Middle Articles

CONTEMPORARY THEMES

Value of Routine Multiple Blood Tests in Patients Attending the General Practitioner

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Summary: The paper describes the investigation of 296 patients selected at random from those attending the general practitioners' surgery and studied by means of multiple biochemical and haematological tests. The tests that would not normally have been requested led to a new diagnosis of clinical significance in 16·9% of patients, in most instances requiring an alteration of the patient's therapy. The effect of the profile tests on patient follow-up, referral of patients to hospital, and the need for subsequent investigations was studied by comparing the patients profiled with a control group of patients not having a blood profile. The place of such an investigation in general practice is considered.

Introduction

Since February 1967 all patients admitted to certain wards at the Queen Elizabeth Hospital, Birmingham, irrespective of diagnosis, have had blood taken and 14 biochemical tests performed. These tests have been named a blood profile. The tests that would not normally have been requested led to a new or additional diagnosis in 8·3% of the first 2,071 ward patients studied (Whitehead et al., 1967; Whitehead, 1968; Carmalt, 1969; Whitehead and Carmalt, 1969). Performing these tests before a patient's admission to hospital may be of greater value in reaching an earlier diagnosis, starting treatment, and reducing the time taken for any subsequent investigations at hospital.

Percy-Robb and Whitby (1967) reported the results of over 1,000 blood samples taken from patients attending general practitioners and analysed them by means of the 12-channel Technicon Sequential Multiple Analyzer (S.M.A. 12) hospital model. They found that instrumental drift resulted in abnormal results, but did not give in any detail the interpretation of abnormal results. Scott and Robertson (1968) and Hodes (1968) performed screening tests in general practice, including haemoglobin and certain biochemical tests. They sent postal invitations to patients to attend for screening, but less than half of those sent letters attended. In these preliminary studies the abnormal biochemical results are given little interpretation. Scott and Robertson (1968) stressed the value of ancillary help and the importance of recording the patient's drug therapy in such investigations.

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The present study was undertaken in order to investigate the use of multiple blood tests irrespective of diagnosis on randomly selected patients attending their general practitioners. Particular attention was given to the effect of this study on diagnosis, treatment, the need for follow-up tests, and referral of patients to hospital. A general practice over 20 miles (32 km.) from the laboratory performing the analyses was selected so that difficulties in communication could be investigated.

Description of Practice and Method of Study

Patients from only one general practice were studied. This is an urban group practice of about 10,000 patients cared for by four doctors, of whom two took part in this study. Except in emergency, however, each practitioner follows up his own patients. The practice has open access to hospital laboratory and radiological services. The study was confined to adult patients attending the surgery at which an appointment system was already in use. Before each surgery started the doctors knew the number of patients due to attend, normally from 15 to 30. By numbering these patients the doctors randomly selected four to be studied at each surgery. Two of the patients were allocated to a control group, while the other pair had 20 ml. of blood taken by venepuncture after the doctor had described the purpose of the scheme. The blood serum was separated at the surgery by a part-time clerical help using a centrifuge. The serum and 2 ml. of blood in a sequestrene tube was placed in a special container and sent by first-class mail to the laboratory for multiple analysis. Specimens were normally analysed the morning after venepuncture, except those collected on Friday; these were stored in the refrigerator for analysis the following Monday.

The general practitioners determined the Westergren sedimentation rates in their surgery. The remaining analyses were performed on single-channel AutoAnalyzers at the laboratory. The serum was analysed for glucose, creatinine, urea, sodium, potassium, alkaline phosphatase, bilirubin, albumin, globulin, calcium, aspartate aminotransferase (S.G.O.T.), iron, uric acid, and cholesterol. Haemoglobin was measured on the sequestrene blood.

At the time of consultation the following details were recorded of all patients in the test and control groups: (1) name, address, year of birth, and sex; (2) reason for consultation; (3) presumptive diagnosis, including any other conditions present but not responsible for the consultation; (4) presumptive course of action—(a) discharged, (b) for follow-up by the general practitioner, or (c) for referral to hospital; (5) discretionary investigations normally asked for; and (6) present drug therapy.

