STUDIES OF THERMAL INJURY. VII.[1] PHYSIOLOGICAL MECHANISMS RESPONSIBLE FOR DEATH DURING CUTANEOUS EXPOSURE TO EXCESSIVE HEAT

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INTRODUCTION

In a previous study in this series (1), attention was called to the fact that acute hyperthermic circulatory failure in some animals was accompanied by, and probably contributed to, by large increases in the potassium concentration of the plasma. An investigation of the circumstances in and the sources from which thermally induced rises in plasma potassium occur has been reported (2).

Although it appears that acute potassium poisoning is probably one, it is obvious that it is not the only mechanism by which cutaneous exposure to heat may cause rapidly fatal circulatory failure. The following experiments were undertaken to investigate more fully the physiological mechanisms by which cutaneous hyperthermia may result in acute circulatory failure and death.

The acute physiological disturbances caused by systemic hyperthermia have attracted the attention of a number of investigators. Heymans (3) injected methylene blue into dogs anesthetized with chloralose. This produced a gradually mounting rectal temperature which reached the lethal level of 43.7° C. to 44.8° C. in 1 to 1½ hours. The heart rate rose gradually from 90 to 120 to 300 to 330 per minute. At first, the respirations were deep and rapid (less than 200 per minute); after the temperature had risen to 41.5° to 43.5° C. they became very shallow and even more rapid (over 300 per minute). Systolic pressure rose and diastolic pressure fell. Respiration almost always failed first, and artificial respiration enabled the heart to continue for a longer time. Reflexes persisted up to the time of respiratory standstill. Uyeno (4) produced hyperthermia in cats, anesthetized with urethane, by exposing them to water of 41° to 42° C. or to a high environmental air temperature. During the 30 minutes of exposure the rectal temperature rose from 35° to 39° C. There was little increase in heart rate, but a pronounced rise in minute-volume output. Shortly after exposure the respiratory rate increased to an average of 200 per minute. This breathing was very shallow (tidal air 2 to 3 ml. per minute) and sometimes resulted in a 29 per cent drop in arterial oxygen saturation. Cheer (5) placed dogs anesthetized with morphine and barbital in a cabinet heated by electric light bulbs. In 2 to 3 hours a lethal (rectal?) temperature of 43° to 45° C. was reached. The heart rate increased progressively until a temperature of 42° to 44° C. was reached, when the heart slowed rather suddenly. Before this stage, electrocardiographic abnormalities were limited to slight abbreviation of the PR interval, slight changes in the QRS complex, and inversion of the T wave. The terminal bradycardia was due to the development of nodal rhythm or of various other types of ventricular rhythm. Systolic and diastolic pressures remained fairly constant up to 41° C., then both dropped, the former more than the latter. The respiratory rate also increased. Respiratory standstill usually occurred before cardiac arrest, vagotomy delaying respiratory failure. A progressive decrease of the blood carbon dioxide was found associated with slight alkalosis and rise of oxygen content which were ascribed to the increased pulmonary ventilation. From the same laboratory, Wiggers and Orias (6) reported observations on the effects of short radio waves on dogs. The cardiac acceleration, increase in rate and depth of the respiration, and primary failure of the respiration were identical with the findings of Cheer (5). However, instead of a decrease in blood pressure, a rise of systolic and diastolic pressure was observed which progressed until death.

Clinical observations on the effect of hyper-

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thermia were made by Ferris (7) *et al.* Patients with heat stroke whose rectal temperatures varied from 39.9° to 44.0° C. exhibited a hot dry skin, a normal or elevated systolic pressure, which dropped to low levels only in the terminal stage, and venous pressures of from 2 to 12 cm. of saline. Their respiratory rate was 28 to 50 per minute. Of 29 patients (all comatose) whose temperatures exceded 41.5° C., 17 died; all others recovered.

