results are shown in Table 17.

To assess the effect of haemolysis whole blood collected in lithium heparin tubes was frozen and thawed to produce "in vitro" haemolysis. Varying amounts of this material were added to plasma obtained from another specimen from the same source. Haemolysis was assessed visually and rated from 0 to +++++. Results are shown in Table 18.

The effect of delay between application of sample to test strip and processing by the instrument was assessed for glucose measurements. Blood was applied to five test strips which were read immediately and after 150, 300, 450 and 600 seconds respectively. This assessment was performed using 8 different specimens. Results are shown in Table 19.

TABLE 17 - EFFECTS OF VARIOUS ANTI-COAGULANTS ON MEASUREMENTS PERFORMED USING THE REFLOTRON

ANALYTE	LITHIUM HEPARIN	SODIUM CITRATE	DIPOTASSIUM EDTA	SODIUM FLUORIDE + EDTA	PLASMA LITHIUM HEPARIN
Glucose *	4.2	4.0	4.4	4.2	4.6
Cholesterol *	4.1	3.7	4.1	4.1	4.2
Triglyceride *	2.6	2.0	2.6	2.6	2.3
Haemoglobin **	100	94	102	103	-
GGT ***	20	-	-	16	-

* mmol/L
** g/L
*** µ/L

TABLE 18 - EFFECTS OF HAEMOLYSIS ON MEASUREMENTS PERFORMED BY RELFOTRON

ANALYTE *	HAEMOLYSIS 0	+	++	+++	++++	+++++
Glucose	4.3	4.1	4.8	4.5	4.6	6.2
Cholesterol	4.3	4.0	3.7	3.2	3.1	4.2
Triglyceride	2.5	2.3	2.2	1.9	1.8	1.7
Haemoglobin	<3.1	<3.1	<3.1	<3.1	<3.1	10.0

* mmol/L except haemoglobin g/L

TABLE 19 - EFFECT OF TIME DELAY ON MEASUREMENTS OF GLUCOSE PERFORMED BY THE REFLOTRON

DELAY	0s	150s	300s	450s	600s
SAMPLES*					
1	16.9	15.7	17.6	14.2	14.9
2	26.6	28.2	24.0	22.6	21.5
3	15.9	15.7	16.2	-	-
4	12.9	16.1	14.9	16.7	13.9
5	20.3	19.6	17.6	20.2	18.7
6	22.9	25.5	25.5	25.5	25.5
7	16.0	17.3	17.7	14.4	12.5
8	15.6	15.6	16.6	12.5	-

* values in mmol/L

SUMMARY

The analytical performance of the instruments assessed in the pre-trial instrument evaluations may be summarised as follows:

Seralyzer

Triglyceride and theophylline: acceptable analytical performance.

Other methods were considered acceptable on the basis of reports in the literature.

Ektachem DT60

All methods gave acceptable imprecision.

Measurements of sodium showed instances of unacceptable inaccuracy. This inaccuracy was particularly obvious in specimens analysed for sodium when other constituents were present in abnormal amounts, such as low or high concentrations of bicarbonate. The manufacturer is aware of this problem and is working towards its resolution.

For the purpose of the subsequent hospital ward side-room and the general practitioners' studies sodium results within the interval 125-150 mmol/L were considered acceptable. It was recommended that values outside this interval should not be accepted and specimens referred to a pathology laboratory for the measurement of sodium.

The value of the intercept was marginally greater than Syx in the inaccuracy study for potassium.

Vision

Imprecision was acceptable for all methods tested. Criteria for inaccuracy were met by all methods except triglyceride where the slope was marginally greater than the criterion established for this study and the intercept greater than Syx.

Reflotron

Imprecision was acceptable for all methods except cholesterol and haemoglobin where the coefficients of variation were slightly larger than the specified criteria.

Measurements of triglyceride, cholesterol and haemoglobin on the Reflotron gave results for inaccuracy which were just outside the criteria selected for acceptable performance. For measurements of triglycerides and cholesterol there were proportional underestimations (slopes of 0.826 and 0.877 respectively) and for measurements of haemoglobin there were proportional overestimations (slope of 1.150). Intercepts for

cholesterol and haemoglobin also did not meet the selected criteria. However, these tests were considered adequate for the general practitioners' study (this instrument was not available for the hospital ward side-room study) as long as users were aware of the small underestimations of triglyceride and cholesterol and small overestimations of haemoglobin when they made these measurements on this instrument.

An unacceptable slope was obtained in the inaccuracy study for glucose when plasma was used for the Reflotron and the comparative instrument.

HemoCue

Acceptable results were obtained for imprecision in the measurement of haemoglobin. Results for inaccuracy gave an intercept slightly larger than Syx. However, this test was considered adequate for the hospital ward side-room and the general practitioners' studies.

All methods on each instrument showed linear responses within the analytical ranges cited by the manufacturers/suppliers.

CONCLUSIONS

As a result of these pre-trial evaluations, all instruments were recommended as suitable for use by non-specialists in the subsequent studies, noting the precautions referred to above for use of methods which did not fully meet criteria of acceptability.

In almost all instances analytical imprecision of the methods assessed not only met the established criteria of acceptable performance but was also considerably better than the median performance of laboratories that participated in the RCPA-AACB Quality Assurance Programmes in Chemical Pathology and the RCPA Quality Assurance Programme in Haematology. Where the criteria for analytical inaccuracy were not met, in most instances the shortcomings were only of a marginal nature.

The Working Party noted with interest the range of approaches to systems for non laboratory testing that had been taken in the designs of the instruments which were evaluated. While all the instruments clearly had the potential for successful use by persons without laboratory training, it seemed possible that each type of instrument might eventually find application in somewhat different non-laboratory situations.

In addition to non-specialist applications, the instruments also represented a useful addition to the range of clinical chemistry systems available to pathology laboratories, particularly in emergency and "after-hours" situations.

Even though in most cases the analytical sytems were only just emerging from the development stage at the time of the evaluation, the results obtained gave evidence that the instruments assessed have significant potential for use in the future development of pathology services. The Working Party considers that, at the time of preparation of this report, the instruments continue to provide good examples of state of the art technology.

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.Boehringer - Mannheim Australia Pty Ltd, Sydney;
.Kodak (Australasia) Pty Ltd; Melbourne;
.Medipac Pty Ltd, Somersby NSW;
.Miles Laboratories Australia Pty Ltd.; Melbourne

In addition to provision of the instruments, assistance with familiarization and operator training was freely given.

Staff of the Division of Clinical Chemistry at the Institute of Medical and Veterinary Science, Adelaide performed the evaluations. Particular contributions were made by Mr T D Geary, Mr T D O'Leary, Ms Jane Badenoch and Ms Kerin Kelly.

