Papers and Originals

Cold Stress and Muscular Exercise, with Special Reference to Accidental Hypothermia

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An investigation of "exposure" accidents among walkers and climbers revealed the fact that wet clothing and walking to the point of exhaustion were the two outstanding features in fatal accidents (Pugh, 1966a). Subsequent experiments in a climatic chamber showed that the combination of exercise, wind, and wetting reduced the effective thermal insulation of a typical clothing assembly to one-tenth of its nominal value determined at rest in dry, still conditions (Pugh, 1966b). The results also showed that when the subject was exercising at a given work rate in the wet-cold situation his oxygen intake was 50% higher than it was at the same work rate in dry conditions. This finding suggested a possible explanation of the premature fatigue commonly described in exposure accidents, and it seemed desirable to study the phenomenon in more detail.

Methods

Experiments were conducted in a climatic chamber at an ambient temperature of 5° C. D.B. (2° C. W.B.). Three young physiologists with experience of hill-walking acted as subjects (Table I). They wore a set of clothing which had been used by one of the hypothermia casualties in the Four Inns Walk (Pugh, 1964). The items were as follows: string vest, woollen shirt and jersey, padded anorak with hood, jeans, heavy woollen socks, gym shoes, and woollen gloves.

TABLE I.—Physical Characteristics of Subjects

Name	Age	Weight (kg.)	Height (cm.)	Surface Area (sq.m.)	Mean Skinfold Thickness (mm.)
Ian Hampton ..	30	59.0	167.0	1.66	3.73
Robert MacGibbon ..	23	73.1	182.5	1.94	3.54
Richard Hillier ..	26	79.7	181.9	2.02	5.61

Two experimental situations were chosen: Situation A, in which the subjects wore dry clothing and were not exposed to wind; and Situation B, in which they wore wet clothing and were exposed to a wind of 15 k.p.h. velocity. In Situation B the subjects wetted their clothing outside the chamber by standing under a shower-bath (water temperature 17-19° C.). After one to two hours in the chamber the outer clothing tended to dry and was rewetted by means of a spray.

The subjects worked on a Van Döbeln-type ergometer at nominal rates of 400, 600, 800, 1,000, and 1,200 kg. m./min. with some adjustment of the higher loads to suit the individual's work capacity. They worked at each of the lower rates for a period of 40 to 60 minutes in Situation A, followed by a period of 40 to 120 minutes in Situation B, the intention being to continue observations in each situation until rectal temperature

reached a steady level. At the higher work rates observation was curtailed by fatigue, but it was usually possible to obtain steady readings by combining a low rate with a high one. In this type of experiment the two situations were taken on different days.

Oxygen intake was measured at suitable intervals by the bag method. When shivering was present two 300-litre bags of expired gas were collected for each determination and the resting collections lasted 10 to 15 minutes. In Situation A resting measurements were made outside the chamber to avoid cold stress. In Situation B resting measurements were made: (1) before exercise on days when Situation A was not studied; and (2) after 25 minutes of rest following exercise when Situation B had been preceded by Situation A.

Rectal temperature was followed continuously with an indwelling thermocouple inserted to a depth of 15 cm. Skin temperatures were measured with thermocouples over 13 regions of the body surface, readings being taken every 20 to 30 minutes (for details see Pugh, 1966b).

In some experiments thermal gradients in mid-thigh (anterior aspect) and in the anterolateral region of the leg about 10 cm. below the knee joint were measured immediately after exercise with an Ellab needle thermocouple† (length 5 cm.; O.D. 0.7 mm.). The needle was inserted at right angles to the skin and readings were taken at measured intervals on withdrawal. The needle was reinserted obliquely to check the more superficial readings. A set of readings took about five minutes to complete.

