Classified according to duration of residence.

	Under 1 Year.		1-2		2-3.		3-5.		5-10.		10-15.		15–20		Over 20.	
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F	M.	F.
Cases	49	63	53	62	74	61	85	85	140	191	81	100	25	55	39	48
Deaths	5	6	3	4	2	4	10	2	4	4	1	4	1	1	—	4
Per ct.	9·9		6·08		4·44		7·06		2·42		2·76		2·50		4·59	

Under sixty years of age and over five years' residence there are 443 cases with six deaths, a mortality of 1·35 per cent., which is about the mean mortality of the general population from 40-45 years of age. Under five years' residence and over sixty years of age the numbers are 127 with 22 deaths, a mortality of 17·3 per cent.

In the different asylums the mortality ranges for cases under sixty years of age from 0·79 to 2·57, and for cases over sixty from 6·44 to 15·00.

The Physiological Action of Alcohol in its Relationship to Animal Heat, and its influence upon the vaso-motor Nervous System. By W. Bevan Lewis, L.R.C.P., Lond., Senior Assist. Medical Officer, West Riding Asylum.

The physiological action of Alcohol upon thermogenesis has been the subject of much dispute, and its effects upon tissue metamorphosis is still a moot point with many authorities in Therapeutics.

As regards large doses of Alcohol, the general belief appears to tend in the direction pointed out by Wood.* When discussing the physiological effects of Alcohol, he makes the following statement:—

"That the antipyretic action of Alcohol is not exerted through the nervous system was proved by Binz, who found that the drug acted powerfully upon the fever of animals after cervical section of the spinal cord, and even prevented the *post-mortem* rise of temperature. It would appear to be a necessary corollary to this that *alcohol in very large doses lowers temperature by directly checking tissue metamorphosis.*"

According to this line of argument, Wood infers that the antipyretic effect of Alcohol is attended with an absolute

* "Treatise on Therapeutics," by H. C. Wood, M.D., 1st Edition, 1874.

lessened formation of heat. The equalisation of temperature in the animal body is due, in great measure, in healthy conditions, to the fact that the *fresh heat formation* is directly compensatory in amount for the heat *lost or dissipated.* When lessened tissue metamorphosis coincides with the maintenance of an equable temperature, a change in the vasomotor regulative centres must be admitted to explain the persistence of a normal temperature; in other words, compensatory heat retention occurs through the agency of the capillary vessels. Supposing, then, that in the normal condition, where the balance between fresh heat formation and heat discharge is exactly maintained, the action of a large dose of Alcohol is brought into play. We shall then get a lessened heat formation as the result of diminished tissue change, whilst the discharge of heat from the body surface remains normal or exceeds the normal amount—hence the body necessarily falls in temperature. This is, as I understand, the assumption of Wood in his deductions from the statement made by Binz. If, however, it can be shown that parallel with a decline of temperature the *absolute heat formation* is *increased* rather than diminished, and this fall of body temperature is also coincident with a greatly increased discharge of heat from the body, the formula becomes much more complex, and the accuracy of the deductions drawn by Wood rendered very dubious. No less an authority than the late Prof. Parkes thus states his dissent from the generally received views that Alcohol lessens tissue change:—"The experiments, already referred to by Count Wollowicz and myself, prove that the metamorphosis of the nitrogenous tissues is in no way interfered with by dietetic doses (of Alcohol). Whether the carbonic acid is really lessened may be also questioned."* We must conclude that the action of *dietetic* doses of Alcohol and the *large* doses spoken of by Binz upon the nutritive processes, must produce diametrically opposite effects to reconcile the discrepancy apparent between the views of Binz, Parkes, and Wollowicz, and it will therefore be interesting from this point of view to consider the action of large and small doses of the drug upon the formation and maintenance of animal heat.

