A STUDY OF MORTALITY IN A BURNS UNIT*

STANDARDS FOR THE EVALUATION OF ALTERNATIVE METHODS OF TREATMENT

J. P. BULL, M.B., B.Ch., AND J. R. SQUIRE, M.D., M.R.C.P.

FROM THE MEDICAL RESEARCH COUNCIL INDUSTRIAL MEDICINE AND BURNS RESEARCH UNITS, BIRMINGHAM ACCIDENT HOSPITAL, BIRMINGHAM, ENGLAND

DURING THE LAST 30 years, medical science has introduced a wide range of potent remedies. For many diseases (and injuries) the new treatments available do not consist of the simple administration of a single drug; rather, multiple advances have been introduced. This more complex situation is well exemplified by the modern treatment of burns. To assess the value of such all-round improvement, the results of treating a comprehensive series of patients must be described in quantitative terms. As ordinarily presented, however, without statistical analysis, these results are frequently meaningless, and surprisingly little critical interpretation has been offered. Bare statements such as "seven thousand patients were treated with a case mortality of five per cent" are still common in medical literature. The following account is intended to show how such work can be converted into valuable data. The methods used involve a statistical treatment which is not familiar to most medical men. A simple table (Table III) has been drawn up which, by arithmetical addition only, permits a comparison between the results of treatment to burned patients given in the Medical Research Council Burns Unit and that used in other centers. In effect, a simple standardization of the results is achieved by these calculations so that account is taken of the differences in severity of lesion and age of patients in each series. The technical methods by which this table has been produced are given in full, so that their validity can be checked, and in order to bring out various interesting implications of the results. It is hoped that the essentials of the method will be applied to conditions other than burns.

The two factors which need standardizing, if results of different centres are to be validly compared, are age of patient and severity of lesion.

(a) *The age* of each patient is easily obtained, and as is well known, has a very marked effect on the outcome of a burn especially in later adult life. It is therefore desirable to record individual ages rather than to assign the patients to coarse age-groups.

(b) *The severity* can be measured by the proportion of the body surface burned. (Berkow[1, 2].) It has become customary to grade patients on this basis, and clinical impressions have been formed as to the extent of burning likely to cause death; thus a full thickness burn of one third of the body surface was at one time regarded as inevitably fatal. Exact studies have confirmed that burn area is a useful criterion of severity (Colebrook, *et al.*,[9] Clarkson and Lawrie,[5] Morrison[12]). Clearly, therefore, the overall mortality of a series

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of burned patients cannot be a satisfactory measure of successful treatment standards unless the area burned in each case is taken into account.

For this study, a specially suitable series of patients was available—all treated by modern methods under Dr. Leonard Colebrook. The analysis of results will serve not only as an attempt to show how to evaluate such a series; we hope it will provide also a challenge to other centers to do as well or better by offering a practical yardstick of the success of alternative methods.

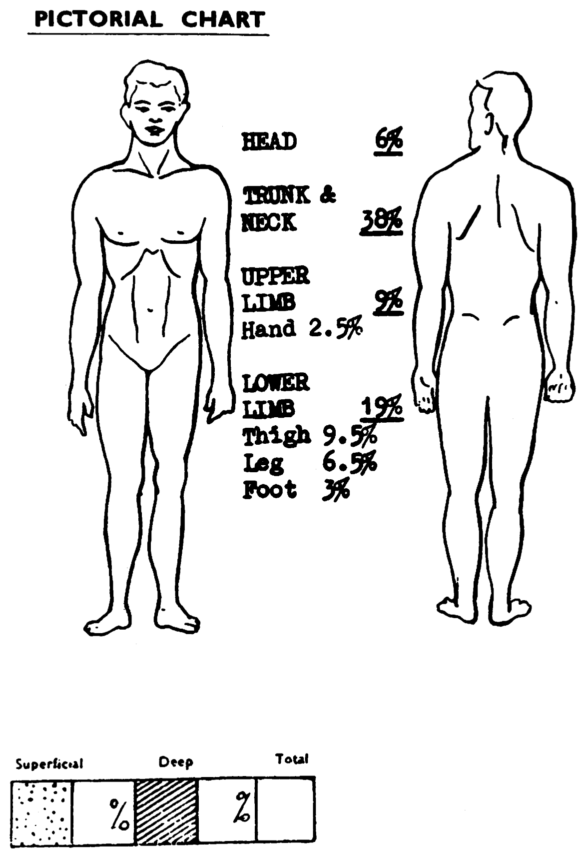

FIG. 1.—Chart used for estimating percentage body area burned.

