vaccine can be adjusted simply by minor changes in the amount of B.C.G. per unit volume. A certain level of tuberculin allergy has been accepted as evidence of successful vaccination, and reactions above and below that level have been called positive and negative.

I would not presume to say that all our anomalous findings will be confirmed or that we have intepreted them correctly; but I think that most of them will survive. Certainly it is evident that much of what we have accepted as common knowledge about B.C.G. vaccine and vaccination is not very well founded; and, if so much of what we thought we knew of the simpler facts be untrue, what can we safely believe about those aspects of vaccination which are more difficult to study and to prove?

I think we can safely believe in the ultimate efficacy of tuberculosis immunisation. We can also, I think, unhesitatingly support mass B.C.G. vaccination programmes in many countries in the world where vaccination is almost all that can be done today to control tuberculosis. B.C.G. is certainly the best known, the most promising, and the most acceptable immunising agent at our disposal. On the other hand, we must seek more dependable information about B.C.G. and tuberculosis immunisation. And this may mean discarding many of our traditional concepts.

STANDARDS FOR THE BASAL METABOLISM OF NORMAL PEOPLE IN BRITAIN

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THIS study was begun at the Middlesex Hospital in 1930, as a direct result of observations on variations in the basal metabolic rate (B.M.R.) in thyrotoxicosis before and after treatment with iodine and before and after subtotal thyroidectomy.

It was noted that, after a successful subtotal thyroidectomy and in the absence of any clinical manifestations of hypothyroidism, the B.M.R., by the standards of Aub and DuBois (1917), was never above 0, and all values lay between 0 and −20. To determine whether or not such a low postoperative range was a natural sequence of removal of the thyroid gland in thyrotoxicosis, a group of fifty nurses in training at the Middlesex Hospital volunteered to have their B.M.R. measured. Their rates also were between 0 and −20. It became apparent that either the standards of Aub and DuBois were too high for people in this country, or that there were some differences in technique in measuring the B.M.R., or both. As there were no British standards for the B.M.R. based on actual measurements taken in this country over a wide range of ages in both sexes, it was decided to begin such a study.

The value of any standard with which a patient's results can be compared depends on the consistency of technique between the workers setting up that standard and those who later use it as a basis for comparison. For convenience we outline below the standard technique adopted, although it has already been described in detail (Robertson 1944).

STANDARD TECHNIQUE OF MEASUREMENT OF B.M.R.

The closed-circuit method was employed, the accuracy of which has already been reported (Robertson 1937). The apparatus used was the Benedict-Roth with recording kymograph. All the machines were alcohol-checked (Barrett and Robertson 1937), but also, each machine was checked once a week by B.M.R. estimations on the same healthy female whose heat output was constant when corrected for age.

Attendance of the people included in this survey was required after the customary fast of at least twelve hours; the last meal had to consist of an egg (or an equivalent amount of protein), bread and butter, and weak tea. The person was weighed on a machine of the fulcrum type, which was repeatedly checked for accuracy. An allowance of $3^1/_2$ lb. was made for the weight of the trousers, shirt, and underwear worn by men, and $2^1/_2$ lb. for the dress and underwear of women, so that estimated nude weights could be used to calculate the surface area of the body. This area was found by applying the formula using height and weight which was originally produced for this purpose by DuBois and DuBois (1916) and approved by Boothby et al. (1936).

After half an hour's rest on a comfortable bed in a quiet room at a temperature of 20°C, duplicate determinations were made of the heat output, and the result was expressed as calories per square metre of body-surface per hour. Similar determinations were made on the next day, when the results were commonly lower than those obtained on the first day. This procedure was continued until no further fall in the heat output was observed—i.e., until the second of the two duplicate readings differed by no more than 5% from the first duplicate on the same day. It should be noted that in these estimations independent readings of the spirogram were made by two or more observers. The test was repeated when the two observers did not agree; in this way it was hoped to avoid a consistent personal bias.