Attempts to analyze the disturbances observed in the intact organism by elevating the temperature in one organ have been made since 1872. Fick (8) heated the blood as it passed through the carotid arteries of the dog and noticed marked hyperpnea without change in heart rate or blood pressure. Cyon (9) isolated the circulation of a dog's head. Perfusion of the head with heated blood produced bradycardia and a drop in blood pressure. Kahn (10) warmed the carotid arteries of unanesthetized dogs without producing a rise in rectal temperature. He observed the development of tachycardia and a moderate rise in blood pressure. Moorhouse (11) heated the carotids and simultaneously cooled the jugular veins in dogs. This resulted in tachycardia, rarely preceded by bradycardia, ascribed respectively to increased sympathetic and vagal activity. Coincidentally, tachypnea and peripheral vasodilatation were observed. Heymans and Ladon (12) severed all connections except the vagal nerves between head and trunk of dogs anesthetized with chloralose. Artificial respiration was applied and the circulation in the head maintained by connecting it to a donor dog. The sublingual temperature of the preparation rose to 45° C. in 1½ hours. There was no change in the heart rate which had risen to 160 after severance of the cervical cord. The head exhibited a progressive and pronounced increase in respiratory rate which persisted until a sublingual temperature of 45° C. was reached when the rate rapidly decreased and the reflexes of the head, which had been active up to that time, disappeared.

The effect of hyperthermia on the heart was investigated by Knowlton and Starling (13) using the innervated heart-lung preparation, perfused with heated blood. From 26° C. to approximately 45° C. the heart rate was a linear function of the blood temperature, the rate at 45° C. being 180 per minute. Above this temperature marked slowing occurred and the heart soon stopped. Arrhythmias occurred above 40° C.

Summarizing these data, it can be said that in the dog, the highest rectal temperature compatible with life lies between 43° and 45° C., when this temperature is reached in 1 to 3 hours. Respiratory failure often seems to precede circulatory failure. Tachypnea, tachycardia, and peripheral vasodilatation seem to be, in part at least, of cerebral origin.

The physiological changes of rapidly developing hyperthermia leading to death within ½ hour have not been heretofore studied. As high environmental temperatures are needed for such experiments, the results are necessarily complicated by the damaging effect of heat on the skin directly. Moreover, these high temperatures will produce damage to the red blood cells that are circulating in the small vessels of skin and underlying tissues (Shen *et al,* 14).

EXPERIMENTAL PROCEDURE

Young pigs, weighing from 6.4 to 18 kgm., and adult dogs, weighing from 7.4 to 8.5 kgm., were used as experimental animals. They were anesthetized with pentobarbital sodium (32 mgm. per kgm. intraperitoneally), shaved, and tied to a wooden animal board. This was lowered into a galvanized iron tank (92 × 46 × 41 cm.). The head of the board rested on a metal bar in the tank, so that it was slightly higher than the foot. A similar tank, placed on a high table, partly projected over the former. This tank was filled with water steam-heated to the desired temperature. In the bottom of the projecting part was a circular opening, 13 cm. in diameter, that could be closed with a heavy rubber and metal stopper. Removal of this stopper resulted in immersion of more than ½ the body surface of the animal in 8 to 10 seconds. During immersion, the temperature of the water, which was continuously stirred, was kept within narrow limits by intermittent introduction of steam. Drainage of the water and termination of exposure could also be accomplished in 8 to 10 seconds. Temperatures ranging from 44° to 75° C. were used.

Previous to exposure, all animals were heparinized (3 mgm. per kgm. intravenously). Because of spasmodic closure of the glottis on immersion, a tracheal cannula was inserted. The carotid pressure was recorded with a mercury manometer. The right auricular pressure was measured by means of a rubber catheter introduced into the superior vena cava or right auricle by way of the external jugular vein and connected with a water manometer. The level of the right auricle as determined by opening the chest at the end of the experiment was taken as point of reference. In pigs the hydrostatic pressure did not influence the auricular pressure. In dogs immersion resulted

in a considerable rise in recorded auricular pressure, so that only changes occurring during exposure could be compared. Pneumograms were obtained by means of a copper cannula thrust between the ribs into the pleural space and connected by means of a rubber tube to a writing tambour. In other experiments, a tracheal cannula provided with a sealed-in side tube connected to the tambour was used.