On return of the multiple blood test results the test group

was reviewed in order to see how many patients required further follow-up, blood tests, or referral to hospital. In addition, for every patient in the test group a questionary was completed by the general practitioners three to six months after the blood test. On this questionary any results marked by the laboratory staff as abnormal were placed in one of three categories: (1) an expected abnormal result, (2) an unexpected abnormal result leading to a new or additional diagnosis, or (3) an unexpected abnormal result, unexplained at the time of completing the questionary.

The criteria for marking a result as abnormal were based partly on the work of Roberts (1967) and are shown in Table I. For haemoglobin results in both sexes below 12 g./100 ml. were marked as abnormal, though this criterion was defined by the World Health Organization (1959) as that for females only.

Fifteen patients were referred to hospital from the control group and eight from the test group. The general practitioners' diagnoses on patients referred to hospital are shown in Table III. Examining the diagnoses of patients in the control group referred to hospital gives no indication that performing a blood profile could have avoided such a consultation.

Of the 293 patients in the control group 33 (11·3%) had blood taken for biochemical or haematological tests within the profile group; these tests requested would represent 1·2% of the total tests if all the control group had full profiles performed. In the patients profiled the practitioners had noted that 3·9% of the total tests performed would normally have been requested.

On return of the profile results 23 (39%) of the 59 patients originally discharged had to be recalled, 17 requiring further investigation.

TABLE I.—*Criteria for Marking Abnormal Results and Assessment of Profile Tests Not Normally Requested*

Test	Criteria for Abnormal Result	Grand Total	Not Normally Requested				
			Total	Total Normal	Abnormal		
					Total Expected	Total Diagnostic	Total Unexplained
Glucose	>150 mg./100 ml.	296	294	280	5	6	3
Creatinine	>1·3 mg./100 ml.	285	284	272	8	3	1
Urea	>45 mg./100 ml.	296	285	269	6	4	6
Sodium	<134 >147 mEq/l.	296	296	284	3	1	8
Potassium	<3·6 >5·0 mEq/l.	294	294	236	57	1	0
Alkaline Phosphatase	>14 K.A. units/100 ml.	295	294	289	3	0	2
Bilirubin	>1·0 mg./100 ml.	294	293	287	0	0	6
Albumin	<3·3 g./100 ml.	295	293	293	0	0	0
Globulin	<2·0 >3·5 g./100 ml.	295	292	273	11	1	7
Calcium	<9·0 >10·5 mg./100 ml.	295	295	289	2	1	3
S.G.O.T.	>35 units/ml.	294	293	287	1	0	5
Iron	<60 >200 µg./100 ml.	264	261	217	25	17	2
Uric Acid	Females >7·0 and males >7·5 mg./100 ml.	285	281	273	2	2	4
Cholesterol	<100 >300 mg./100 ml.	295	288	256	14	1	17
Haemoglobin	<12·0 g./100 ml.	278	184	128	11	37	8
E.S.R.	>15 mm./hour	288	237	207	27	0	3
Total		4,645	4,464	4,140	175	74	75
Total as % of grand total			96·2	89·1	3·8	1·6	1·6

Results

Effect on Patient Follow-up and Investigation

Nearly 600 patients have been studied, 296 in the test group and 293 in the control group. The action of the general practitioners at the time of consultation is shown in Table II. In

TABLE II.—*Proposed Action at Time of Consultation*

	Control Group	Profile Group
Patients discharged	103 (35·1%)	59 (19·9%)
Patients followed up by practitioner ..	175 (59·8%)	229 (77·3%)
Patients referred to hospital	15 (5·1%)	8 (2·7%)
Total	293	296

35·1% of the control group and 19·9% of the test group the patients were discharged—that is, not asked to reattend—while 59·8% of the control group and 77·3% of the test group were asked to reattend the general practitioners. There was therefore a higher rate of reattendance in the test group.