CLINICAL MATERIAL

The study is based on a review of 794 patients with burns requiring in-patient hospital treatment. All were under the supervision of Dr. L. Colebrook, the first 72 at Glasgow (1942-3) and the remaining 722 consecutive in-patients at the Birmingham Accident Hospital admitted during 1945, 1946 and 1947; all were treated to completion. The only cases which have been excluded are those in the 0 to 14 age group treated in Glasgow in 1942–3, since the results in this group differ materially from subsequent experience because, it is now recognized, in the early days transfusion technic for younger patients had not been fully developed. The remaining Glasgow cases, with the complete Birmingham series, may be taken as representative of the results obtainable with the modern treatment of burns. The main features of this treatment are:

(1) Segregation and treatment of the patients in a specially organized Burns Unit.[6]

(2) Adequate fluid replacement by oral and intravenous routes.[9]

(3) The utmost precautions against added infection, and, in particular, cross-infection.[4, 7, 8]

(4) Local chemotherapy, reinforced occasionally with general medication.

(5) Skin grafting as required.

(6) Generous dietary treatment.

It should be pointed out that no deaths have been excluded, even if the burn was not apparently the primary cause of death—any patient dying in hospital was included. The study does not include any out-patients—they all had minor burns, and no deaths were reported among them.

Very full details were available from case records of the Birmingham patients. The details of the Glasgow patients used in this study were derived from Appendix I of the Medical Research Council Report Special Series No. 249.[9] The proportion of the body area burned had in every instance been estimated at the time of admission with the help of a pictorial chart and table reproduced in part in Figure 1. As an indication of how a burn was interpreted, a photograph is shown of a typical 25 per cent burn (Fig. 6).

PRELIMINARY SURVEY OF MORTALITY IN TERMS OF SEVERITY AND AGE

For the preliminary inspection of the data, each patient has been plotted on a diagram (Fig. 2) showing the age in years and the percentage of the body area involved by the burn. Those who survived are shown as clear circles, those who died as crosses. Owing to the large number of infants and children under five years with less than 10 per cent burns, none of whom died, a small area of the diagram is occupied by "208 survivors not plotted" for reasons of space. Inspection of Figure 2 confirms that both age and the area burned are factors in determining mortality.

For example, of 13 patients aged 0 to 10 years with 20 to 29 per cent area burns, only one died. Of four patients of this age group with 60 to 75 per cent area burns, all died (*i.e.,* the greater the area involved, the higher the mortality). Again considering 20 to 29 per cent area burns, but now among patients 60 or more years of age, out of a group of 12, only one survived (*i.e.,* for comparable areas, elderly patients have a worse prognosis).

These findings reaffirm what has been long known from clinical impressions, but it will be seen that the present extensive series, with materially consistent treatment and good documentation, provides an opportunity for assessing these two factors with considerable accuracy. It may be objected that a small deep burn may endanger life more than a larger area of superficial burning, and therefore that proportion of the body area burned is not the best measure of severity. Most of the patients in this series had areas of both full- and partial-thickness skin loss, and the area of each was recorded. By plotting the results from these patients on a diagram showing deep and superficial