In this study the lowest reading observed in the series was taken as an estimate of the true basal level of metabolism. As Vogelius (1945) has shown, graphs of the results of repeated estimations reveal a clear training

TABLE I—OBSERVED HEAT OUTPUT AT SPECIFIED AGES
(Calories per square metre body-surface per hour)

Age last birthday (yr.)	Males			Females		
	No. of persons	Mean heat output	Standard deviation	No. of persons	Mean heat output	Standard deviation
3	6	61·0	7·27	6	54·8	3·06
4	34	58·1	4·90	24	52·6	4·07
5	33	54·2	5·21	41	53·3	5·71
6	48	53·8	1·31	28	52·1	3·35
7	27	51·3	3·32	27	51·1	3·14
8	21	49·5	5·60	18	47·2	4·14
9	13	50·0	4·97	30	45·2	3·68
10	16	47·9	4·54	13	45·3	3·66
11	34	47·7	3·77	18	43·0	3·97
12	41	43·5	3·82	31	40·5	3·48
13	30	42·2	3·74	39	38·2	2·99
14	33	42·8	3·44	36	37·3	2·57
15	20	41·9	2·67	33	36·7	2·54
16	24	39·6	3·41	24	35·4	2·90
17	24	39·0	3·29	22	35·4	2·72
18	21	39·5	3·37	32	35·2	2·24
19	22	38·9	2·58	224	34·7	2·50
20	42	38·2	2·26	116	34·3	2·35
21	15	37·8	1·90	50	34·5	2·17
22	19	36·7	2·13	35	33·7	2·19
23	14	37·5	3·01	30	33·8	1·83
24	19	37·5	2·48	26	33·8	2·72
25	21	36·8	3·06	31	33·4	2·60
26	21	37·0	2·85	14	34·1	1·61
27	33	37·1	2·64	18	34·4	2·33
28	30	37·3	2·19	25	34·0	2·08
29	29	36·7	2·47	17	33·8	2·13
30	28	36·8	2·45	15	34·1	2·20
31	24	36·5	2·50	16	34·0	2·48
32	21	37·0	2·38	15	34·5	2·75
33	27	35·8	2·36	8	34·0	2·07
34	21	35·0	2·20	21	33·4	2·06
35	21	36·0	2·20	12	33·6	1·38
36	20	35·6	2·37	11	32·8	2·09
37	19	35·9	2·99	20	34·2	1·98
38	10	35·4	2·80	16	32·3	2·98
39	13	35·2	2·48	21	32·3	2·18
40	22	36·1	2·08	21	32·8	2·84
41–44	19	34·9	2·64	37	32·5	2·30
45–49	11	34·1	2·70	36	31·3	2·69
50–54	11	34·5	2·54	25	31·9	2·35
55–59	6	33·5	3·21	6	30·2	1·47
60–64	8	32·5	1·85	10	32·3	1·83
65–69	9	32·2	2·49	17	30·3	1·65
70–74	4	33·3	3·10	8	30·5	1·60
75 or more	3	32·0	3·46	..	..	..