As yet my experiments have been limited wholly to animals, yet I conceive they will prove worthy of consideration, since any addition to our knowledge of the physiological action of so universal an article of dietetics as Alcohol must prove of interest to all my readers. The interest universally

* "Practical Hygiene," 4th Edition, page 275.

shown in articles by our leading physicians in recent numbers of the "Contemporary Review" upon the physiological action of Alcohol proves also how keen is the mental appetite for information upon this very engrossing subject by the public at large, and I take it therefore as the distinct duty of every physician to obtain as clear an insight into the action of Alcohol as possible, and to base his treatment by its agency upon as exact a knowledge of its physiological effects—as far as this can be acquired.

The method adopted was similar to that employed in certain calorimetric observations upon the action of several potent alkaloids in the production of animal heat, which were detailed in the sixth volume of the West Riding Asylum Medical Reports. The calorimeter made use of was the improved form recommended by Dr. Burdon Sanderson, and the animals experimented upon were chiefly rabbits. The animals were chosen in a state of perfect health, weighed carefully, and one or more calorimetric observations made in the normal condition prior to the administration of the drug, the intervals of each observation extending over a quarter of an hour. Alcohol was then given (carefully diluted), being introduced into the animal's stomach by a simple arrangement whereby rapidity and efficiency were secured without entailing any but the slightest amount of discomfort to the animal. A description of the calorimeter and the method of estimating by its means the amount of heat generated in the animal body may be found in most text books devoted to this branch of enquiry, as also in the article alluded to in the West Riding Asylum Reports. I shall, therefore, not digress so far as to enter upon these points, but shall proceed at once to discuss the results of observations tabulated below, and which are chosen from a large number of experiments as typical of the action of Alcohol upon thermogenesis when given in doses of varying strength.

In the following Table we observe the effects a *small dose* (one and a half drachms) of alcohol upon a plump healthy rabbit weighing 2363 grammes. During the first quarter of an hour's interval the total heat formation was 3387 gram. units, equivalent to 1·4 units of heat for each gramme of body weight. Observation 3 gives the maximum heat formation at 6412, *i.e.*, 2·7 heat units per gramme of body weight, whilst the three succeeding observations registered between 1·18 and 1·7 heat units. For the present we will pass over the central column of Table 1, as we may more conveniently

consider the amount abstracted from or added to the temperature of the animal's body at a subsequent period.

TABLE 1.

(Observations Extending over ½ of an Hour).*

Rabbit treated with 90 mins. Alcohol.

Weight of Animal, 2363 Grms.	Total Heat Formation.	Loss or Gain in Body Temperature.	Fresh Heat Formation per Gramme of Body Weight.
Observation--1	3387	— 1745	1·4
,, 2	2243	— 323	0·95
,, 3	6412	+ 1745	2·7
,, 4	2800	Nil.	1·18
,, 5	4014	+ 215	1·7
,, 6	4014	+ 215	1·7

Let us now observe the effect of a larger dose of alcohol (120 mins.), noting the fact that the animal now experimented upon weighs 633 grammes less than in the preceding case, a fact which must be taken into consideration in estimating the potency of the dose administered.

TABLE 2.

(Observations ½ hour each).

Rabbit given 120 mins. Alcohol.

Weight of Animal, 1730 Grms.	Total Heat Formation.	Loss or Gain in Body Temperature.	Fresh Heat Formation per Gramme of Body Weight.
Observation--1	Too minute for registry.	— 1837	Too minute for registry.
,, 2	3693	— 132	2·135
,, 3	3693	— 132	2·135
,, 4	4153	+ 187	2·4
,, 5	4058	+ 161	2·34
,, 6	4058	+ 161	2·34

* In each column the figures represent *gramme-units of heat.*

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Here the heat produced is still more marked than in the first experiment. The primary effect seen during the first observation (Table 2) is very noteworthy. So small is the heat formation during this interval that the delicate thermometer used (extremely sensitive and registering 1-20ths of a degree Fah.) failed to detect any change in the temperature of the Calorimeter. The second and third intervals, however, register 2·135 heat units for each gramme of body weight, the last three observations giving 2·4, 2·34 and 2·34 respectively. The experiment, therefore, extended over a period of one and a half hours from the exhibition of the two-drachm dose of Alcohol. In order to appreciate these results, we must enquire into the heat production normal to the same animal and prior to the administration of Alcohol. (See Table 3).