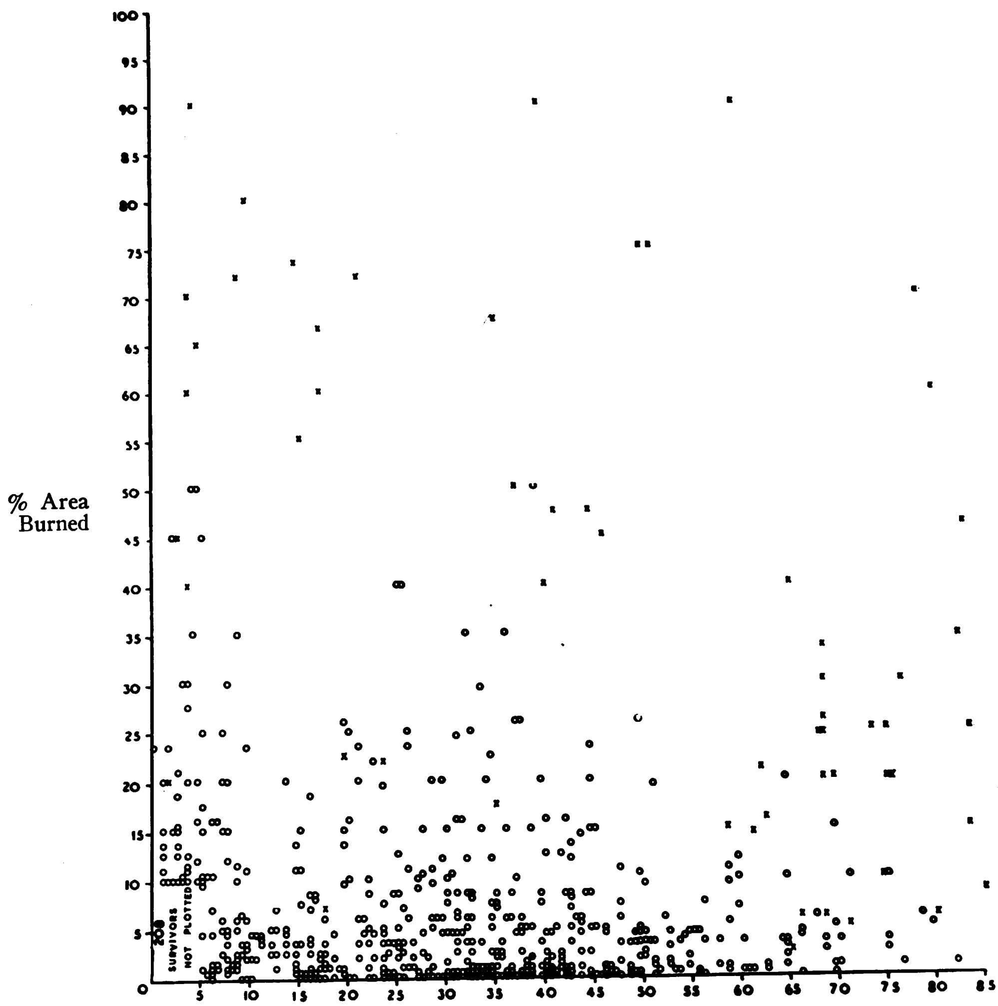

FIG. 2.—Diagram showing the distribution of the 794 patients in respect of (a) age in years, (b) burn area expressed as percentage of total body surface. Patients who survived shown:— o; died:— x.

areas, the trend of mortality was found to be best expressed in terms of "deep area plus one-fourth superficial area," *i.e.,* area for area a deep burn seemed to be four times as serious as a superficial burn. This refinement might be of value in comparing closely matched and highly documented cases, but since the exact diagnosis of burn depth is often difficult, subject to revision during the healing stages, and likely to vary with the judgment of different clinicians, the more simple if less accurate measure based on the total area of the burn has been adopted.

Since the two factors, age and area burned, influence the mortality, it is convenient at first to consider only one factor, the severity of the burn, by dividing the series into suitable age groupings. For this purpose, patients with ages 0 to 14, 15 to 44, 45 to 64, and 65 or more years were studied separately. By calculating the proportion of patients dying with burns of different areas within each group, rough curves relating case mortality to the percentage area burned could be constructed. Such a graph is shown in Figure 3.