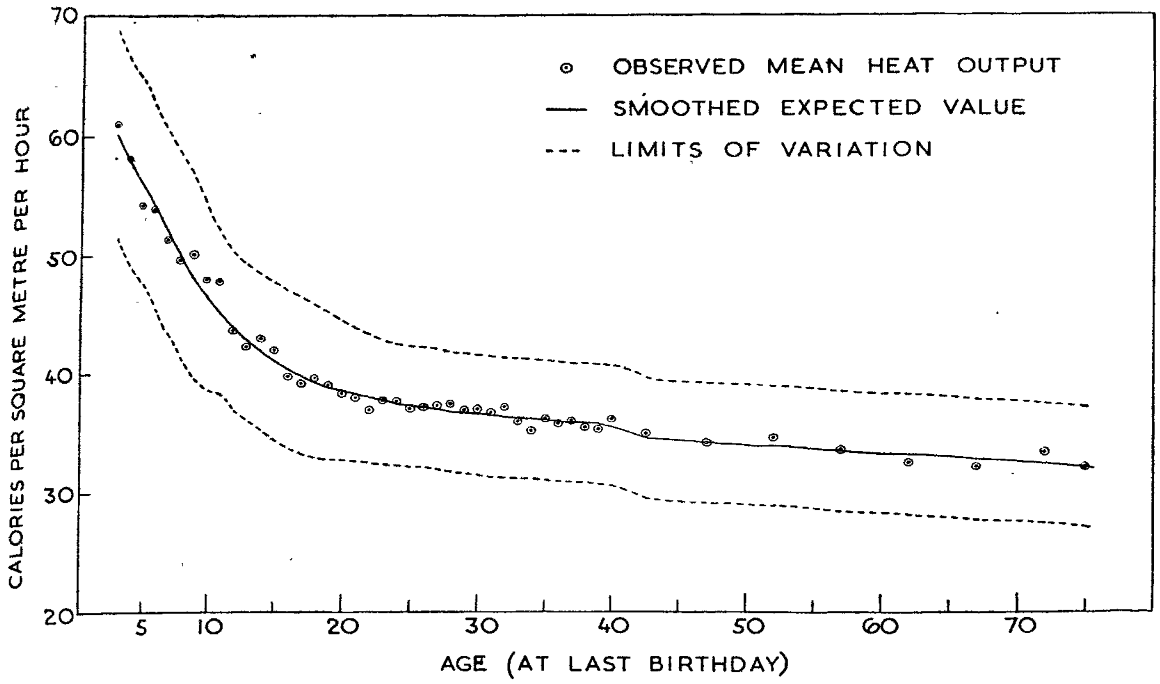

Fig. 1—Observed and expected mean heat outputs at ages and limits of variation (males).

effect: successive readings fall rapidly at first, but after about the first four estimations the curve describing the trend of results flattens out quickly. It seems reasonable therefore to take either the lowest recorded value or the mean of the last two readings made as an estimate of the asymptote or basal metabolic level which the curve is approaching. It could be argued that where the latest is also the lowest value in a short series of four readings it is more likely to be nearer to the true basal level than the mean of the third and fourth readings. On the other hand, in longer series, where the curve has flattened out, the mean might be the more appropriate indicator of the basal level. Since in practice we are here dealing with shorter rather than longer series, and since too we accept that stabilisation has been reached only when the last two readings differ by less than 5%, the difference between taking the lower of the two rather than their average is relatively small.

This method of repeating observations until stability is apparently achieved is in contrast to the usage adopted by Boothby et al. (1936), whose paper on standards for B.M.R. in normal people appeared while this work was in progress. They took as their basal value "the first determination made for the individual unless at the time of the test and before its calculation it was noted as unsatisfactory for reasons of restlessness, observable nervous tension, or an elevated temperature." They criticised the policy of taking several readings and maintained that results would vary according to the number of readings taken. Thus, even if several readings were taken on a subject, the first only was used for computing their normal standards. They further stated that "if one departs from the practice of using a single determination made under standard conditions, the number of determinations should strictly be identical for each individual." Thus the element of training was excluded from their normal standards as they suggested it would be in its clinical application.

Robertson (1944) has criticised these views on the following grounds:

(1) So-called nervous tension is not uncommon at the initial test, particularly in thyrotoxicosis.

(2) Initial readings are commonly higher, and sometimes much higher, than subsequent or true basal determinations. Thus of 223 people aged 19, 156 (70%) gave initial readings which were higher than those on the second day, 48 (22%) gave results 10% or more higher, 21 (9%) gave results 15% or more higher, and 11 (5%) gave readings as elevated as 20% or more higher. In no case was the initial reading at the time of test considered unsatisfactory, and a kymographic record of the respirations is a very sensitive guide. These observations were made on nurses who had volunteered for the test; apprehension is much more likely in nervous patients, with or without thyrotoxicosis. To estimate a person's B.M.R. on the initial observation alone is to run the risk of reporting a raised B.M.R. as due to pathological rather than psychological causes.

(3) If standards are based on initial readings alone, the metabolic assessment of people who have ever had the test before presents a problem, since to have had experience of the test means some degree of the training which Boothby and his colleagues suggested should be excluded.

(4) The controlling influence of iodine on the B.M.R. in thyrotoxicosis as a diagnostic test becomes much less sensitive; for indeed it would be difficult to determine whether a fall in the B.M.R. in a subsequent test after iodine was due to the element of training or to iodine.