Results

During exercise in Situation A (dry clothing, no wind) the subjects were comfortably warm and sweated at high work rates. In Situation B (wet clothing, wind) they experienced severe general discomfort, and it was found necessary to allow them to wear plastic bags over their gloves and shoes to reduce painful cooling of the extremities. Shivering began either before or immediately after entering the chamber and persisted throughout the experiments except when the work rate was greater than 800-1,000 kg. m./min. depending on the individual. At work rates below 800-1,000 kg. m./min. the subjects found work more tiring in the wet-cold situation, and afterwards described symptoms such as extreme misery, loss of morale, blankness, and light-headedness. They did not, however, become confused, disorientated, or amnesic as described by Adolph and Molnar (1946), who made observations on nude subjects working outdoors at 0° C.

When the work rate was increased to 800 kg. m./min. shivering and discomfort diminished, and by 900-1,000 kg. m./min. had subsided completely. At this stage the subjects no longer

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felt cold or discomfort, nor was the work more tiring than in the warmer situation.

O₂ Intake and Work Rate

Individual results have been plotted in Fig. 1, and Table II summarizes the data for all subjects. Mean O₂ intakes in Situation A agreed closely with average values from this and other laboratories. In Situation B O₂ intakes at work rates of 400–800 kg. m./min. were 0.4–0.5 l./min. higher than in Situation A, but there was no increase in O₂ intake at higher work rates. The metabolic response to cold during exercise was approximately equal to that brought about by a 300 kg. increase in work load, and amounted to 15–20% of the subjects' estimated maximum O₂ intake. Mean resting O₂ intake in Situation B increased from 0.3 to 1.0 l./min.

TABLE II.—Mean Values of Oxygen Intake and Rectal Temperature for Three Subjects During Rest and Prolonged Exercise: (A) in Dry Clothing Without Wind; (B) in Wet Clothing in Presence of Wind

Work Rate (kg. m./min.)	Oxygen Intake (l./min.)			Rectal Temperature (°C.)		
	A	B	Difference	A	B	Difference
Rest	0.28 (6)	1.02 (11)	+0.74	37.19 (6)	36.57 (11)	−0.62
400	1.06 (5)	1.60 (5)	+0.54	37.55 (5)	36.51 (6)	−1.04
600	1.60 (4)	2.00 (8)	+0.40	37.93 (4)	37.39 (5)	−0.54
900	2.17 (5)	2.18 (9)	+0.01 (N.S.)	38.13 (4)	37.77 (9)	−0.36
1,200	3.06 (1)	2.91 (1)	+0.15 (N.S.)	—	—	—

FIG. 1.—O₂ intake and work rate during ergometer exercise. Situation A: dry clothing, no wind (●). Situation B: wet clothing, 15 k.p.h. wind (×). Ambient temperature 5° C. Subject I.H. was working submaximally at 1,100 kg. m./min. Data on R.H. are incomplete.

Body Temperature

In both situations rectal temperature varied with work load, but mean skin temperature was relatively constant and independent of work rate (Fig. 2). Mean skin temperatures at room temperature outside the chamber were 33–34° C. During exercise in Situation A the values were 30–32° C., which are normal values for clothed subjects exercising in a cool environment. In Situation B mean skin temperatures fell to 18–22° C. Regional skin temperatures were similar to previous findings (Pugh, 1966b) (Table III). Notable features were the low temperatures over the lower limbs due to poor insulation afforded by jeans, and the low forehead temperature.

During exercise in Situation A rectal temperature rose to steady levels in 40 to 60 minutes (Fig. 3). The final values were closely comparable with the data of Nielsen (1938) and were representative of the normal "set points" to which body temperature is regulated at each work rate. During exercise in Situation B rectal temperatures assumed values within 0.0 to −0.4° C. of the "set point" so long as the work rate was greater than 800 kg. m./min. At work rates below 800 kg.