APPENDIX I

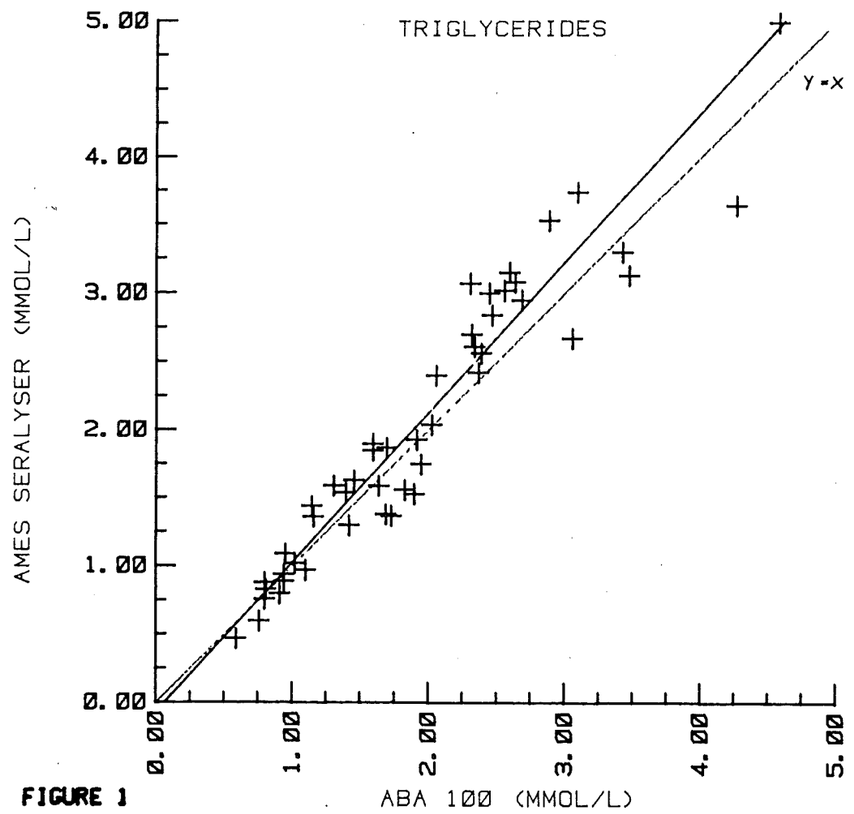
MEAN VALUES AND MEDIAN STANDARD DEVIATIONS[1] OBTAINED BY LABORATORIES PARTICIPATING IN THE RCPA-AACB CHEMICAL PATHOLOGY[2] AND RCPA HAEMATOLOGY QUALITY ASSURANCE PROGRAMMES

ANALYTE		MEAN	MEDIAN SD	CALCULATED CV(%)[3]
Sodium	(mmol/L)	137.5	1.70	2.5
Potassium	(mmol/L)	3.75	0.100	5.3
Glucose	(mmol/L)	12.5	0.41	6.6
Urea	(mmol/L)	11.5	0.42	7.3
Urate	(mmol/L)	0.40	0.022	11.0
Bilirubin	(mmol/L)	55	3.3	12.0
Triglyceride	(mmol/L)[4]	1.65	0.070	8.5
Cholesterol	(mmol/L)[4]	7.5	0.17	4.5
ϒ-Glutamyl transferase	(μ/L)	75	3.5	9.3
Theophylline	(mol/L)[4]	82.5	4.90	11.9
Haemoglobin	(g/L)[5]	101.9	1.40	2.7

1. 50th percentile value for imprecision
2. Cycle 8 (13-5-85 to 19-8-85), except where stated
3. 2 x Median SD - Mean x 100 (%)
4. January, 1986
5. June, 1985

APPENDIX II

Plots of individual results used in the linear regression analyses to assess the performance of the analytical systems.



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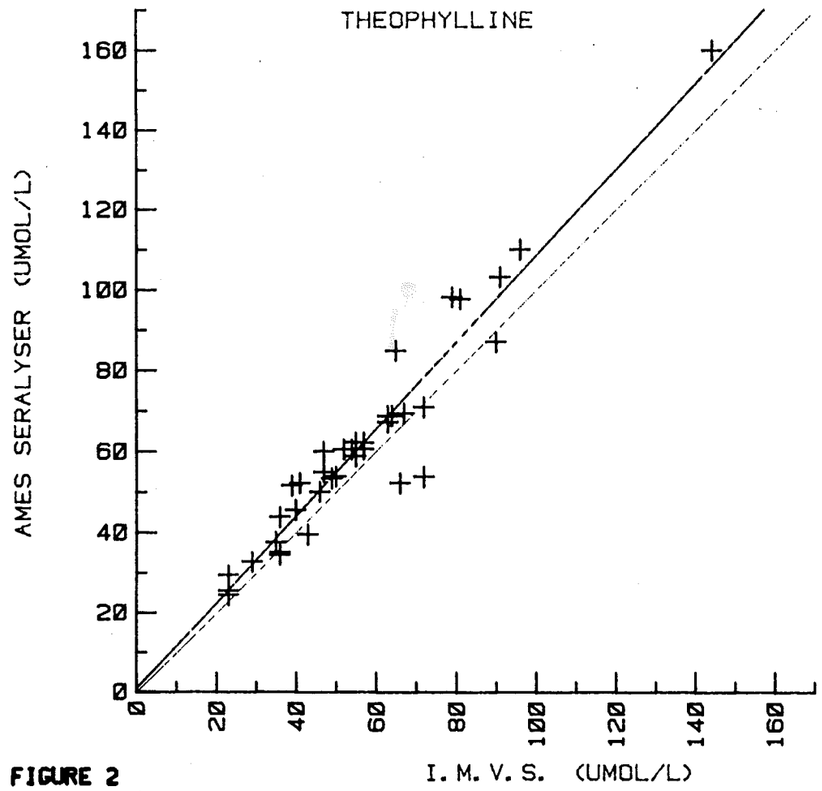

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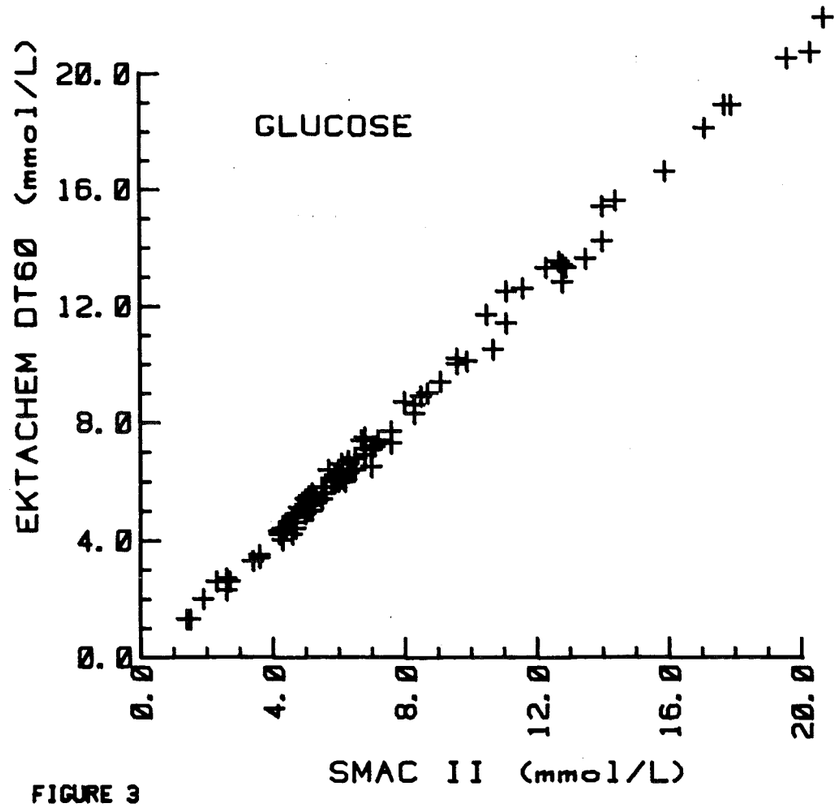