In this study of the basal energy output of 987 males and 1323 females, aged between 3 and 80 years, we have followed the convention also adopted for the American standards by Boothby and his colleagues by expressing this basal output in terms of calories per square metre of body-surface per hour. Justifiable objections have been raised to the use of such per-weight and per-surface-area standards (e.g., by Tanner 1949) on the grounds that they imply that heat output always bears a constant ratio to surface area. It is perhaps fortunate that, for the limited range of values within a single age and sex

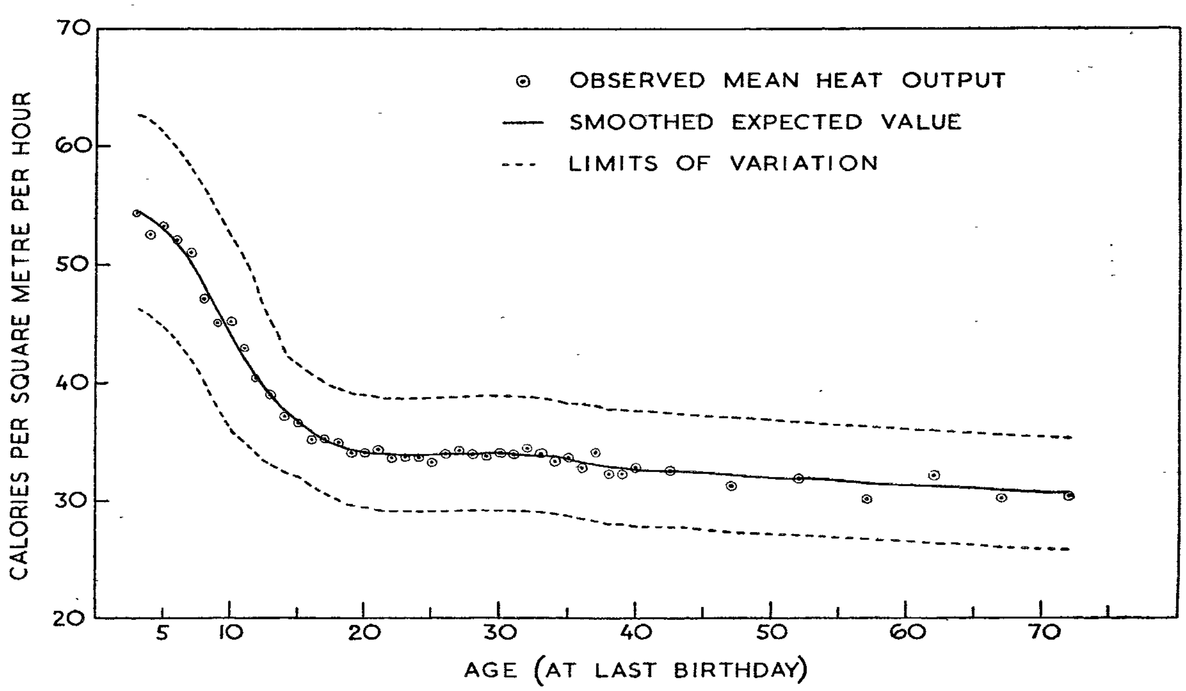

Fig. 2—Observed and expected mean heat outputs at ages and limits of variation (females).

group, the relation between heat output and surface area described by the regression line of output on area is approximated reasonably well by the assumption of a constant ratio between the two biological measurements. From the practical point of view, therefore, it is legitimate to compare the ratio of heat output to surface area in a person with the mean and likely range of similar ratios for a group of healthy people of the same sex and age.

Clearly, no method of estimating and expressing the level of metabolic activity in a simple practical but unexceptionable way has yet been evolved. It must be remembered that the standards set up by this study refer to a B.M.R. measured under standard conditions by standard methods which, although they may not be theoretically perfect, at least have the essential merit of consistency, since all the observations were made by one of us (J. D. R.) between 1930 and 1950.

TABULATION OF RESULTS

As already mentioned, the basal heat output is expressed as a ratio to the surface area derived from height and weight. The mean number of calories per square metre per hour has been calculated for members of each sex for each year of age between 3 and 40 years, and these means are set out in table I. For those aged more than 40, observations were grouped into 5-year age-groups. Plotting these means gave the pattern seen in figs. 1 and 2. Compared with a similar curve from the American standard data, it shows much less irregularity, particularly for the years of adolescence, but the same tendency to asymptote at ages over 40.