m./min. rectal temperatures, after a variable interval, drifted downwards towards new levels depending on the work rate. At 400 kg. m./min. the values were still falling asymptotically after 80 to 120 minutes of observation. The above changes are illustrated in Fig. 2, in which mean rectal temperature has been plotted against work rate for Subjects R.M. and R.H., who were of comparable size and fitness. The time course of rectal temperature at a work rate of 400 kg. m./min. in Situations A and B is illustrated in Fig. 3, and Fig. 4 illustrates changes associated with change of work rate and with the onset of exhaustion. After exercise rectal temperature fell steeply if the

FIG. 2.—Mean values of rectal temperature during ergometer exercise. Subjects R.M. and R.H. ● Dry clothing, no wind. ○ Wet clothing, wind. × Data of Nielsen (1938) shown for comparison. Figures indicate mean skin temperatures. Vertical lines represent ranges. Note progressive departure from "set point" at the lower work rates in wet-cold conditions.

TABLE III.—Regional Distribution of Skin Temperature in Situation A (Dry Clothing, No Wind) and Situation B (Wet Clothing, Wind). Ambient Temperature 5° C.

Region	Skin Temperature (°C.)	
	Situation A (Warm)	Situation B (Cold)
Forehead	31.1	20.4
Hands	31.4	10.8
Feet	26.9	15.9
Lower limb	28.9	15.8
Upper limb	32.8	25.0
Trunk	33.2	25.1

FIG. 3.—Rectal temperature during exercise at 400 kg. m./min. in Situation A (dry clothing, still air) and Situation B (wet clothing, wind). Subject R.H. Ambient temperature 5° C. Figures show O₂ intake in l./min. Note rise of rectal temperature over 40 min. in A and progressive fall in spite of increased O₂ intake in B.

value during exercise was close to the “set point” but remained steady if rectal temperature during exercise had already fallen to a low level. There was insufficient evidence to show whether or not the post-exercise fall was influenced by exhaustion; nor was there any clear relation between rectal temperature and resting metabolism (Fig. 1), the reason being that metabolism in the cold responds to a combination of factors of which rectal temperature is only one.

FIG. 4.—Rectal temperature at varying work rates in the wet-cold situation. Subject I.H. work rates in kg. m./min. are shown above the temperature line and O₂ intake in l./min. below it. Note rise of rectal temperature with increase of work rate, falling rectal temperature and work rate associated with fatigue, and sharp fall of rectal temperature on cessation of exercise.

Muscle Temperatures

Muscle temperatures for R.M. are shown in Fig. 5. In the thigh, after work at 400–600 kg. m./min. the thermal gradient extended inwards to a depth of 2 cm. in Situation A and of 4 cm. in Situation B. Owing to the low skin temperatures in Situation B the gradients were much steeper and a considerable bulk of muscle had cooled below 32° C. Post-exercise deep thigh temperatures were 38.5–39.0° C. in both situations. The values were 0.9–1.7° C. higher than rectal temperatures in Situation B and 0.4° C. higher in Situation A.

Muscle temperatures in the leg were 3–6° C. lower than in the thigh in Situation B, but only slightly different in Situation A. After 40 minutes without exercise in Situation B

FIG. 5.—Thermal gradients in the thigh and leg in subject R.M. Rectal temperatures (T_R) are shown for comparison.

the thermal gradient in the thigh extended further inwards and was steeper than after exercise, but the opposite was true of the leg—perhaps because of the greater convective surface-cooling associated with movement. After exercise in Situation B the subjects were stiff and clumsy, but were still able to perform a full knees-bend.

Clothing Insulation

Determination of clothing insulation was not a primary purpose in this investigation, as this had been done previously. However, the data collected permitted further estimates on three subjects which are summarized in Table IV and confirm the previous findings (Pugh, 1966b).

TABLE IV.—Effect of Exercise, Wind, and Wetting on Apparent Clothing insulation in $\frac{\text{kcal.}}{\text{m}^2 \text{ h}}$ with Clo Units in Parentheses.