TABLE III.—*Diagnoses of Patients Referred to Hospital*

Control Group	Profile Group
Foreign body in finger	Before return of profile:
Otitis media	Rheumatoid arthritis
For insertion of intrauterine coil	Brachial neuritis
Asthma	Chronic bronchitis
Chronic bronchitis	Varicose veins
Multiple sclerosis	Osteoarthritis
Cataracts	Inguinal hernia
Mitral stenosis	Polyneuritis
Lump in breast	?Acoustic neuroma
Carpal-tunnel syndrome	After return of profile:
Lump in breast	Uraemia (urea 309 mg./ml.)
Fractured finger	Known diabetes mellitus (glucose
Carcinoma of lung	410 mg./100 ml.)
Sciatica	Known pyelonephritis (urea 175 mg./
Gastric ulcer	100 ml.)

Of the 229 patients asked to return to the surgery before the profile results were known, 64 required further investigations and 3 were referred to hospital (see Table IV).

TABLE IV.—*Action On Return of Profile Results*

	Patients Originally Discharged	Patients Already Being Followed Up
Discharged	36	—
Follow-up by general practitioner:		
No tests	6	162
Further tests	17	64
Referred to hospital	0	3
Total	59	229

Diagnoses and Treatment in Test Group

Of the 4,645 tests performed in the profile group, 4,464 would not have been requested (Table I); 74 of these unrequested tests led to a new diagnosis in 50 patients—that is, in 16·9% of patients in the profile group. The diagnoses resulting from the unrequested tests and the range of haemoglobin in those found to be anaemic are shown in Table V. In addition to the data given in this table one patient, a man born in 1901, was found to have myxoedema (cholesterol 358 mg./ 100 ml.). In his case the follow-up protein-bound iodine was low. The general practitioner recorded a new diagnosis when the result was significant in management of the patient. A further 64 (21·6%) patients had an unexplained abnormal result which would not have been requested.

Unsuspected biochemical abnormalities such as hyper-cholesterolaemia in 17 patients and hyperuricacidaemia in four patients were recorded as unexplained abnormal results and not diagnostic results, since treatment was not considered necessary for such patients. In 57 (19·3%) of the patients in the profile group the serum potassium levels were over

TABLE V.—*Diagnoses Resulting From Profile Tests*

Iron-deficiency Anaemia (40 Patients)

Haemoglobin* (g./100 ml.)	6—	7—	8—	9—	10—	11—
No. of patients	1	1	10	7	14	7

Diabetes Mellitus (6 Patients)

Glucose level (mg./100 ml.)	155	155	157	273	310	345
Year of birth of patient	1922	1926	1888	1886	1903	1891†

Renal Disease (4 Patients)

Creatinine (mg./100 ml.)	Urea (mg./100 ml.)	Year of Birth of Patient
1·0	51	1909
1·4	51	1898
1·9	72	1888
14·4	309	1891

*In three patients the haemoglobin was requested but the result was unexpected and diagnostic and the serum iron was diagnostic and not requested. One woman with a haemoglobin of 12·6 g./100 ml. and serum iron 50 μg./100 ml. was diagnosed as a case of iron deficiency.
†This patient had unsuspected uraemia.

5 mEq/l.; most of these were thought to result from haemolysis and were therefore marked as expected abnormalities.

With regard to the effect on the patients' treatment, the profile results led to 27 patients (9·1% of those profiled) having iron therapy. In some patients, drugs likely to cause intestinal bleeding were withdrawn or replaced with other drugs; while one patient was found to have bleeding haemorrhoids, which were removed surgically. In the 14 patients in whom the haemoglobin has so far been repeated after therapy, the initial haemoglobin results varied from 8·7 to 11·7, mean 10·4 g./100 ml., with rises after treatment of 1·0 to 6·7, mean 3·5 g./100 ml.

One patient with myxoedema started thyroxine therapy, while five patients with diabetes mellitus were given diet with or without hypoglycaemic agents.