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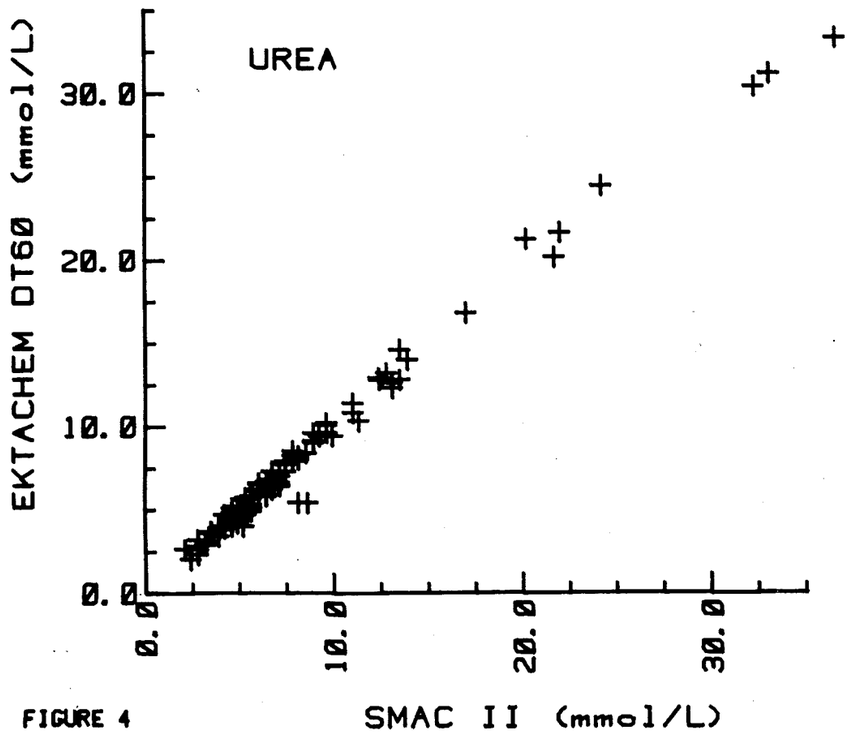

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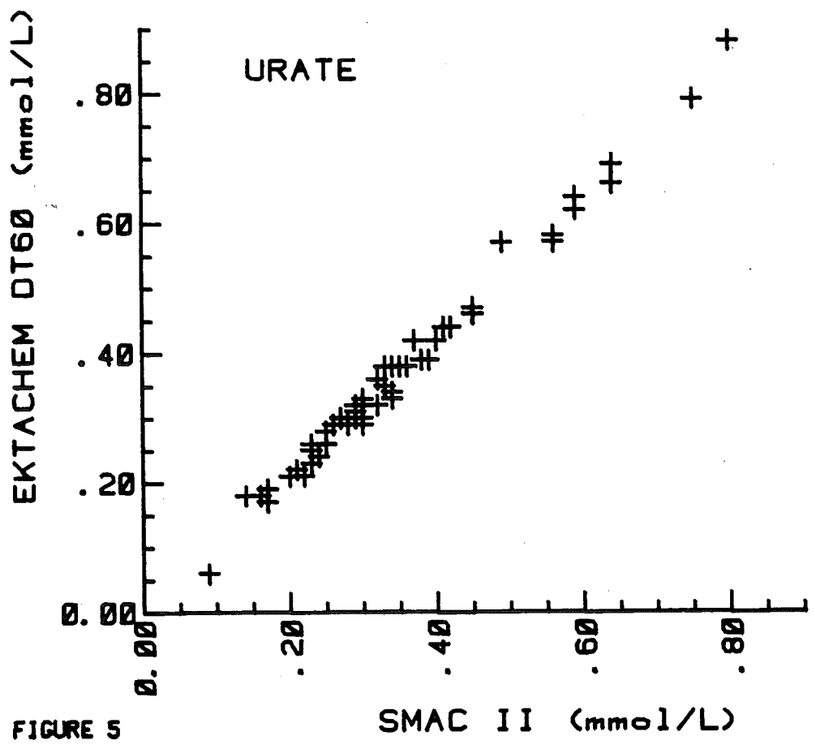

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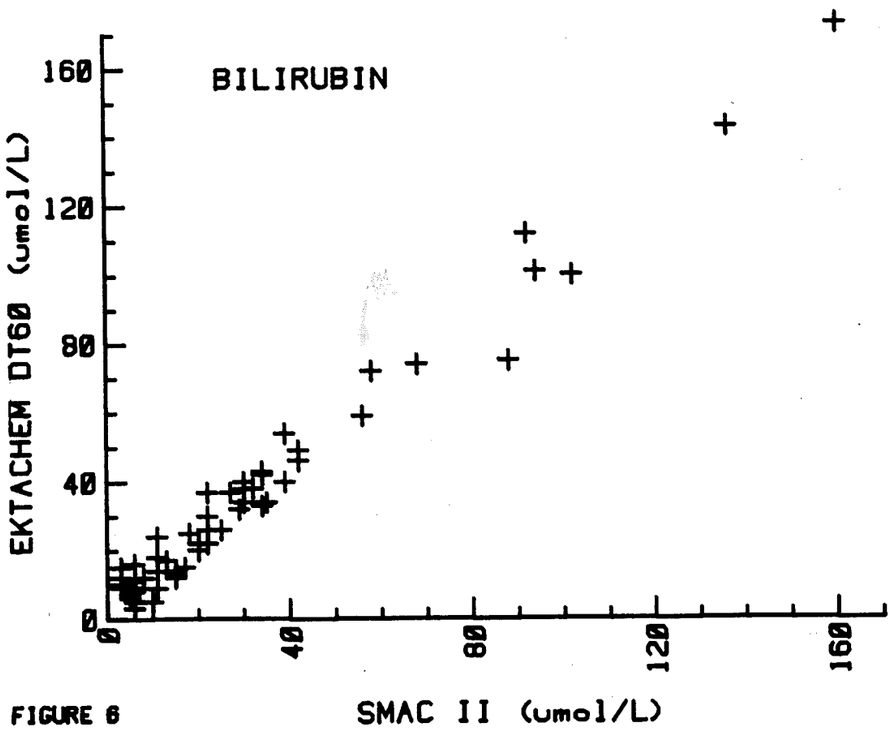