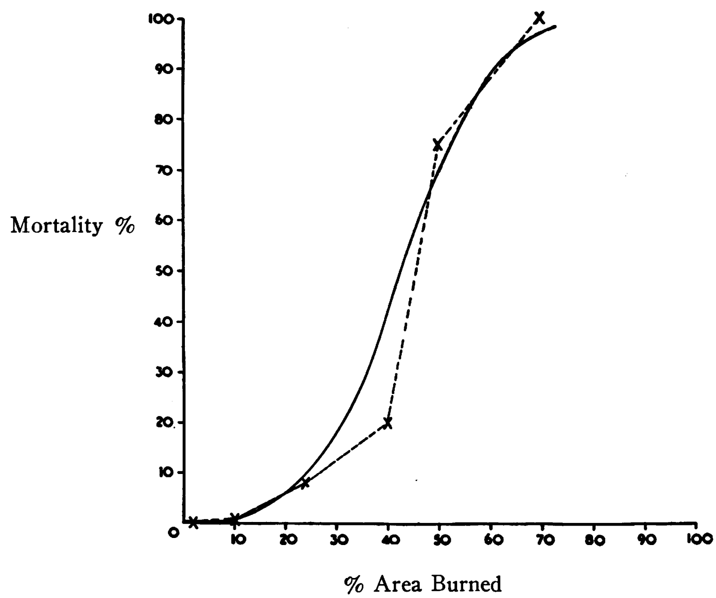

FIG. 3.—Diagram illustrating characteristic relationship between case mortality (percentage of patients dying) and severity index based on percentage area burned, plotted for various area groups of patients 15 to 44 years old. Solid line represents Probit fit.

The data plotted in this way suggest an S-shaped curve similar to that found by Clarkson & Lawrie.[5] Such a sigmoid relationship implied that even for relatively mild burns (*e.g.*, 5 to 15 per cent in adults age 15 to 44) a few individuals, less able than the average to withstand burning, succumb. On the other hand, although an insufficient number of severe burns are available to demonstrate the point with certainty, it is reasonable to assume that in the region of the curve where the mortality is tending to approach 100 per cent, there would be a few exceptionally strong individuals who would survive a burn severe enough to cause death in the "average" person. (This assumption is to an extent shown to be valid by the subsequent calculations.)

Those familiar with toxicity experiments on batches of animals, with the action of antiseptics on bacteria, or with many other biological studies involving populations of appreciable size, will recognize the essential similarity of this S-shaped curve to those plotted from other biological phenomena. For instance the mortality among batches of animals plotted against various doses of a toxic drug (or against the logarithm of these doses) usually shows a sigmoid relationship. It has been supposed that this form of relationship depends on the variation of one individual from another within any living population group—a variation in susceptibility about an average level which in quantitative degree corresponds with the usual "normal" distribution curve. In experiments with large numbers, this supposition has been tested and found to fit the facts; it can therefore be justifiably extended to cover an analogous situation such as the mortality from burns.

Early quantitative studies of this variation of susceptibility to toxic agents in animals were made by Gaddum.[11] Since then, the mathematical technic for handling such material has been developed by Bliss,[3] and in the form now known as "Probit Analysis" has been clearly explained and set out by Finney.[10] So far as is known, this valuable method has not previously been applied to any mortality findings in man.

In essence, the Probit technic implies that data of the type shown in Fig. 3 can be replotted with the vertical scale of response (percentage mortality in this case) altered so as to convert a sigmoid curve into a straight line. This result is obtained if the original sigmoid relationship depends on a "normally distributed" factor such as individual susceptibility. On the altered scale a Probit value of 5 corresponds to 50 per cent mortality; of 6 and 4 to 84 per cent and 16 per cent respectively, of 7 and 3 to 97.7 per cent and 2.3 per cent, etc. Having effected this straight line transformation, simple (though laborious) methods are available for calculating the best-fit formula for the data, testing the probable linearity of the relationship, assessing the certainty with which future results can be predicted and so on. In series suitable for considering in Probit terms, the conclusions are drawn from every part of the data, due relative importance being attached to each. Thus in the analysis of the burned patients, every death and every survival counts, while chance variations in the results from different groups are fitted in with the overall experience.

APPLICATION OF PROBIT ANALYSIS, AGE GROUPING RETAINED

The results plotted in Fig. 2 were first grouped as shown in Table I. Within each age group is tabulated the number of patients who suffered burns affecting various proportions of the total body surface. Alongside is shown the proportion of patients which died in each sub-group.

Thus of five patients age 0 to 14 years with an approximate mean area burned of 50 per cent, one died, giving an observed case mortality of 20 per cent.

Table I affords the starting point for calculation of Probit values, and the results finally obtained are shown at its foot. The Probit lines drawn from these formulae are shown in Figure 4. Here, the Probit values which constitute the vertical (or Y) scale are shown on the left, and the corresponding percentage mortalities are shown on the right. Mathematical testing shows that the lines afford a satisfactory fit with the original data, and gives no indication of a departure from linearity in the direct relationship between Probit values calculated from mortality and the percentage body area burned.