	Rest		Work	
	No. of Observations	Value	No. of Observations	Value
A. Dry clothing, no wind	2	0.465 (2.58)	5	0.204 (1.13)
B. Wet clothing, wind	1	0.105 (0.58)	8	0.071 (0.39)

Insulation was calculated as $\frac{T_s - T_a}{H}$, where T_a and T_s are ambient temperature and mean skin temperature and H is non-evaporative heat loss from body surface in kcal./m² h. 1 Clo unit = 0.18 $\frac{\text{kcal.}}{\text{m}^2 \text{ h}}$ and is equivalent to insulation afforded by ordinary business clothing.

Discussion

The cold stress examined in these experiments was judged to be comparable with that commonly encountered in natural conditions when casualties occur. The relatively high dry-bulb temperature of 5° C. and moderate wind velocity were offset, with respect to the cooling demand on the body, by a high rate of evaporative cooling due to low humidity. Ambient temperature corrected for evaporative cooling can be calculated from observed values of clothing and tissue insulation (Pugh, 1966b) if the equilibrium value of rectal temperature is known. Extrapolation of cooling curves suggested a value of about 34° C. at a work rate of 400 kg. m./min., and the equivalent ambient temperature worked out at 0° C. Winds of gale force would of course increase the environmental cooling power, as well as being an important contributory cause of exhaustion (Pugh, 1966a).

It appears that mountaineers and experienced hill-walkers habitually operate at O₂ intakes of about 2–2.5 l./min. (Pugh, 1958, 1964, and unpublished results), or 50–60% of capacity (maximum O₂ intake), in which case they would be relatively immune from discomfort and extra fatigue in average wet-cold situations because they would be working above the cut-off level of the cold response. On the other hand, persons who for one reason or another have a lower physical working capacity will become exhausted through working too close to capacity if they walk fast enough to keep warm; and if they maintain a slower pace they will suffer an obligatory increase of O₂ intake of perhaps 30–50%, as well as intense discomfort.

In the conditions simulated in this investigation the extra O₂ intake amounted to 14–19% of the subjects' estimated maximum O₂ intake. Precise data are not available on the relation between O₂ intake relative to capacity and endurance in outdoor sports other than athletics,

but one would expect tolerance times to be halved in persons working at 75% of capacity compared with 60%. On the other hand, if a person under cold stress reduces his pace so as to keep his O_2 intake at 60% capacity he will then be expending as much energy in covering a given distance as he would be going 30–50% further in warmer conditions, not to mention the greater discomfort.

We did not compare tolerance times in this investigation, but the subjects' statement that they found work at rates below 900 kg. m./min. more tiring in the wet-cold situation can readily be accepted. Adolph and Molnar (1946) found that their subjects, working nude at 0° C., became confused and exhausted in one hour while working at a rate they maintained easily for four hours in warmer conditions. These authors regarded the pain and discomfort of severe cold stress as important a cause of exhaustion as the extra O_2 intake.

The results in Fig. 1 show considerable variation in the O_2 intake and work rate at which the metabolic response to cold stress subsided. Indeed, the position of the horizontal section of the O_2 intake/work rate line can be regarded as a measure of the effective cold stress on the individual. This would depend on a combination of factors such as clothing insulation, physical type, thickness of subcutaneous fat and sensitivity to cold (Strømme, Lange Andersen, and Elsner, 1963). Individual variation in effective cold stress under given environmental conditions may explain the apparently random incidence of hypothermia casualties among parties of hill-walkers who are accustomed to walking together and who might therefore be assumed to be evenly matched. For if a party caught out by bad weather increases its pace in order to keep warm, those whose O_2 intake is above the cut-off point of the cold response experience no extra fatigue and comparatively little discomfort. On the other hand, those who are exposed to greater effective cold stress may be still operating below the cut-off point and will become exhausted much sooner.

In youth movements and organized parties where individuals do not choose their companions, the factor of variation in physical work capacity is another obvious source of danger, and one cannot help wondering whether the arbitrary division of young people into groups without reference to their exercise history is justified in activities such as hill-walking and mountaineering.