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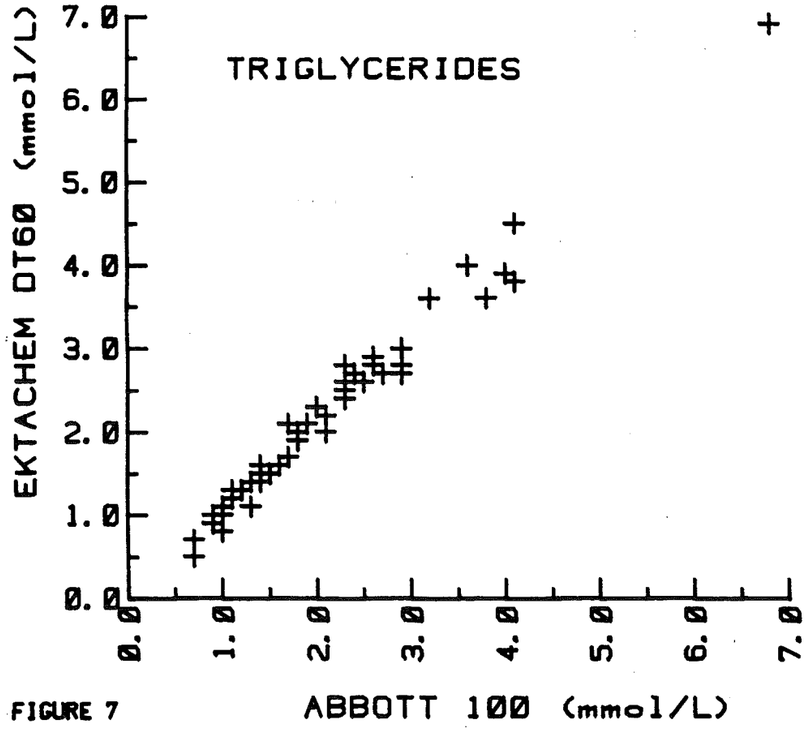

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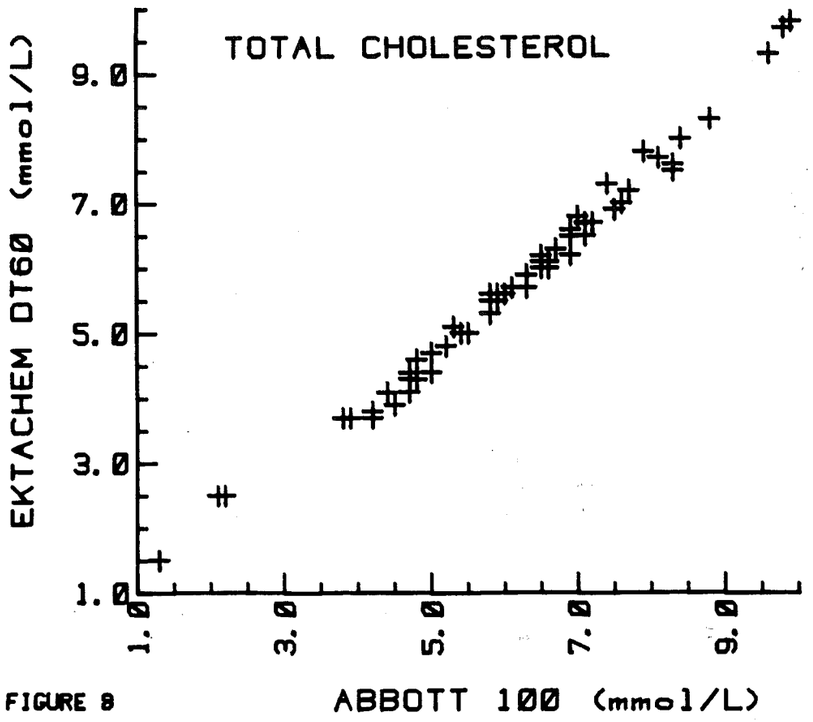

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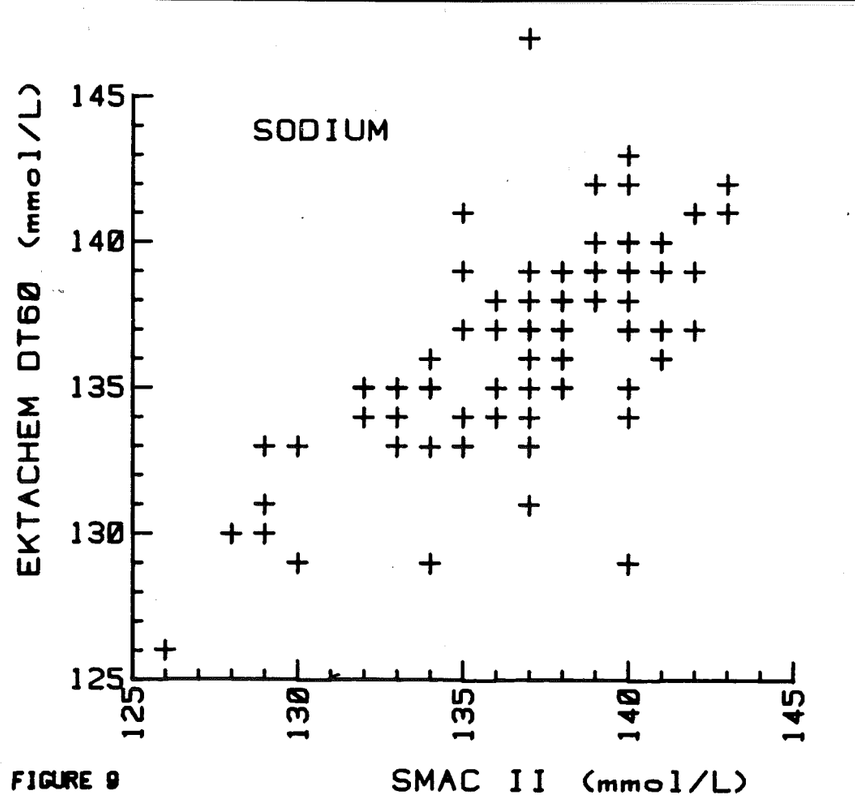

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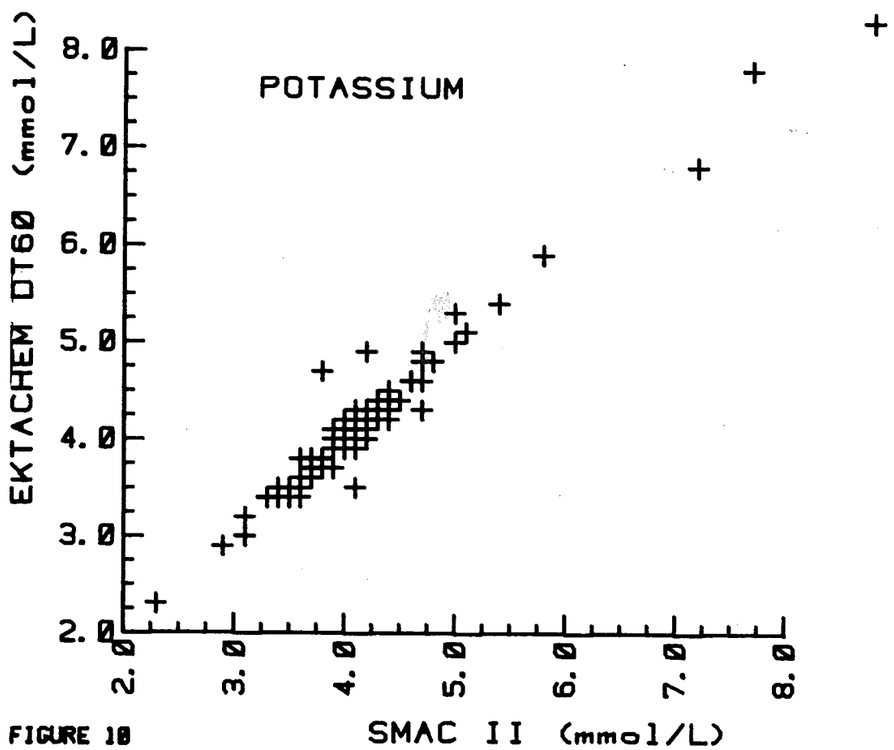