TABLE 3.

(Observations, ½ hour each).

Rabbit in Normal Condition.

Weight of Animal, 1730 Grms.	Total Heat Formation.	Loss or Gain in Body Temperature.	Fresh Heat Formation per Gramme of Body Weight.
Observation--1	1649	+ 98	0·96
„ 2	1649	+ 98	0·96
„ 3	1649	+ 98	0·96
„ 4	1649	+ 98	0·96
„ 5	1109	— 478	0·64
„ 6	1855	Nil.	1·08

A glance at this Table will suffice to show how much smaller the heat formation is in the normal condition and how greatly exaggerated it becomes upon the exhibition of Alcohol. The contrast may be, perhaps, shown more clearly and strikingly by arranging the estimates of heat units per gramme of body weight in parallel columns. (See Table 4.)

To illustrate the effects of still larger doses of Alcohol the observations taken in the case of an animal weighing 2033 grms. are chosen as typical of the action of these larger doses. The animal experimented upon was given 180

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minims of Alcohol, and, as in all former experiments, each Calorimetric observation extended over an interval of a quarter of an hour.

TABLE 4.

Gramme Units of Heat formed per Gramme of Body Weight.

	Animal in Normal Condition.	Animal after 120 Mins. of Alcohol.
Observation—1	0·96	Inappreciable.
„ 2	0·96	2·135
„ 3	0·96	2·135
„ 4	0·96	2·4
„ 5	0·64	2·34
„ 6	1·08	2·34

The following Table gives a summary of the results of nine consecutive observations :—

TABLE 5.

(Observations, ¼ hour each).

Rabbit treated with 180 mins. Alcohol.

Weight of Animal, 2033 Grms.	Total Heat Formation.	Loss or Gain in Body Temperature.	Units of Heat formed per Gramme of Body Weight.
Observation 1	2701	— 2151	1·32
„ 2	4792	— 1974	2·35
„ 3	4934	— 936	2·43
„ 4	4064	— 462	2·
„ 5	8720	— 379	4·28
„ 6	3910	+ 352	1·92
„ 7	3910	+ 352	1·92
„ 8	3910	+ 352	1·92
„ 9	3910	+ 352	1·92

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The normal amount of heat formed each quarter of an hour in this animal, prior to the administration of Alcohol, varied between 0·45 and 1·53 heat units per gramme of body weight. Under the influence of 180 minims of Alcohol, however, this heat product is steadily augmented, until in the fifth interval succeeding the exhibition of the drug it rises to 4·28 heat units, representing an aggregate formation of 8720 gram. units of heat. It cannot fail to strike the attention on glancing over the results in Table 5 that the augmentation in the heat product is not only strongly marked, but most persistent after these larger doses of Alcohol. Thus, in consulting Table 7, where but 40 mins. of Alcohol have been given, the heat increment reaches its height during the *second interval*, and declines after the first half hour; in Table 1, where 90 mins. of Alcohol was the amount administered, the highest heat product was registered during the *third interval*, beginning to fall after three quarters of an hour. In Table 2, representing the results of 120 mins. of Alcohol, the "heat climax" was obtained during the *fourth interval*, and fell but *very slowly*, remaining at 2·34 (*i.e.*, only ·06 below the heat climax) until one hour and a half had elapsed from the administration of the Alcohol. A still stronger dose of Alcohol, *i.e.*, 180 minims being given in our last case (Table 5), the heat climax of 4·28 was registered at the termination of the *fifth interval*, one hour and a quarter from the administration of the dose. This relationship between the time of the attainment of the heat climax and the dose of the drug administered was so striking and so constant a feature that it deserves to be separately tabulated (Table 6.)

TABLE 6.

Illustration of the Relationship between the Period of Highest Heat Formation and the Dose of Alcohol.

Dose of Alcohol given.	Period of Heat Climax.	Time elapsed since Administration of Alcohol.
40 Minims.	During Second Interval	½ hour.
90 Minims.	,, Third ,,	¾ hour.
120 Minims.	,, Fourth ,,	1 hour.
180 Minims.	,, Fifth ,,	1¼ hours.