The above results provide a rational explanation of events on the Four Inns Walk 1964, in which there were numerous exposure casualties (Pugh, 1964). Severe weather conditions developed shortly after the start of the 50-mile (80-km.) race. Lightly clad leading teams completed the course in times comparable with those of previous years; but among slower teams, who wore clothing similar to the outfit used in this study, casualties began to occur about five hours after the start and there were three fatalities.

Thermoregulation

It is seen from Table II that the metabolic response to cold stimulation at a mean skin temperature of 20° C. was inhibited at a rectal temperature of 37.8° C. The data cannot be correlated with results of experiments on subjects immersed in baths or exposed nude in air because of the different regional distribution of skin temperature (Carlson, 1954). But they are consistent with the hypothesis put forward by Benzinger (1962) that the posterior hypothalamic centres which mediate impulses from the cutaneous cold receptors receive afferent inhibitory impulses from the preoptic centres, which are sensitive to cranial temperature.

Pooled results suggested a linear relation between extra O_2 intake due to cold and rectal temperature, but the individual results showed a more or less constant increase in O_2 intake below 800 kg. m./min., and one might argue that only those muscles not engaged in active work were available for

shivering. This would explain the greater rise of resting O_2 intake as well as the finding that O_2 intake at low work rate did not increase as rectal temperature fell (Figs. 3 and 4). Further work is needed to settle this question.

The lowest rectal temperature observed in the series was 35.2° C. in R.M. working at 400 kg. m./min., and extrapolation suggested a value of 34.0–34.5° C. after five hours. It is known that Channel swimmers can continue swimming with rectal temperatures as low as this (Pugh *et al.*, 1960), though a non-cold-adapted swimmer studied by Pugh and Edholm (1955) regularly failed with muscle weakness when his rectal temperature reached 34.5° C. The results illustrated in Fig. 4, however, imply that exhaustion may come on while rectal temperature is still above 37.0° C. (see also Adolph and Molnar, 1946), but in this case rectal temperature falls extremely rapidly after cessation of active exercise. We did not feel justified in following this stage longer than 30 minutes in our subjects, but there is evidence that the metabolic response to cold passes off when rectal temperature falls below 34° C., and this would greatly hasten body-cooling (Burton and Edholm, 1955).

The role of local muscle-cooling in accidental hypothermia is difficult to evaluate without further investigation. Clarke, Hellon, and Lind (1958) found the maximum tension exerted during voluntary sustained contractions of the forearm muscles showed little or no reduction with decreasing muscle temperatures to about 27° C., but when temperature was reduced below 27° C. tension rapidly decreased. In their experiments the muscle temperatures were measured about half-way between the skin and the centre of the forearm, and the large temperature gradients through the forearm led to the suggestion that at muscle temperatures lower than 27° C. the outer and cooler layers of the muscle fibres were inactive.

The present findings are consistent with the view that muscle temperatures might fall low enough to cause serious weakness by the time rectal temperature had fallen to 34.5° C. Low muscle temperatures may also be related to other symptoms of incipient hypothermia such as stiffness, stumbling, and cramp.

Clothing

The clothing results confirm previous findings that the combination of wind, exercise, and wetting reduces clothing insulation to very low values. They also show that in the wet-cold situation insulation was 50% higher in rest than during exercise. In an outdoor situation a further improvement in effective insulation could be obtained by getting out of the wind and adopting a curled-up posture. Accordingly parties caught by bad weather will usually survive if they bivouac in good time while their metabolic response to cold is still intact.

Summary

Observation of O_2 intake and body temperature on clothed subjects during ergometer exercise in a simulated wet-cold situation (mean skin temperature 20° C.) showed that at work rates up to 800 kg. m./min O_2 intake increased by 0.4–0.5 l./min. compared with control observations at similar work rates without cold stress. At work rates of 900 kg. m./min. and over there was no metabolic increase in response to cold. At the lower work rates rectal temperature fell towards new levels depending on the work rate. At high work rates rectal temperature remained at, or close to, the normal set point for the given work rate. Muscle temperatures and clothing insulation were also investigated. The findings are discussed in relation to accidental hypothermia in outdoor activities.