An attempt was therefore made to describe these observations by one curve for each sex extending over the age range 3–40 for which individual year means were available. Changes in metabolic activity with increasing age may well be regarded as a growth phenomenon, and it seemed biologically reasonable to use a logistic curve for the fitting process. Clearly too, no simple logistic would fit the apparent changes in the speed of metabolic adaptation at different ages. According to the methods suggested by Pearl (1940) a skew logistic curve with a quintic exponent was fitted to the data, with the result seen in figs. 1 and 2. For males (fig. 1), where the numbers in each group were fairly equal, no weighting was needed; but for females (fig. 2) the means at ages were weighted by the numbers of observations upon which they were based. The resultant fit is quite adequate; the analysis of variance for each sex for the age range between 3 and 40 displayed in table II shows that the residual variation not accounted for by the fitted regression line differs insignificantly from the error variance.

TABLE II—TESTS FOR GOODNESS OF FIT OF CURVE TO OBSERVED HEAT OUTPUT

Analysis of variance				
Sex	Source of variation	Sum of squares	D.F.	Mean square
Males: Aged 3–40 yr.	Fitting of logistic Deviations from logistic Within age-group	43,445·99 350·49 9119·44	7 30 878	6206·57 11·68 10·39
	Total	52,915·92	915	..
Aged 41 and over	Fitting straight line Deviations from line Within age-group	57·09 12·63 441·24	1 6 63	57·09 2·11 7·04
	Total	510·96	70	..
Females: Aged 3–40 yr.	Fitting logistic Deviations from logistic Within age-group	38,525·43 281·87 9181·33	7 30 1146	5503·63 9·40 8·01
	Total	47988·63	1183	..
Aged 41 and over	Fitting straight line Deviations from line Within age-group	52·17 40·84 679·10	1 5 132	52·17 8·17 5·15
	Total	772·11	138	..

It might be pointed out in passing that the skew form of the logistic curve used to achieve this fit is supposedly more appropriate to the growth of collections of cells whose speed of multiplication is subject to some central control than to the increase in size of a population of independent units—e.g., to the growth in size of a person rather than to a rise in a population. In other words, the methods used in this study to measure the change with increasing age of individuals' B.M.R. appear to produce results which are at least consistent with rational expectation. In this respect they differ from the results obtained by Boothby et al. (1936), where the result of the first test is used as an indicator of the basal level of metabolic activity. For ages over 40 a straight line gave a good fit to the trend of the mean heat output per square metre per hour in both sexes.

The smoothed values, which are supposedly free from erratic sources of variation, could be derived from the formulæ thus used to describe the data:

For males (aged 3–40)

$$\text{Heat output is cals./sq. m./hr.} = 30 + \frac{35}{1 + e^{u}/10}$$

where $u = 1{\cdot}3724343 + 0{\cdot}54564663x - 0{\cdot}027774833x^2 + 0{\cdot}0^{3}76481273x^3 - 0{\cdot}0^{4}10880471x^4 + 0{\cdot}0^{7}62750139x^5$, and x is age in years.

For males (aged 41 or more)

$$\text{Heat output} = 37{\cdot}405365 - 0{\cdot}06944x.$$

For females (aged 3–40)

$$\text{Heat output} = 30 + \frac{30}{1 + e^{u}/10}$$

where $u = 0{\cdot}9683040 - 0{\cdot}22383820x + 0{\cdot}0685533x^2 - 0{\cdot}0^{2}40652313x^3 + 0{\cdot}0^{4}95117564x^4 - 0{\cdot}0^{6}78506248x^5$.