TABLE I.—*Burns Mortality Results, Summarized from Figure 2, Used in Calculating Probit Values*

Age Group: 0–14 Years			Age Group: 15–44 Years		
Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality	Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality
2	191	0%	2	175	0%
10	107	0%	10	83	1.2%
20	23	4.3%	20	31	9.7%
30	6	0%	30	7	0%
40	3	33%	40	5	20%
50	5	20%	50	4	75%
60	1	100%	60	2	100%
70	4	100%	70	3	100%
80	1	100%	90	1	100%
90	1	100%			
Total number of patients in group............	342			311	

Age Group: 45–64 Years			Age Group: 65† Years		
Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality	Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality
2	66	0%	2	14	7.1%
			6	9	55.6%
10	18	5.6%	10	3	33.3%
			15	2	50%
20	6	50%	21	6	100%
30	1	0%	30	8	100%
			35	1	100%
45	1	100%	45	1	100%
			60	1	100%
75	2	100%	70	1	100%
90	1	100%			
Total number of patients in group............	95			46	

Probit formula obtained from above data:

0–14 years, $Y = 1.29 + 0.0728X$ 15–44 years, $Y = 1.94 + 0.0709X$

45–64 years, $Y = 1.97 + 0.1343X$ 65+ years, $Y = 3.61 + 0.1532X$

(X = % area burned)

From the lines in Fig. 4 (or the formulae in Table I), estimates can readily be made of the severity of burn likely to produce any level of mortality. For instance, the severity corresponding to 50 per cent mortality can be read directly from Fig. 4, *e.g.*, in the 0 to 14 age group, a 51 per cent body area burn, on the basis of this series, is likely to produce death in 50 per cent of the patients treated. Just as the toxicity of a drug is best expressed in terms of the dose needed to kill 50 per cent of a batch of experimental animals (usually known as the Lethal Dose for 50 per cent or L.D.$_{50}$), so we may assess the treatment of a series of burned patients in terms of the area of burn producing death in 50 per cent of cases (*i.e.*, Lethal Area for 50 per cent, or L. A.$_{50}$). An improvement in treatment will be reflected in a rise in the L. A.$_{50}$ in a comparable group of patients. The degree of certainty with which this figure can be given depends on the number of patients studied, and on how severely each one was burned; it can be expressed as falling between certain "fiducial limits," *i.e.*, the range within which the true result should be found 19

