CONVENTIONAL TESTS IN THE STUDY OF THYROID DISEASE*

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The present work was prompted by the inadequacy of any one simple laboratory test to serve as a clinical guide to thyroid function. Tests involving the use of ^{131}I (Mason and Oliver, 1949; Foote and MacLagan, 1951; Foote, Mackenzie, and MacLagan, 1952) are applicable only to untreated cases of thyroid disorder. Plasma protein-bound iodine estimations (de Mowbray and Tickner, 1952; Fraser, 1954) are unlikely to pass into routine use owing to inherent technical difficulties. Oxygen consumption measurements ("basal metabolic rate"), though relatively non-specific, usually provide the method of reference, if not of choice, for the various chemical tests advocated from time to time.

We aimed at a set of tests of the conventional chemical type suitable for the routine measurement of thyroid function both as a diagnostic tool and as a guide to subsequent treatment. For this reason we evaluated the results of five measurements and chose two of these, the serum cholesterol level and the urinary pigment excretion, as being the most useful. We then evolved two ways in which to assess thyroid function from these two chemical data: correlation with the observed basal metabolic rate ($\text{O}_2\text{-B.M.R.}$) gave a discriminating function the solution of which we have called the "derived B.M.R."; comparison with the final diagnoses of the same patients gave a qualitative "chemical diagnosis." The choice between these two forms of expression is one of individual preference, and we are at present using both forms in a comparative study of radio-iodine and conventional tests. The results we present here are themselves a continuation of the series first reported by Tárnoky (1952).

Clinical Methods

Clinical Material.—This consisted of 87 women patients. They were both in- and out-patients and

were referred to the laboratory for $\text{O}_2\text{-B.M.R.}$ determinations as an aid to the diagnosis or exclusion of hyper- or hypothyroidism. Hypopituitarism was suspected in two cases. The number of male patients was quite small, and it was decided to limit the investigation to females. A provisional diagnosis (PD) of each case was provided by the physician at the time of the test. A final clinical opinion (FD) of 80 cases was obtained after at least 12 months' treatment and observation.

Ward Procedure.—Robertson's (1944) conditions for $\text{O}_2\text{-B.M.R.}$ estimations were observed. Urine passed at the end of the respiratory test was used for pigment and creatinine analyses. Venous blood was taken after the $\text{O}_2\text{-B.M.R.}$ estimation on the first day.

Laboratory Methods

The following characteristics were measured: the $\text{O}_2\text{-B.M.R.}$ following Robertson's (1944) method; serum creatinine (sCR) and creatine (scr) (Peters, 1942; Griffiths, 1951, 1954); serum cholesterol (King, 1951); urinary creatinine (UCR) (King, 1951); urinary pigment (UPG) by direct colorimetry of acidified urine in 1 cm. colorimeter tubes, with an Ilford 601 filter. These last two measurements were expressed as the urinary pigment (1000 E)/creatinine (mg./100 ml.) ratio (Ostow and Philo, 1944; Vorzimer, Cohen, and Joskow, 1949; Moreland and Gurgiolio, 1955).

Results

Simple correlation between pairs of measurements (Table I) proved to be of limited value on account of the markedly abnormal distribution of several of the variates. We used these results for screening purposes when seeking to match an equation based on several data to the $\text{O}_2\text{-B.M.R.}$ (accepted as the method of reference) or the final diagnosis (as the clinical criterion).

Fitting Two Chemical Measurements to $\text{O}_2\text{-B.M.R.}$: "Derived B.M.R."—Since the $\text{O}_2\text{-B.M.R.}$, serum cholesterol, and urinary pigment/creatinine values had highly significant correlations (Table I) we began by fitting our formulae for $\text{O}_2\text{-B.M.R.}$ in terms of the other two measurements, using the

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TABLE I
SIGNIFICANCE OF CORRELATION (r) BETWEEN PAIRS
OF CHEMICAL MEASUREMENTS IN SUSPECTED THYROID
DISORDER