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The earliest indication obtained of the action of small doses of the drug always pointed in the direction of a primary check to heat formation, this action being scarcely recognisable when larger doses were administered. In the latter case, if it occurs, the effect is too fugitive to be detected except in a much shorter interval after administration of the alcohol, whilst when small doses are given there is a distinct tendency to protraction of this stage. Thus, in a rabbit weighing 2662 grammes, to which but 40 mins. of alcohol had been given, the primary check to thermogenesis occurs during the first quarter of an hour, when 0·46 heat units were registered, the healthy standard in this animal being 0·95.

TABLE 7.

(Observations, ¼ hour).

Rabbit given 40 minims of Alcohol.

Weight of Animal, 2662 Grms.	Total Heat Formation.	Loss or Gain in Body Temperature.	Fresh Heat Formation per Gramme of Body Weight.
Observation 1	1224	— 1575	0·46
„ 2	7118	— 814	2·7
„ 3	3428	+ 814	1·3
„ 4	4060	— 119	1·5

Passing now from the total amount of heat formation as the results of the injection of Alcohol, to the effect on the animal's temperature we find the primary effect one of marked loss of body heat during the first interval. In the *normal condition* the animal to which 40 mins. of Alcohol were given (Table 7) obtained an increment of 173 heat units to its body temperature during the first interval, lost an equivalent amount during the next, and again gained 421 heat units during the third interval. Such slight variations are usual in the normal state of the animal, however carefully the Calorimetric Observations are performed, as in no case can the condition of the animal in the calorimeter be made perfectly natural to it. So slight, however, are these variations that they have a scarcely recognisable effect upon the general accuracy of experimental results. Glancing at the middle column of Table 7, we observe that 40 mins. of

Alcohol had the effect of depriving the animal of 1575 heat units during the first quarter of an hour, and of 814 in the next interval, the third period being marked by an increment of 814. This loss from the body temperature *increases in amount with the dose*—thus after 180 mins. the loss during the first interval was 2151, and during the second 1974 (Table 5). If we compare the effects of the smaller and larger doses of 40 and 120 mins. in Tables 7 and 5 we perceive that the body temperature is not only reduced far more in degree by the larger dose, but the reduction in temperature is more persistent, being protracted up to the fifth interval—a period of 1¼ hours after administration of the drug. As a further illustration of this point we will compare the results of 120 mins. of Alcohol upon body temperature with the slight variations already referred to as occasionally produced by the somewhat unnatural condition of the animal. (See Table 8).

TABLE 8.

(Observations, ¼ hour).

Loss or Gain in Body Temperature expressed in heat units.

Weight of Animal, 1730 Grms.	Rabbit in perfect health and normal state.	Same Animal after 120 mins. Alcohol.
Observation—1	+ 98	— 1837
„ 2	+ 98	— 132
„ 3	+ 98	— 132
„ 4	+ 98	+ 186
„ 5	— 477	+ 161
„ 6	Nil.	+ 161

These results tabulated above speak for themselves. One point worthy of notice, however, is that the slight increment added to the animal's temperature in the normal state goes on up to the fourth interval, and then the balance becomes almost re-established by a sudden fall of 477 heat units, whilst in the sixth interval the temperature becomes stationary, no registry of rise or fall having been obtained. This sudden restitution of the normal temperature is probably indicative

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solely of vaso-motor changes. I need scarcely call attention to the very pronounced and protracted fall of body temperature shown in Table 5, amounting in the aggregate to 5902 heat units in the course of an hour and a quarter from administration of the spirit. In these larger doses the normal of temperature is reached by a tardy process of small increments, there being no tendency shown to the rather sudden re-establishment of the balance, which is usually apparent after the administration of small doses of the drug.

In all our cases we observe one very important point demonstrated, viz:—that the injection of Alcohol is invariably followed by an augmentation of the total heat formation, and that though thermogenesis may receive a slight check as a primary effect of the Alcohol, the ultimate issue is invariably the *formation* and *discharge* of a much increased heat product often double or treble the normal amount.