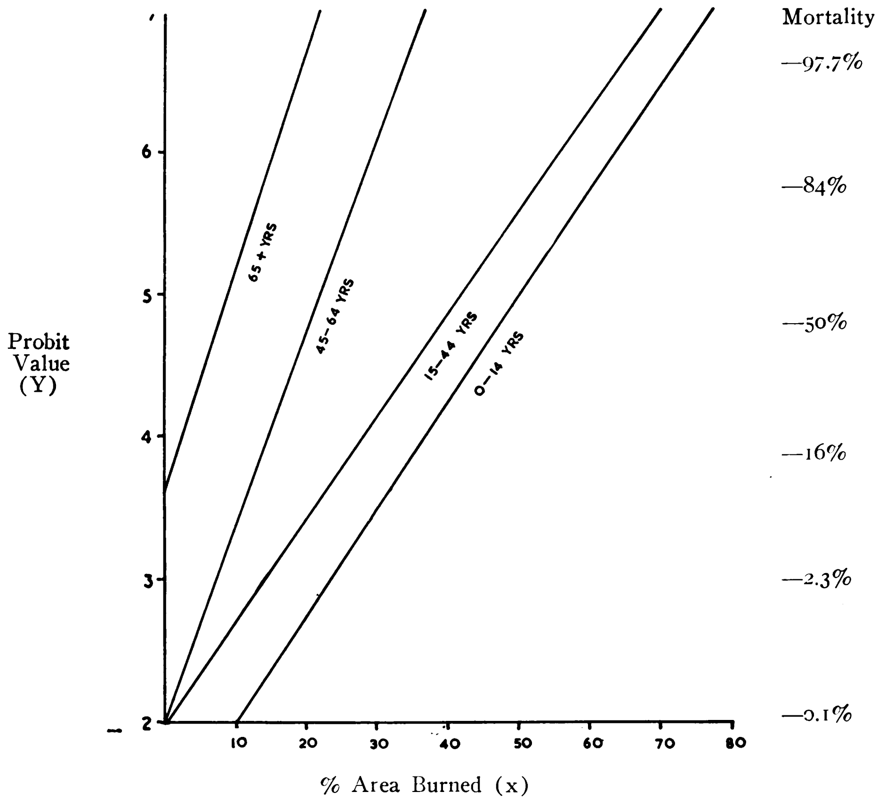

FIG. 4.—Probit values of case mortality related to severity index (*i.e.*, percentage area burned) for each age group, plotted from formulae given in Table I. Typical results derived from this figure are shown in Table II.

times out of 20. In Table II, the areas of burn found likely in this series of patients to produce 50 per cent and 25 per cent levels of mortality (the L. A.$_{50}$ and L. A.$_{25}$ values) are tabulated, together with the fiducial limits of these values.

Table II shows clearly the quantitative effect of age in decreasing the patient's powers of resistance to burn trauma. Thus among patients age 0 to 14 (average five years) it took a 51 per cent area burn to cause death in

50 per cent of cases; a corresponding effect was produced by a 23 per cent area burn in the age group 45 to 64 (average 55 years) and only a 9 per cent burn in the elderly group age 65 or more (average 71). These changes are highly significant.

RESULTS CO-ORDINATED TO SHOW MORTALITY EXPECTED AT ANY AGE

Ageing is a continuous process, and age grouping is an artificial, though convenient, abstraction. The results calculated for the series may now be considered as a whole by plotting graphically, the L. $A_{.50}$, L. $A_{.30}$, etc. against age. Such a diagram has been constructed in Figure 5. Each contour line showing the percentage area burn likely to produce death in 50 per cent, 30 per cent, etc., of cases is based on four points determined from the appropriate Probit line. The points show no suggestion of any discontinuity, and smooth lines have therefore been drawn between them. It is noticeable that there is no evidence, either in this graph or in the raw data, for a worse prognosis in very young children than in older children or adults with any given

TABLE II.—*Comparative Lethality of Burns at Different Ages Derived from Probit results*

Age Group Years	Mean Age Years	No. of Patients In Group	Area of Burn Corresponding to 50% Mortality		Area of Burn Corresponding to 25% Mortality	
			LA_{50}	Fiducial Limits*	LA_{25}	Fiducial Limits*
0–14	5	342	51%	43%–64%	42%	32%–54%
15–44	31	311	43%	37%–55%	34%	28%–42%
45–64	55	95	23%	17%–40%	18%	13%–28%
65 or more	71	46	9%	6%–15%	5%	0%– 8%

* Fiducial limits have been calculated for P =.95 (i.e.. range within which result may be expected to fall 19 times out of 20).

percentage area burn of the body. Since this is contrary to the clinical impressions of many surgeons, the original case notes have been carefully checked to exclude complicating factors (*e.g.,* a preponderance of scalds rather than burns among young children). The conclusion appears sound, though it should be noted that the present series does not include any severely burned infants under one year of age (Fig. 1) so that no statement can be made about patients in this age group.

PRACTICAL METHOD OF COMPARING DIFFERENT SERIES

Any other long series can be compared with the results given here by repeating the calculations described above. After deriving Probit values, a statistical comparison could be made between the lines obtained, both in respect of their position (*e.g.,* the L. $A_{.50}$s) and of slope (*i.e.,* the variability of susceptibility to burn trauma). Since the numbers of patients studied are usually less extensive and since the necessary calculations are tedious, a more convenient method of comparison is put forward.