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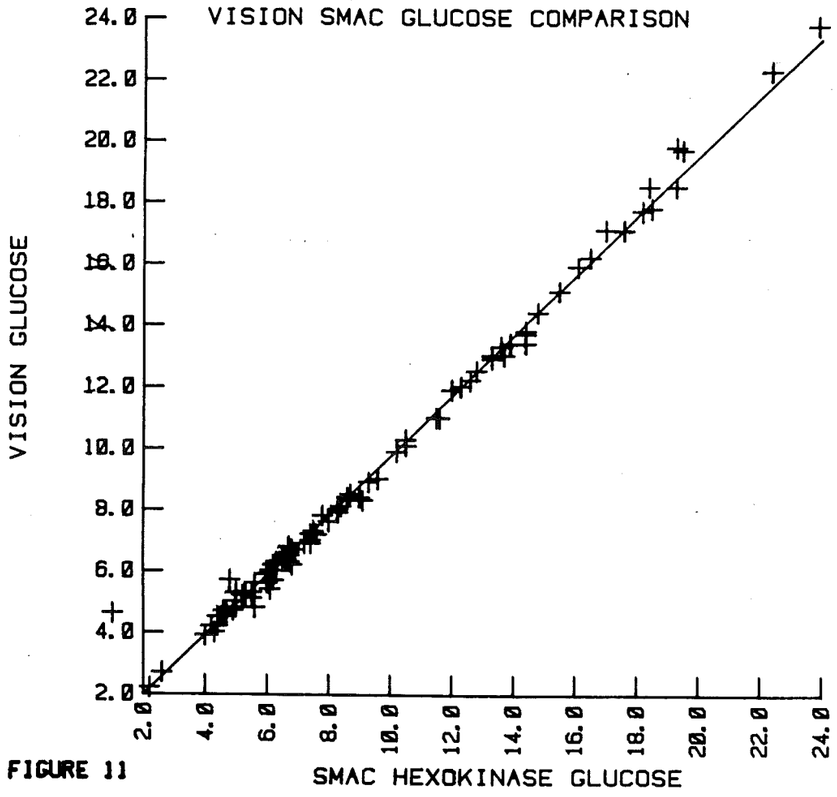

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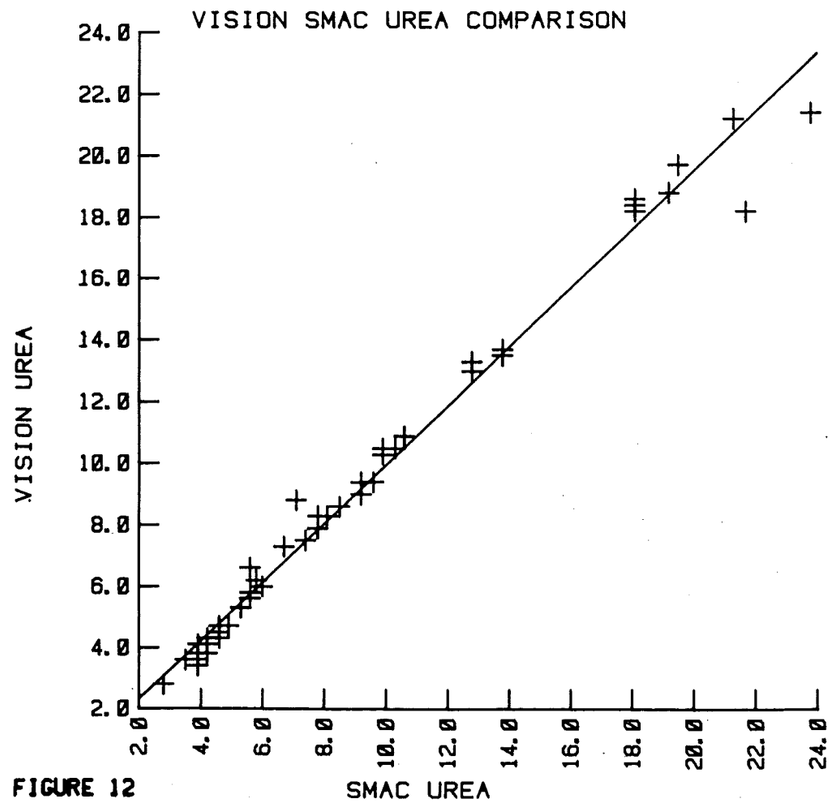

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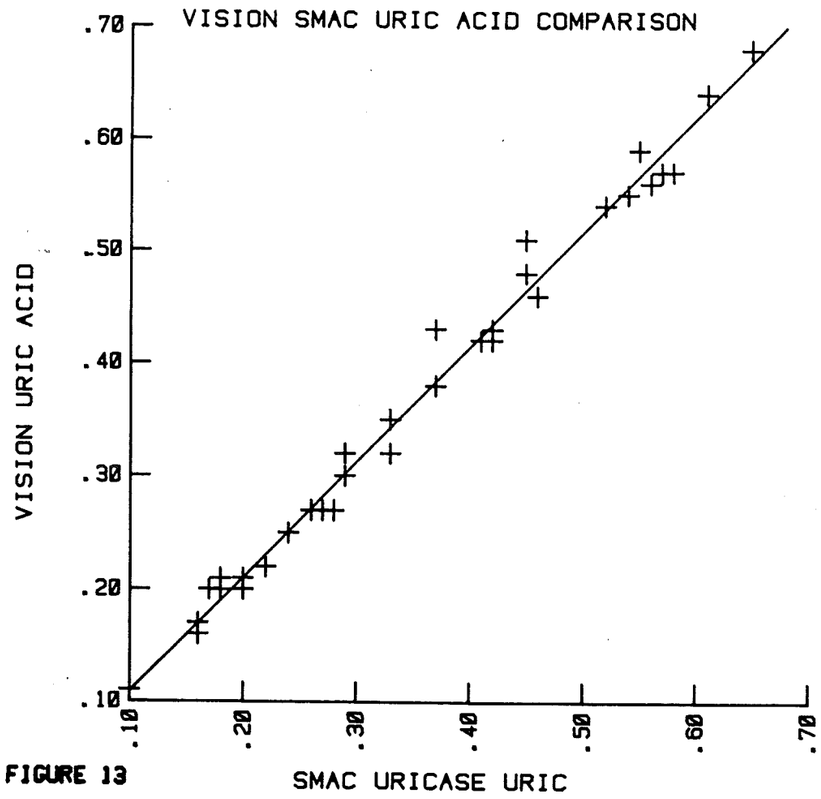