	UCR	UPG UCR	sch	sCR	scr
PD+ } O ₂ -B.M.R.	+0.167	+0.400	-0.266	-0.213	+0.295
PD- } O ₂ -B.M.R.	+0.041	+0.068	-0.312	-0.317	-0.123
PD+ } UCR		+0.053	-0.044	-0.078	+0.106
PD- } UCR		-0.160	-0.368	-0.376	+0.101
PD+ } UPG			-0.442	-0.066	+0.014
PD- } UPG			-0.403	-0.187	+0.226
PD+ } sch				+0.116	-0.029
PD- } sch				+0.528	-0.213
PD+ } sCR					+0.346
PD- } sCR					-0.013

method of least squares. Inclusion of serum creatine levels gave only a slightly improved fit which justified neither a further chemical determination nor an additional complication of the formula. A discriminating function based on two measurements

$$\text{derived B.M.R.} = 13 + 7.5 \frac{\text{UPG}}{\text{UCR}} - 0.1 \text{ S. cholesterol}$$

agreed with the observed O₂-B.M.R. with a probable error of ± 15 percentage units (Fig. 1). The extent of agreement of the observed O₂-B.M.R. with the final diagnosis is shown in Table II, and that of the derived B.M.R. with the diagnosis in

FIG. 1.—Scatter diagram of O₂-B.M.R. and derived B.M.R. in suspected thyroid disorder.

TABLE II
COMPARISON OF O₂-B.M.R. WITH FINAL DIAGNOSIS

	O ₂ -B.M.R.		
	-	N	+
FD+	0	10	33
FD normal	2	13	8
FD-	8	6	0

TABLE III
COMPARISON OF DERIVED B.M.R. WITH FINAL
DIAGNOSIS

	13 + 7.5 $\frac{\text{UPG}}{\text{UCR}}$ - 0.1 sch		
	-	N	+
FD+	0	9	34
FD normal	0	14	9
FD-	4	8	2

Table III. The number of correct forecasts by the two methods (52 cases by derived, 54 by O₂-B.M.R.) is not significantly different.

Fitting Two Chemical Measurements to Final Diagnosis: "Chemical Diagnosis."—The following procedure is one which we have found of equal value in a direct comparison with the final diagnosis. To detect cases of hypothyroidism we use the serum cholesterol measurements alone, with a minimum figure of 320 mg./100 ml. as the boundary line. To detect hyperthyroidism we use the pigment creatinine ratio alone, with a minimum figure of 3.15 as the boundary line. This raises the number of correct forecasts to 56 (Table IV). A complication arises in this procedure when the

TABLE IV
COMPARISON OF THYROID ASSESSMENT FROM TWO
CHEMICAL MEASUREMENTS WITH FINAL DIAGNOSIS

	sch ≥ 320	N	UPG/UCR ≥ 3.15
FD+	0	3+1*	39
FD normal	3	10	10
FD-	7	3+2*	2

* sch and UPG/UCR findings conflict. Case 6: sch 350; UPG/UCR 3.2; PD+; FD+; O₂-B.M.R. 0%; derived B.M.R. +2%; 7 weeks later sch 330; UPG/UCR 2.9; O₂-B.M.R. +16%; derived B.M.R. +2%. Case 39: sch 425; UPG/UCR 4.6; PD-; FD- and subacute combined degeneration of the cord; O₂-B.M.R. -60%; derived B.M.R. +5%. Histamine test meal: achylia. Case 62: sch 375; UPG/UCR 4.4; PD-; FD-; O₂-B.M.R. +2%; derived B.M.R. +9%.

two tests give definite but conflicting results, e.g., with a serum cholesterol level of over 320 mg. (-forecast) and a urinary pigment/urinary creatinine of over 3.15 (+forecast) for the same patient. This happened in three cases in our series. These would be reported to the clinician as giving a conflicting chemical diagnosis; for statis-

tical purposes we have provisionally regarded the chemical forecast as normal and indicate the numbers by an asterisk in Table IV, which also gives details of these cases.

Although assessment in this way gives a higher number of correct forecasts than by the simultaneous use of the two data, the difference between these two methods is not significant and either form of expression may be used. As obtained in this series, both give results which approximate to O_2 -B.M.R. figures. When used in serial testing of patients under treatment, successive measurements in any one patient will probably be less scattered by personal idiosyncrasies than single measurements in a group of cases; and it would not be unreasonable to look for a more consistent operation of the test.

Summary

The basal metabolic rate, urinary pigment and creatinine concentrations, and serum cholesterol, creatinine, and creatine levels in 87 cases of suspected thyroid disorders are compared. The pigment excretion (urinary pigment/creatinine ratio) and serum cholesterol have been found the most valuable of these data.

Two procedures have been developed for expressing the results from the two chemical findings. In one, a "derived B.M.R." is obtained from a discriminating function involving both

data. In the other a "chemical diagnosis" is based on these figures taken separately.

Both procedures are designed to supersede respiratory basal metabolic rate determinations and to be carried out as complementary to radioiodine methods in the assessment of thyroid function.

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