Following the profile results three patients were referred to hospital (Table III); two were known to have diabetes or renal disease, but the biochemical results disclosed an unsuspected deterioration in their condition, while the third patient required inpatient treatment for renal failure. As a result of tests performed subsequent to the profile a further two patients were referred to hospital, one already mentioned for haemorroidectomy and the other, a subject with back pain and a previous colectomy for carcinoma, for reassessment when found to have a persistently raised serum calcium.

Age of Patients in Profile Group

The sex and age distribution of patients in the profile group is shown in Table VI. There were more females than males

TABLE VI.—*Sex and Age Distribution of Profile Group*

Age in Years:		15-19	20-29	30-39	40-49	50-59	60-69	70-85	Total
Males	No.	1	17	13	23	17	27	12	110
	%	0·9	15·5	11·8	20·9	15·4	24·5	10·9	—
Females	No.	2	19	29	46	42	29	19	186
	%	1·1	10·2	15·6	24·7	22·5	15·6	10·2	—

and about half the patients were below 50 years old. Difficulties arise in comparing results with those of the hospital ward patients, where there were more males than females and 60% were over the age of 50 (Whitehead, 1968).

Discussion

The whole scheme worked well, including the bleeding of patients by the general practitioners, centrifuging and dispatch of specimens by the part-time clerical help, and return of reports by post. This confirms the possibility of performing such procedures on a larger scale. The main problem with the blood specimens was haemolysis, which resulted in nearly one-fifth of the patients in the profile group having serum potassium results over 5 mEq/1.

Unrequested results led to a new diagnosis in 16·9% of the patients in the profile group, many of whom required an alteration in treatment. Iron-deficiency anaemia was the major finding and, while the indication for screening for anaemia in the general population remains uncertain (Cochrane and Elwood, 1968), all the patients found to be anaemic in this series were attending the general practitioner with a variety of symptoms, and when reassessed after treatment all had a rise in haemoglobin. They should therefore be treated for anaemia until it is shown to be of no benefit. Diabetes, renal disease, and one patient with myxoedema accounted for the remaining diagnoses considered to be clinically significant, though other unsuspected biochemical abnormalities such as raised serum cholesterol or uric acid were found, but these were not classified as a new diagnosis because treatment was not considered necessary.

There are many advantages in performing such tests in general practice rather than hospital. It is our experience that in hospital practice the finding of an abnormality like diabetes mellitus in a patient admitted for routine surgery can lead to delay in treatment of the surgical condition, not only inconveniencing the patient but also increasing the cost of hospital treatment. If such abnormalities were detected previous to hospital care therapy might be given and so prevent any delay on admission to hospital. Further, results of certain tests may be considered irrelevant to the present diagnosis if such tests are performed in hospital, but subsequent results may prove the information valuable—for example, raised uric acid in a patient subsequently developing arthritis. Under present conditions results of such tests performed in hospital are not adequately conveyed to the general practitioner. If tests altered by hospital investigation, like protein-bound iodine, are added to the profile, then the earlier such a test is performed in the course of a patient's investigation the less likely a false result will be produced. Thus in a random survey of protein-bound iodine in 424 patients on admission to the Queen Elizabeth Hospital, 23 (5·4%) had high abnormal results due to recent radiological investigations.

In hospital or health-screening clinics the problem arises of managing patients with abnormalities of doubtful significance detected on unsolicited tests. If such tests are performed under the auspices of the general practitioner, however, since he and his partners assume continuous care for such patients, a conservative policy can be adopted without the need for unnecessarily alarming the patient. The general practitioner should also know of any drug therapy the patient is receiving which may be important in certain tests.

Performing many tests on a specimen of blood taken at one point in time has the advantage that if an abnormality is detected other results may help to exclude or confirm the presence of certain diseases and therefore save the need for follow-up investigations. Thus if a raised cholesterol is found the profile can be examined for the presence of diabetes mellitus, the nephrotic syndrome, or liver disease.

Normal results are of considerable value; they may reassure the doctor or patient that certain diseases are not present. Thus in an anaemic patient a normal urea should exclude uraemia as the cause of anaemia. The normal results may also be used to assess the suitability of patients for various treatments, such as hepatotoxic drugs and certain forms of surgery. In later years previous results may be useful as a baseline if disease subsequently develops.