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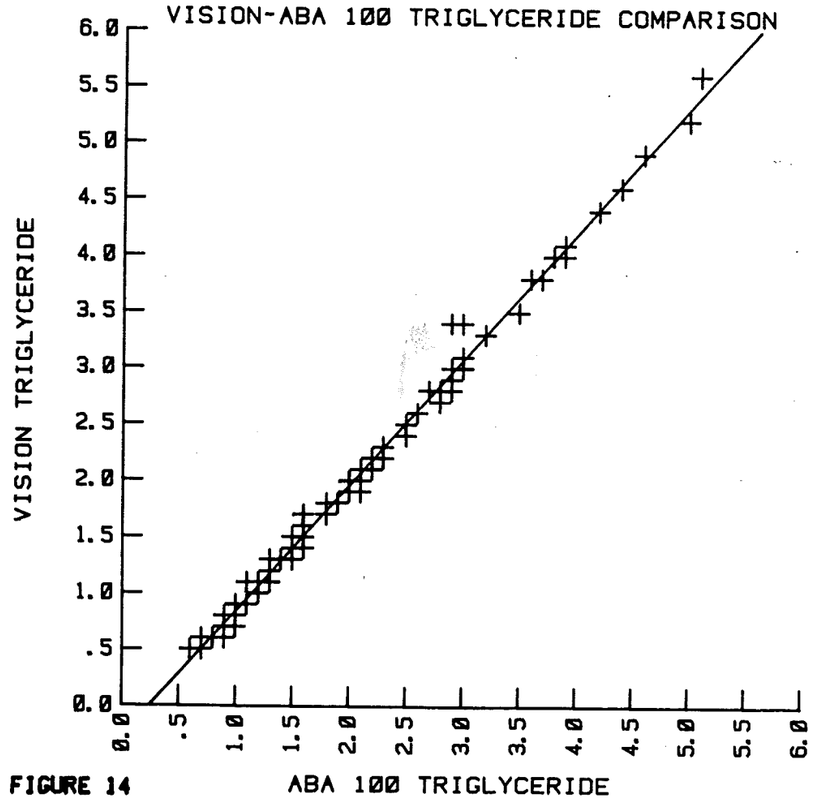

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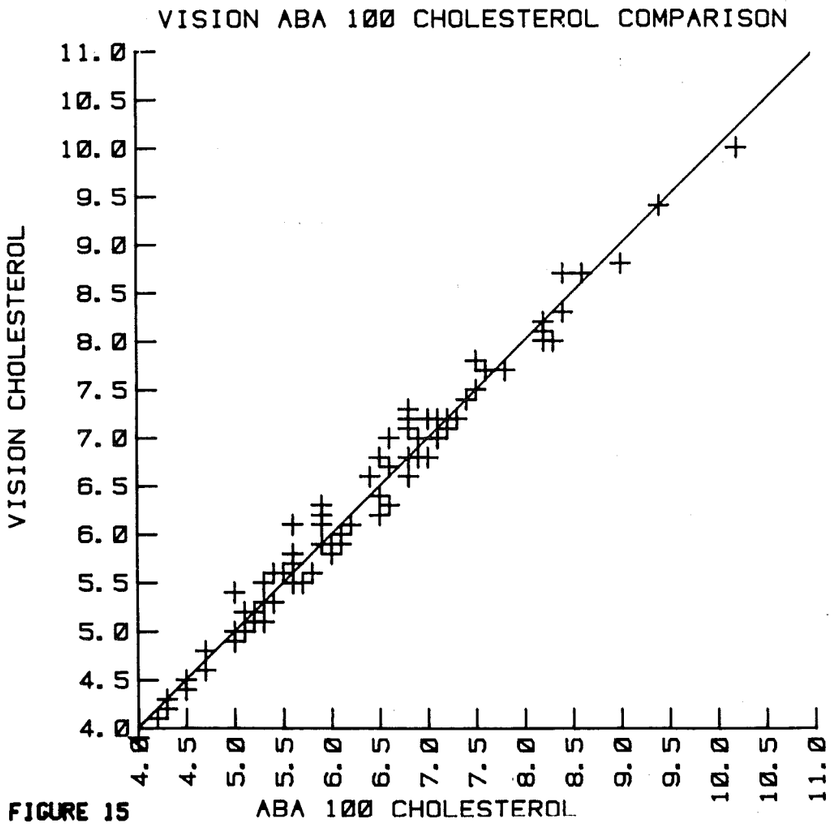

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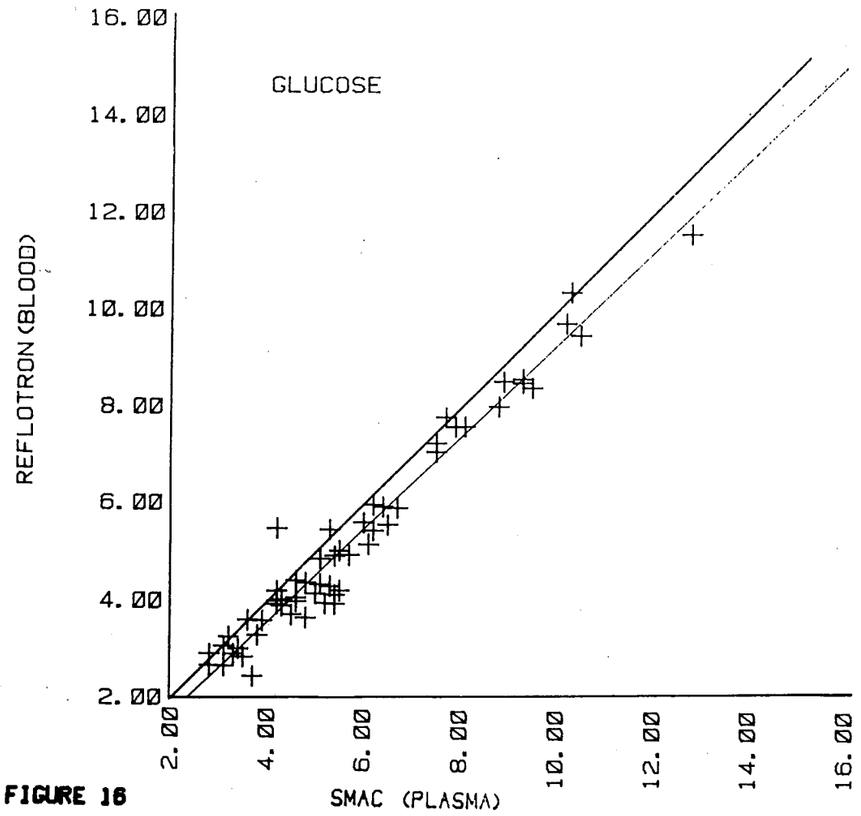