From the mortality contours at all ages (Fig. 5), a grid (Table III) has been constructed showing the probability of death for any given combination

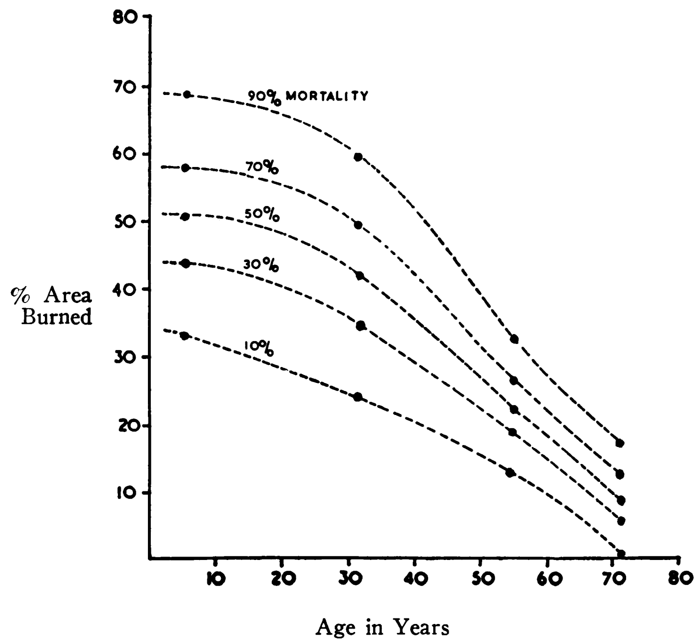

FIG. 5.—Contour lines dividing zones of equal mortality with various combinations of age and severity. The points are derived from the Probit values plotted in Figure 4, and have been used to prepare grid shown in Table III.

TABLE III.—*Grid of Approximate Mortality Probabilities for Various Combinations of Age and Area*

% of Body Area Burned	Age — Years 0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75†
73 or more	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
68–72	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1.0	1.0	1 0	1.0	1.0	1.0	1.0	1.0
63–67	.8	.9	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1 0	1.0	1.0	1.0	1.0	1.0
58–62	.7	7	.8	.8	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
53–57	.6	.6	.7	.7	.7	.8	.8	.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
48–52	.5	.5	.5	.5	.6	.7	.7	.8	.9	1.0	1.0	1 0	1.0	1.0	1.0	1.0
43–47	.3	.3	.4	.4	.5	.5	.6	.7	.8	.9	1.0	1.0	1.0	1.0	1.0	1.0
38–42	.2	.2	.3	.3	.3	.4	.5	.6	.7	.8	1.0	1 0	1.0	1.0	1.0	1.0
33–37	.1	.2	.2	.2	.2	.3	.3	.4	.5	.7	.9	1.0	1.0	1.0	1.0	1.0
28–32	.1	.1	.1	.1	.1	.2	.2	.3	.4	.5	.7	.9	1.0	1 0	1.0	1.0
23–27	0	0	0	.1	.1	.1	.1	.1	.2	.3	.5	.7	.9	1.0	1.0	1.0
18–22	0	0	0	0	0	0	.1	.1	.1	.2	.3	.5	.7	.9	1.0	1.0
13–17	0	0	0	0	0	0	0	0	0	.1	.1	.2	.4	.7	.8	1.0
8–12	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.4	.6	.8
3–7	0	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.3	.6
0–2	0	0	0	0	0	0	0	0	0	0	0	0	0	.1	.1	.3

These figures are approximations to a single place of decimals. A reading of 1.0 therefore implies "most probable value greater than 0.95."

of age and burn area. These probabilities are shown as decimal fractions of unity so that a 90 per cent mortality appears as 0.9. All figures are given to the nearest decimal place. From the table set out in this way simple addition

FIG. 6.—Photograph on admission of a typical 25 per cent burn of a child 2½ years old.

will give the expected number of deaths. To use this table for comparative purposes, a list of patients treated should be prepared giving age and percentage body area burned. Each patient can then be given a probability of mortality from the table. For example a patient aged 5 years with a 40 per cent burn will be scored "0.2," another aged 50 with a 25 per cent burn will be scored "0.5" and so on through the list. The total number of deaths expected from the whole series is then obtained by addition of all the probabilities. This total must then be compared with the number of deaths actually experienced in the series. If this actual number is less than the expected deaths it suggests that better results have been obtained possibly as a consequence of improved treatment. It is not feasible to apply a conventional criterion of "significance" to such a comparison, but any marked improvement or inferiority in treatment of a reasonable number of patients will be demonstrated.

This method will also show the particular type of patient contributing to any disparity. For this purpose, sub-totals, observed and expected, are compared, for example, for young and old patients, or for medium and large burns. In this way, it might be possible to demonstrate that another Burns Unit, while sustaining about the expected number of deaths when all patients were considered, had substantially better results with old persons, but less good results with children. Such comparisons should clearly lead to an interchange of information with mutual advantages.