For females (aged 41 or more)

$$\text{Heat output} = 35{\cdot}15375 - 0{\cdot}06149x.$$

In practice, however, it is simplest to refer to the tabulated values for each year of age given in table III. By themselves, of course, the means give no indication of the range and frequency distribution of deviations from this "normal" average. The standard deviation, which is the best measure of this variability between persons of the same age, declines in size from birth until adolescence in both sexes and is fairly constant in adult life. Stability is reached earlier in females among whom the variances in the age-groups from 13 onwards are shown by the Bartlett test to differ insignificantly. Similarly the within age-group variances at ages between 3 and 12 years do not differ appreciably. Standard deviations have been calculated from variances based on all the observations within these homogeneous segments of the age scale, and they have been used, after appropriate smoothing at the junction of the two segments, to mark the "control limits" seen in fig. 1. For males three homogeneous sections were found at 3–10 years, 11–20 years, and 21 and over, and similar "control limits" have been derived from the standard deviations based on all observations within these age-groups.

In the practical use of these results it is most convenient to refer to table III, where the mean heat output in calories per square metre of body-surface per hour is set out for healthy people of a specified sex and age together with the corresponding limits of usual variation between people in the same age-group. These "control limits," which correspond to heat outputs two standard deviations above and below the expected mean, mark the values between which should lie most (95%) of such readings made on healthy people of that sex and age. If the patient's basal heat-output rate is outside these limits it may be regarded as significantly unusual and therefore potentially pathological. Thus we might have a male patient aged 29 whose heat output per square metre per hour is 39 calories. We note that, although this differs by 2·5 calories from the expected or normal average of 36·5 calories, the divergence is equal to the standard deviation of 2·5 calories; hence the patient's test result lies within the limits of normal variation. Only if the output were greater than 41·5 or less than 31·5 would we suggest, on this evidence alone, that the patient's B.M.R. was abnormal in the sense here used.

These standards are based upon observations made on apparently healthy volunteers. These were nurses, medical students, and members of the staff of the Middlesex Hospital, children attending welfare clinics and on tonsillectomy waiting-lists, and members of the public who came in response to newspaper appeals. In so far as these "normal people" are typical of the British population, these tables of their heat output at different ages, measured by the technique described, should form a useful standard for clinical work on basal metabolism in this country.

TABLE III—EXPECTED MEAN HEAT OUTPUT AND LIMITS OF VARIATION

(Calories per square metre body-surface area per hour)

Age last birthday (yr.)	Males			Females		
	Expected mean	Lower limit	Upper limit	Expected mean	Lower limit	Upper limit
3	60·1	51·5	68·8	54·5	46·4	62·6
4	57·9	49·2	66·5	53·9	45·8	62·1
5	56·3	47·7	65·0	53·0	44·9	61·1
6	54·2	45·6	62·8	51·8	43·6	59·9
7	52·1	43·4	60·7	50·2	42·1	58·3
8	50·1	41·4	58·7	48·4	40·2	56·5
9	48·2	39·6	56·7	46·4	38·2	54·5
10	46·6	38·6	54·4	44·3	36·3	52·5
11	45·1	37·7	52·2	42·4	35·1	50·6
12	43·8	36·8	50·4	40·6	34·0	47·7
13	42·7	36·0	49·3	39·1	33·2	45·1
14	41·8	35·2	48·4	37·8	32·6	42·7
15	41·0	34·4	47·6	36·8	32·2	41·7
16	40·3	33·7	46·9	36·0	31·3	40·8
17	39·7	33·1	46·3	35·3	30·7	40·2
18	39·2	32·9	45·6	34·9	30·1	39·7
19	38·8	32·7	45·0	34·5	29·7	39·3
20	38·4	32·6	44·3	34·3	29·5	39·1
21	38·1	32·5	43·7	34·1	29·3	38·9
22	37·8	32·4	43·1	34·0	29·2	38·8
23	37·6	32·3	42·6	34·0	29·1	38·8
24	37·3	32·2	42·3	33·9	29·1	38·8
25	37·1	32·1	42·1	34·0	29·1	38·8
26	37·0	32·0	42·0	34·0	29·2	38·8
27	36·8	31·8	41·8	34·0	29·2	38·8
28	36·6	31·6	41·6	34·0	29·2	38·9
29	36·5	31·5	41·5	34·1	29·2	38·9
30	36·4	31·4	41·4	34·1	29·2	38·9
31	36·3	31·3	41·3	34·0	29·2	38·8
32	36·2	31·2	41·2	33·9	29·1	38·8
33	36·1	31·1	41·1	33·8	29·0	38·7
34	36·0	31·0	41·0	33·7	28·9	38·5
35	35·9	30·9	40·9	33·5	28·7	38·3
36	35·8	30·8	40·8	33·3	28·5	38·2
37	35·7	30·7	40·7	33·1	28·3	38·0
38	35·7	30·7	40·7	32·9	28·0	37·7
39	35·6	30·6	40·6	32·8	28·0	37·6
40	35·5	30·5	40·5	32·6	27·8	37·5
41–44	34·5	29·5	39·5	32·5	27·7	37·4
45–49	34·1	29·1	39·1	32·2	27·4	37·1
50–54	33·8	28·8	38·8	31·9	27·1	36·7
55–59	33·4	28·4	38·4	31·6	26·8	36·4
60–64	33·1	28·1	38·1	31·3	26·5	36·1
65–69	32·7	27·7	37·7	31·0	26·2	35·8
70–74	32·4	27·4	37·4	30·7	25·9	35·5
75 or more	32·0	27·0	37·0	..	..	..