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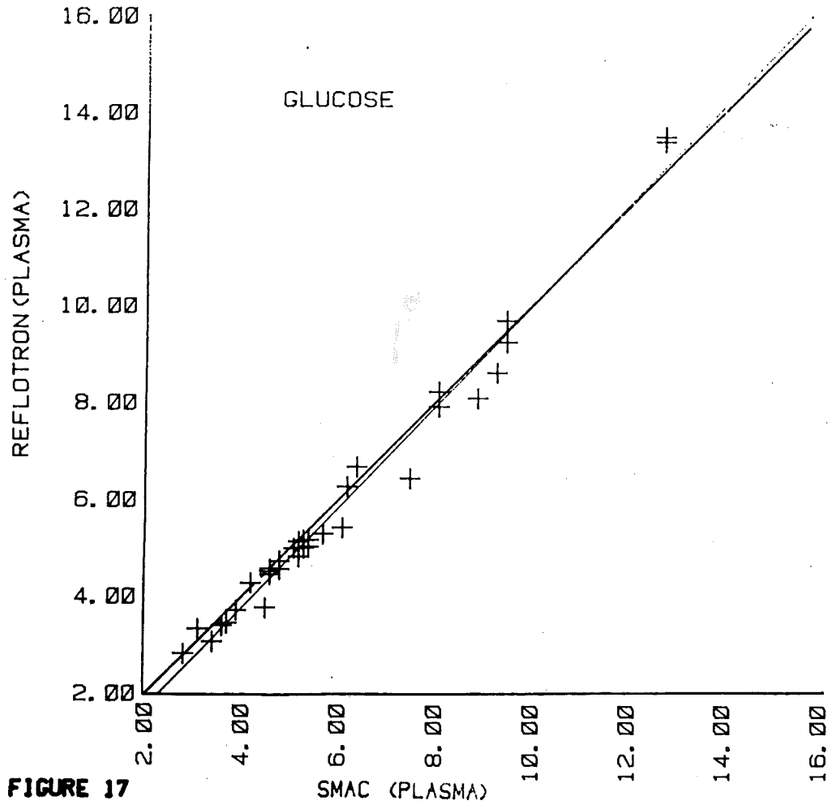

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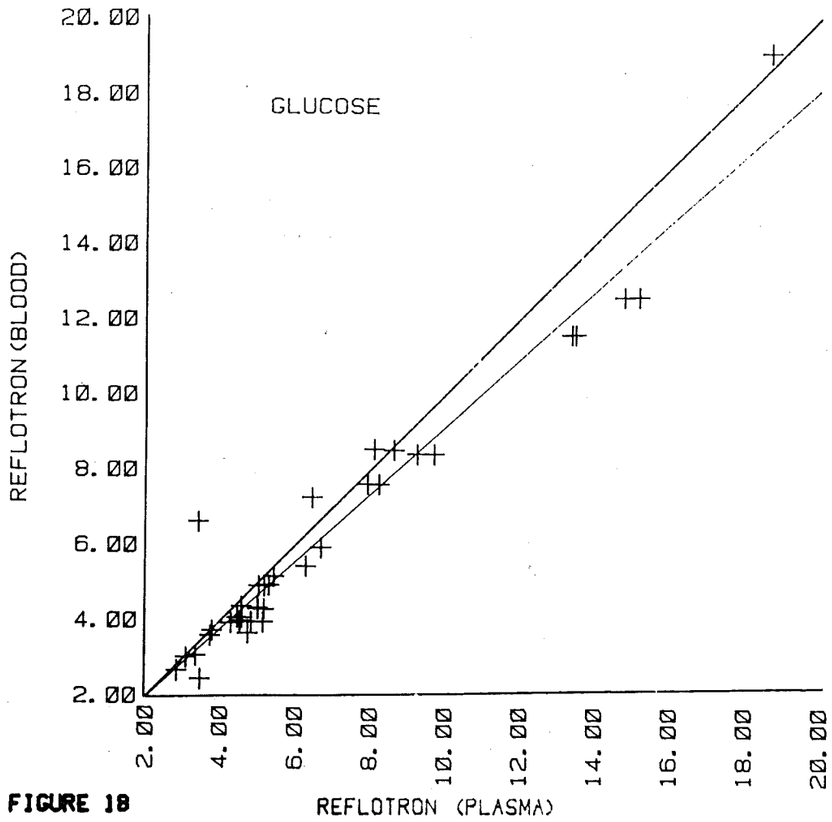

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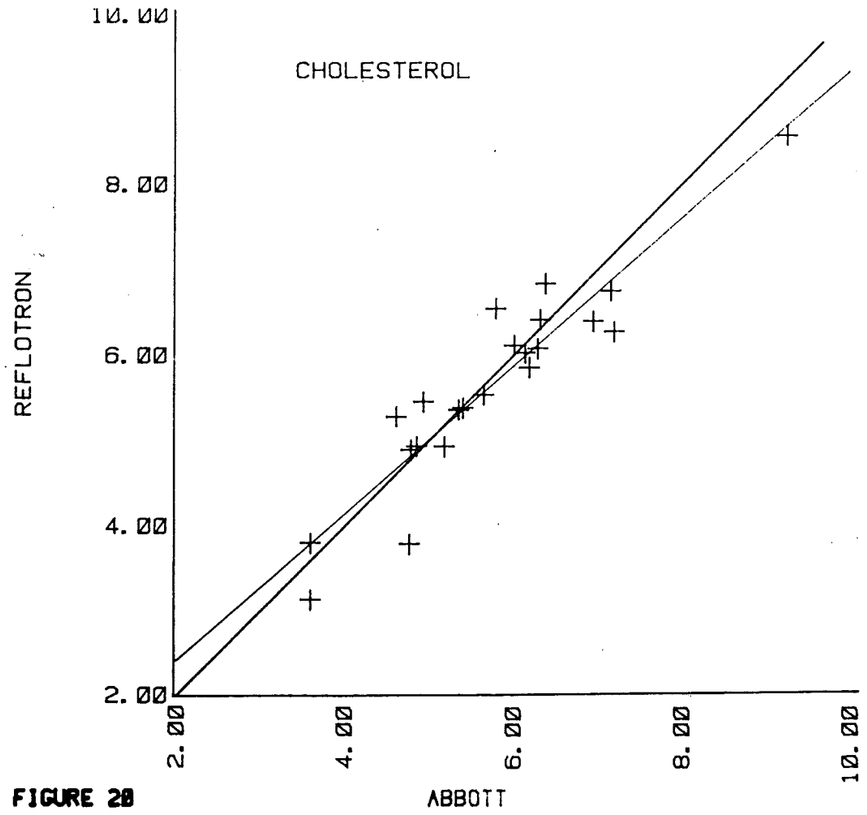

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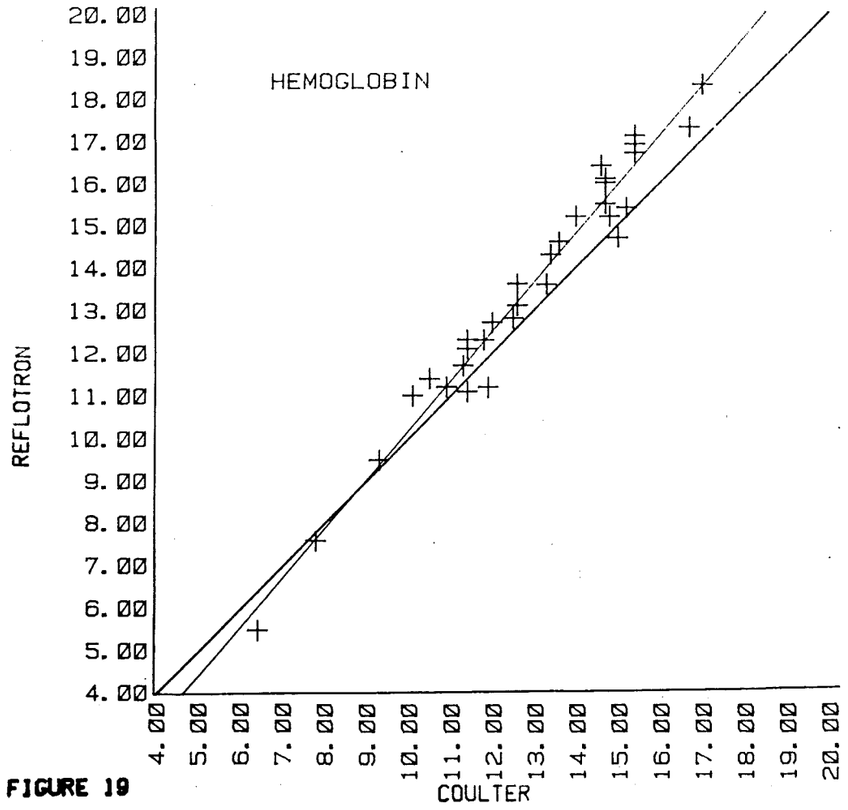