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Hodgkin's Disease*—II

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General Manifestations

Hodgkin's disease differs from most other invasive neoplasms chiefly in its recurrent spontaneous regressions, its fever (often remitting), its varied and severe infections (frequently of the rarer and opportunistic kinds), its anergy, immunoglobulin abnormalities, anaemias, lymphoid depletion, pruritus, loss of weight (sometimes severe at the onset of the disease), its tendency to affect near relatives, and its association with certain virus diseases. It is indeed characterized by those general symptoms which are concerned with its origins as a proliferative disorder of immunologically active cells complicated by the wide destruction of lymphocyte and blood-forming tissue effected by the treatments given. The most dramatic demonstration of anergy in this disease is the acceptance of foreign skin grafts, shown in some lymphomas and notably in Hodgkin's disease by Kelly, Good, and Varco (1958) and by Green and Corso (1959), and repeated for me by my colleague, Mr. C. I. Cooling, on several of my patients (Fig. 5).

FIG. 5.—Three thicknesses of skin graft from a father to his son with Hodgkin's disease, showing no immune reaction. Grafts intact to death. A, 11 April 1960. B, 3 May 1960.

It is often difficult to pin down the beginnings of Hodgkin's disease. Previous illness may be attributed to other causes by the patient or dismissed or not inquired into by the doctor. The closer the inquiry the more frequently is a history of illness before the first node enlargement obtained and the more often is there a story to be heard of spontaneous remission, with nodes increasing and then decreasing in size. Ten patients

in our series of 350 seen during 1945–64 gave a clear-cut history of such remissions. The longest period during which remissions took place without treatment was 12 years; a node was removed and confirmation of the diagnosis obtained at the start of this long period. This patient is one of only two in our series in whom regression was noticed in lymph-node sites other than the neck (where it is easiest to detect), but she also showed spontaneous regression and return of metastases in the lungs. Some of the other patients noticed neck nodes enlarging and diminishing but tending to get larger and stay longer each time. One patient had attacks of fever and pruritus with each exacerbation. Most of these patients had one remission, and came to treatment when symptoms recurred. The regressions were repeated over one to three years in three patients, a regression lasted two years in one patient, and regressions lasted three to six months in five patients.

Fever, loss of energy, and loss of weight (sometimes severe) may occur before the lymphadenopathy is noticed. Out of 271 staged patients, 108 had developed these general symptoms by the time they were first seen. Loss of weight was severe in 32, 16 of whom said they had lost a stone (6.4 kg.) or more. Of these 108 patients 45 (42%) had general symptoms before they or their doctors detected any node enlargement. Seventeen of the 45 had general symptoms manifest less than six months before lymph-node enlargement was detected; in 11 patients the interval was six months to one year; in 13 the interval was one to two years; and in four more than two years. From the start some of these patients—perhaps all—had nodes involved, possibly in the mediastinum or abdomen, but nevertheless a general illness may be the first sign of the disease in 16% or more of all new cases seen. One patient felt ill for a long time; repeated examinations showed nothing abnormal, and he joined a merchant ship as doctor for a year, hoping that the change would help him to recover. He got worse, and by the end of the year had further weakness, dyspnoea, pruritus, and anaemia, with swelling of his ankles. An enlarged node was first detected and removed two years after he began to feel weak; he was dead three months later.

Relation to Other Disorders

The relation of Hodgkin's disease to certain other disorders is a fascinating study in itself, and cannot be more than touched on here. The commonest of these associated disorders is herpes zoster, the generalized form of which—indistinguishable from varicella—is to be seen most frequently in patients with lymphomas (Burgoon, Burgoon, and Baldrige, 1957; Williams, Diamond, Craver, and Parsons, 1959). Dayan, Morgan, Hope-Stone, and Boucher (1964) reported four cases of the generalized

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