During the earlier stages of its operation, and whilst this primary check to heat formation is more or less recognisable the greatest diminution in body temperature occurs,* whilst the attempt at restitution of the normal temperature is almost always coincident with the registry of the heat climax.†

It will prove of interest to compare the results obtained from the administration of Chloral with those we have just recounted. For this purpose I add a table abstracted from my former article in the West Riding Asylum Reports (Vol. 6), somewhat modified for more ready comparison.

TABLE 9.

(Observations, ½ hour).

Rabbit treated with 20 grains of Chloral.

	Total Heat Formation.	Loss or Gain in Body Temperature.	Heat units formed per Gramme of Body Weight.
Observation—1	10815	— 1008	7·7
„ 2	10815	— 1008	7·7

* See Table 2, Obs. 1; also Table 7, Obs. 1.
† See Table 1, Obs. 3; also Table 2, Obs. 4; also Table 5, Obs. 5.

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TABLE 10.

(Observations, ½ hour).

Rabbit treated with 17 grains of Chloral.

	Total Heat Formation.	Loss or Gain in Body Temperature.	Heat units formed per Gramme of Body Weight.
Observation—1	Inappreciable	— 542	Inappreciable
„ 2	16907	— 825	11·3
„ 3	15344	— 1922	10·3

Here we note a greatly increased heat formation together with a large evolution from the body temperature. The first experiment in which 20 grains had been administered exhibits, in the course of one hour, 2016 heat units abstracted from the animal's temperature, represented by a fall of fully 6·3° Fah.

The effect of Chloral therefore upon thermogenesis is closely allied to that of Alcohol, a fact which we cannot afford to lose sight of in the administration of these drugs as remedial agents. The *extreme vaso-motor paresis* produced by the combination of these two remedies has been a fact palpable to my mind for many years. In the treatment of insanity I have had frequent opportunities of observing the distressing symptoms which follow the administration of Alcoholic stimulants upon those who have taken Chloral, in doses of twenty or thirty grains. A throbbing headache, causing very great distress, marked flushing of the face, and a strong chloral odour in the breath are the prominent symptoms, and these may be often noted for 18 to 24 hours after the administration of the Chloral. These symptoms may be present in any subject, but are less marked in younger patients—whilst in later life the cephalalgia and general malaise accompanying extensive and severe vaso-motor paresis are so distressing that I now make a point of never combining them in the treatment of such cases.

To summarise the results of these researches into the effect of Alcohol upon thermogenesis :—

1. A primary check to heat formation most marked and protracted when *small doses* of Alcohol have been given.

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2. A pronounced fall in body temperature most marked during the first quarter of an hour, and therefore coincident with the primary check to thermogenesis (1).

3. A greatly increased heat formation varying directly with the strength of the dose administered.

4. This increased heat product is manifested over a more prolonged period after larger doses of Alcohol.

5. This increase in the heat product is gradually augmented from time to time until the heat climax is reached, a period usually coincident with the registry of the lowest body temperature.

6. The heat climax is more protracted or postponed, and also greatest in degree with the stronger doses of Alcohol.

7. The greatest loss of heat units from the temperature occurring, as before stated, during the first interval, subsequent intervals are marked by a still progressive loss, which, however, becomes less towards the period of heat climax, when a restitution of the *norma* of temperature begins.

8. With *small* doses of Alcohol this restitution of body temperature is usually sudden or comparatively rapid in operation; after *large* doses the return to the *norma* of temperature is spread over a longer period, being extremely tardy when very large doses have been administered.

9. These observations are directly in antagonism to the views already quoted, that "*Alcohol in very large doses lowers temperature by directly checking tissue metamorphosis.*"

10. The above considerations appear to justify the conclusion that the *characteristic* action of Alcohol is that of greatly increasing the heat product, whilst dispersion of the fresh formed heat is facilitated by peripheral vaso-motor paresis, and that it is only in very small doses that we get a temporary lowering of heat formation.

11. The action of Chloral, as affecting thermogenesis, being similar to that of Alcohol, we obtain by their combination a most powerful vaso-motor depressant, and one which should be used with great caution.