At several points in this paper the emphasis has been placed on the careful reassessment of profile data associated with the subsequent follow-up of patients by the general practitioner.

For this to be effective there needs to be much improvement in the methods by which patient information is recorded in general practice. The present general practice national health service records are inadequate for recording the necessary information and filing results of investigations.

It is important to realize that performing such multiple blood tests in no way reduces the time needed for history-taking and clinical examination by the general practitioner; rather, in many instances, the results have stimulated the doctors into further clinical examination of certain patients. Thus most blood tests are not diagnostic of any one disease but require interpretation with regard to the clinical findings and possible confirmatory investigations. A wrong interpretation could lead to incorrect diagnosis and treatment.

In the earlier studies already referred to on hospital in-patients, when assessed two weeks after the blood tests 36·1% of patients had unexplained abnormal results in tests that would not normally have been requested. Follow-up of a group of these patients reduced this subsequently to 15·5% (Carmalt, 1969). In the present study 21·6% of patients had unexplained abnormal results, though this assessment was made three to six months after the blood tests were performed. These unexplained abnormal results included the patients with raised cholesterol and uric acid for which no therapy was indicated. Follow-up of these unexplained results could mislead the doctor from the main diagnosis, though a proportion may indicate treatable disease.

With regard to the follow-up of patients by the general practitioners, more patients in the profile groups than in the control group were given a further appointment at the initial consultation; this is probably because the doctor waited for the profile result before discharging the patient. The profile tests resulted in further work for the general practitioners, since 81 (27·4%) of the patients profiled required follow-up tests and 23 (39%) of the patients initially discharged had to be recalled for follow-up, with or without further investigations. The proportion of patients with a new diagnosis from un-solicited tests, however, was the same in the groups either followed up or initially discharged by the general practitioner. Before the profile tests more patients in the control group than in the profile group were referred to hospital, but there was no evidence that referral of any patient in the control group could have been prevented by performing multiple blood tests. After the profile tests three patients were referred directly for hospital treatment, while two further patients were referred subsequent to further blood tests. There was there-fore no evidence in this general practice that the use of multiple blood tests reduced the rate of referral of patients to hospital, though these general practitioners had open access to labora-tories and did not have to refer patients to hospital for such investigations.

In the future preliminary investigation of patients may change from hospital outpatient departments to general practitioner clinics with access to pathological laboratories (Wilson, 1969). This could both reduce outpatient visits and lead to the admission of certain patients to hospital without the need for outpatient consultation. If multiple blood tests are to form part of this service the problems arise regarding which patients should be investigated in such a manner and what group of tests should be used. The range of tests given in this paper are not necessarily ideal. The electrolytes results gave a low yield of information. We would recommend that any range of tests should include those to screen for anaemia and diabetes and for kidney, thyroid, and liver diseases. Serum calcium should also be retained, as, particularly in the hospital patients, the determination led to diagnoses of osteomalacia and hyperparathyroidism, both treatable conditions and com-pletely unsuspected on clinical grounds.

The choice of tests should remain flexible in the light of further experience and advances in therapy, particularly of such conditions as hypercholesterolaemia.

Patients suitable for multiple tests are those with obscure symptoms of uncertain aetiology—for example, undiagnosed weight loss—and those with predominantly psychiatric symp-toms where organic disease cannot be excluded. The geriatric patients are a group who might benefit from general screen-ing, as may other patients on certain therapy—for example, oral contraceptives. Finally, patients should have these tests performed before some outpatient consultations, since bio-chemical profiles have been shown to yield valuable informa-tion at such clinics (Carmalt, 1969).

In examining the investigations of patients by general practitioners the present training of medical students emphasizes the use of laboratories in the investigation and treatment of patients. If doctors entering general practice are to be able to practise the high standard of medicine they have been taught in medical school, the advances in laboratory methods, including the use of multiple tests, should become available to the general practitioner on a wider scale than at present. Such endeavours should come before scarce resources are deployed on well-population screening.

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