Our thanks are due to Prof. E. C. Dodds, in whose department this work was begun, and to Mr. A. V. Bridgland, Chairman of the Trustees of the London Clinic, where it was completed; to Sir Alan Daley, Mr. Somerville Hastings, and the press for their help in enlisting the coöperation of suitable people; and above all to the volunteers themselves.

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REPAIR OF DURAL DEFECTS WITH GELATIN FILM

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DEFECTS in the dura mater remaining after the removal of certain intracranial tumours or the excision of cortical scars have always presented a problem to the neurological surgeon because adherence of the brain to overlying structures, with subsequent formation of fibrous scar tissue, may give rise to epileptic attacks.

In attempts to prevent adhesion of the brain many different tissues have been used to close these dural defects, including fascia lata, periosteum, temporal fascia, and muscle. Likewise, the dura remaining in the wound has been split into two layers so as to bridge the defect with the extra area of membrane so produced; but though this can be done with small defects and a thick dura, it may not be possible in the frontal region, where the dura is closed thin: the larger defects provide problems insoluble by such a process.

Various foreign substances have also been used, among them 'Cellophane,' amniotic membrane, tantalum foil, fibrin foam, and 'Gel-foam' film. From the multiplicity of methods it is evident that the ideal substance has not yet been discovered.

The use of gelatin film was reported by Busch et al. (1949) but it was considered unsuitable for repairing dural defects. Weisel et al. (1950) gave a detailed account of gelatin film implanted into chest wounds as a temporary closure for pleural defects, and found that the implants were completely absorbed between the eight and fourteenth days: tissue reaction was minimal, and the normal pleural regeneration did not seem to be hindered by the presence of the gelatin film. I compare here the results achieved with tantalum foil and with gelatin film in relation first to the postoperative convalescence and secondly to the incidence of subsequent epilepsy.

PRESENT INVESTIGATION

This series of cases dates from 1945, and in the first few years tantalum foil was used to close almost all the dural defects. Then, however, Messrs. Allen & Hanburys produced a gelatin film large enough to close the largest defects. This film is a thin transparent membrane, supplied sterilised in tubes, which closely resembles cellophane until it is moistened with saline solution, when it immediately becomes soft and is easily tucked in beneath the edges of the dural defect. No fixation of the implant appears necessary, because it sticks quite easily to the underlying brain.

The series consists of 60 cases of intracranial meningioma after the removal of which dural defects remained, 30 being treated with tantalum-foil implants and 30 with gelatin film. The series is consecutive except for half a dozen cases in which fibrin foam or film was used; these have been excluded as providing too small a number of cases to give data comparable with those of the gelatin or tantalum groups.

TABLE I—SITE OF MENINGIOMAS

Tantalum series		Gelatin series	
Frontal cortical	5	Frontal cortical	6
Parietal cortical	9	Parietal cortical	8
Parasagittal	11	Parasagittal	10
Sphenoid wing	3	Sphenoid wing	3
Temporal	2	Suprasellar	2
		Subtentorial	1
Total	30	Total	30