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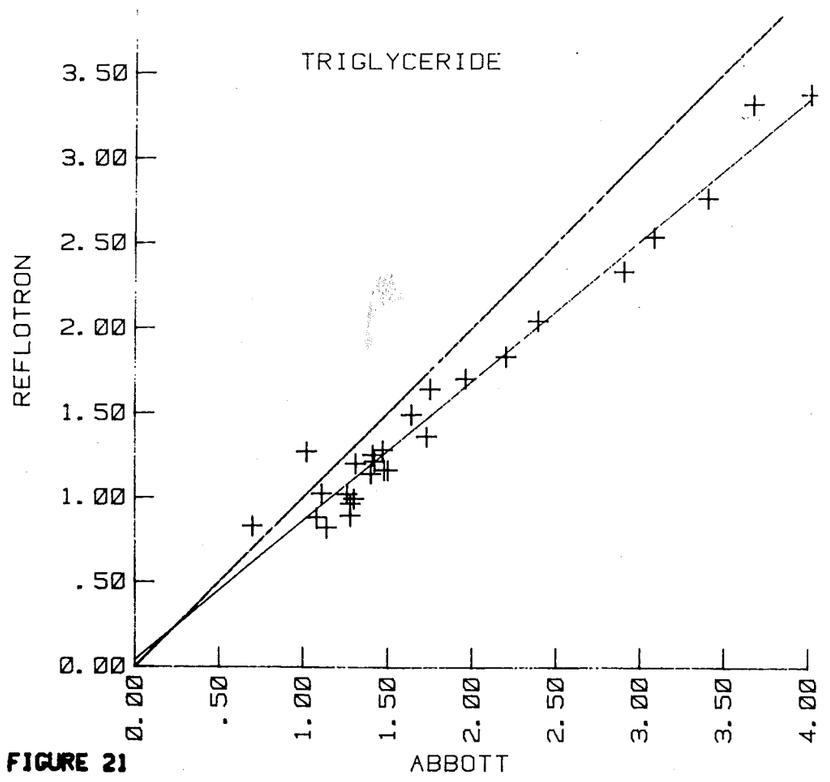

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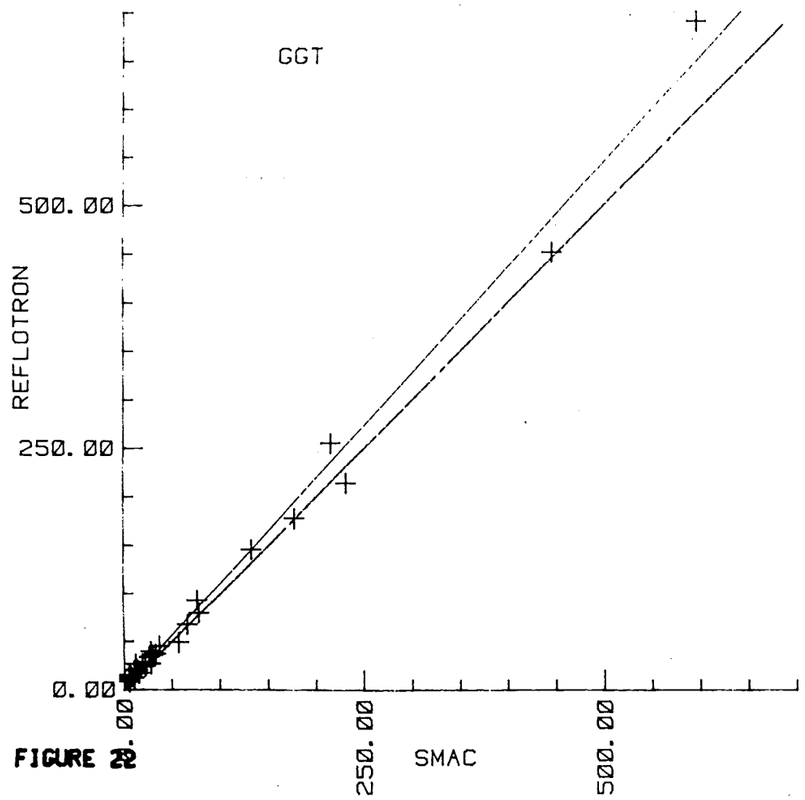

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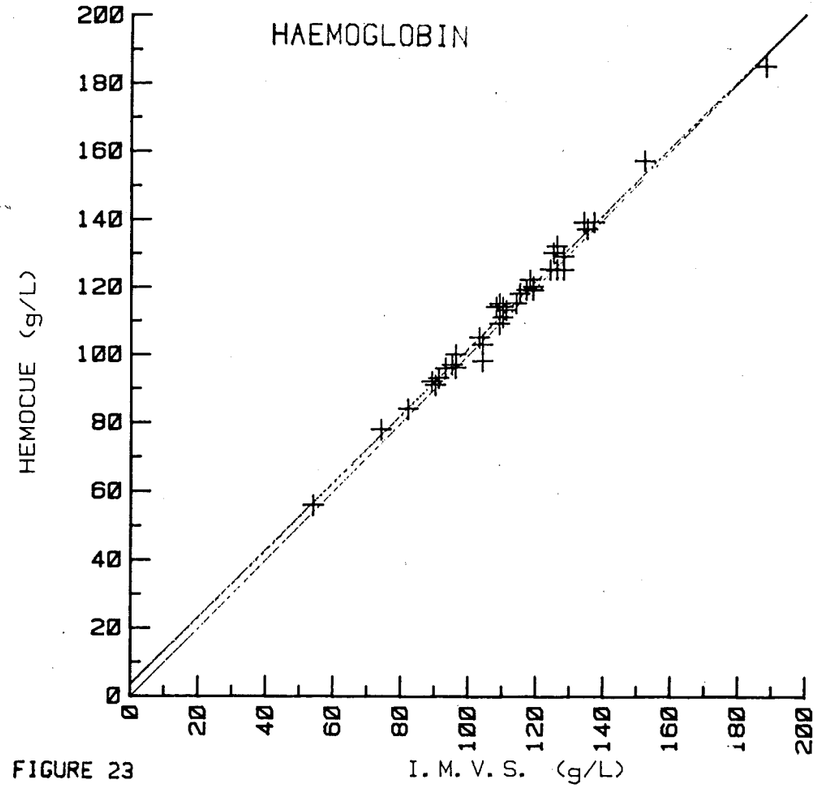

FIGURE 23