DISCUSSION

If the idea of a sigmoid relationship between mortality and burn severity is accepted, then no matter how severely burned the patient may be, some probability of his survival remains. This statement is of great clinical importance, and is preferable to the old idea that a burn of a certain proportion of the body surface was necessarily fatal. If each burned patient is regarded as having a chance of recovery, every effort will be made to help by means of treatment. As pointed out in the footnote to Table III, the probabilities shown as 1.0 are only approximations indicating a mortality of over 0.95, *i.e.*, a chance of survival of less than 1 in 20. Such chances cannot be regarded in this clinical situation as negligible, and may increase with improved methods of treatment.

In this study, death or survival has been the only criterion of successful treatment considered. This limitation was intentional so as to simplify analysis and discussion. Quantitative indices of disability time or degree of final recovery would be susceptible to similar studies. Mortality also can be subdivided in the assessment of results into "early" and "late" deaths in relation to the time of being burned. In this series, there is little to indicate any marked alteration in the relative numbers of early and late deaths, as compared with pre-war studies. It is probably justifiable to conclude that roughly as many lives have been saved by improved resuscitation, especially with plasma transfusion, as by the control of infection.

Enough has been said to indicate the practical applications of this analysis to the evaluation of burn treatment. The technic should also be applicable to other conditions, though in each case suitable severity criteria must be worked out. These may take a simple physical form (*e.g.*, degree of trauma) clinical (raised or lowered blood pressure, basal metabolic rate), biochemical (liver function) or other forms based on instrumental findings such as the radiograph or electrocardiogram. Again mortality need not be used to assess results, since many other findings can be transformed on to Probit scales.

Apart from the importance of quantitative assessment in specific conditions, it is probable that correlation of results expressed in this way for the whole human age range would lead to the discovery of an underlying regularity among the results. It is tempting to speculate further on the meaning of the changes in Probit lines calculated from the present series. For instance, there is a suggestion that the rise in susceptibility from the age of 10 years up to 70 years, as judged by the fall in L. $A._{50}$ for instance, follows a course similar to that found for the "force of mortality" in studies of vital statistics. It is greatly to be hoped that similar studies on large series of burns or other conditions will lead to further investigation of this fundamental relationship between age and resistance to trauma or disease.

SUMMARY

1. The mortality findings among 794 burned patients treated in hospital by a Burns Unit are reported.

2. The importance of the age of the patient and the extent of the body surface area burned in determining mortality is demonstrated.

3. The analysis of these findings by the Probit technic is explained, and the results of this analysis for separate age groups are given.

4. The results by age-groups are graphically correlated to show the expected mortality for any given age and area.

5. A grid table is provided for making a simple comparative assessment of the results obtained in other series.

6. Similar analyses for conditions other than burns are suggested, and the likelihood of finding a general "law of ageing" discussed.

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BIBLIOGRAPHY

1 Berkow, S. G.: Arch. Surg. Chicago, **8**: 138, 1924.
2 ——————: Amer. J. Surg., 11: 315, 1931.
3 Bliss, C. I.: Quart. J. Pharm., 11: 192, 1938.

4 Bourdillon, R. B., & L. Colebrook: Lancet, i, 561, 601, 1946.
5 Clarkson, P., and R. S. Lawrie: Brit. J. Surg., **33**: 311, 1946.
6 Colebrook, L.: Nurs. Times, **41**: 4, 1945.
7 Colebrook, L., J. McK. Duncan, and W. J. H. Butterfield: Lancet, i, 321, 1947.
8 Colebrook, L., J. McK. Duncan, and W. P. Dallas Ross: Lancet, i, 893, 1948.
9 Colebrook, L., T. Gibson, J. P. Todd, A. M. Clark, A. Brown, A. B. Anderson: Med. Res. Council Spec. Rep. Ser. Lond., No. 249, 1945.
10 Finney, D. J.: Probit Analysis. Cambridge Univ. Press, 1947.
11 Gaddum, J. H.: Med. Res. Council Spec. Rep. Ser. Lond., No. 183, 1933.
12 Morrison, B.: Arch. Dis. Childhood, **22**: 129, 1947.