Electrocardiograms were taken with an amplifier type of electrocardiograph. It was only possible to take the first standard lead, as the hind legs of the animal were under water. In some experiments, curarized animals were used and artificial respiration was applied throughout the exposure. Intocostrin (Squibb), 1 mgm. per kgm. diluted with saline, was slowly injected intravenously. The side reactions were limited to a short (20 to 30 seconds) period of mild excitation. The drug had no effect on the arterial pressure. A second smaller dose usually had to be given 20 to 40 minutes later. A Palmer respiration pump for small animals which allows the air to escape spontaneously on expiration was used. When venous pressures were recorded the animals were immersed in such a man-

TABLE I

Rectal temperature, arterial pressure and electrocardiogram of 12 pigs immersed in hot water

A—Normal sinus rhythm (normal rate, tachycardia or bradycardia). Normal duration of QRS complex.
A′—First or second degree A-V block. Normal duration of QRS complex.
A″—Complete A-V block. Normal duration of QRS complex.
B—Slight, BB—Moderate, BBB—Pronounced } Widening of QRS complex without P wave.
BBB—Can often be interpreted as ventricular fibrillation.

Time		Rectal temp.	Arterial pressure	ECG
min.	*sec.*	*° C.*	*mm. Hg*	
Pig 876 (7.7 kgm.) 48° C. Died after 26.5 min.				
Control		34.3	118	A
16	00	44.0	66	A
24	30	45.2	42	A
26	30	45.7	76	BB
Pig 875 (6.4 kgm.) 48–50° C. Died after 35 min.				
Control		35.0	130	A
27	30	42.2	64	A
29	00	42.8	64	A
34	15	43.7	26	A
Pig 878 (12.0 kgm.) 47° C. Died after 50 min.				
Control			110	A
29	00		70	A
37	20		50	A
49	30	44.9	30	A
Pig 879 (11.8 kgm.) 44–47° C. Died after 106.5 min.				
Control		36.8	106	A
33	00	43.1	54	A
Out of hot bath* from 33.5 to 48.5 min.				
49	53	42.0	116	
79	30	44.1	86	A
105	00	44.5	14	A

Time		Rectal temp.	Arterial pressure	ECG
min.	*sec.*	*° C.*	*mm. Hg*	
Pig 895 (18.0 kgm.) 49° C. Curare. Died after 32 min.				
Control		37.8	148	A
15	00	41.9	172	A
25	30	43.7	76	A
31	30	44.0	10	A′**
Pig 943 (8.3 kgm.) 47° C. Curare. Died after 36 min.				
Control		37.7	126	A
17	00	42.6	126	A
29	00	44.5	136	A
Pig 897 (16.4 kgm.) 47° C. Curare. Died after 56 min.				
Control		37.9	146	
24	00	43.5	146	A
47	00	44.0	90	A
55	00		36	A′
Pig 946 (9.5 kgm.) 47° C. for 23 min. Curare. Died after 42 min.				
Control		40.1	82	A
17	00	43.0	120	A
26	00	44.4	40	A
34	30	44.6	26	A

Time		Rectal temp.	Arterial pressure	ECG
min.	*sec.*	*° C.*	*mm. Hg*	
Pig 944 (10.4 kgm.) 47° C. for 25 min. Died after 99 min.				
Control		38.1	108	A
14	00	43.5	120	A
26	00	45.4	100	A
37	00	44.1	90	A
Pig 867 (7.3 kgm.) 64–65° C. Died after 15 min.				
Control			146	A
5	30		72	A
10	30		72	A
15	00	46.0	12	BB
Pig 872 (7.3 kgm.) 64–65° C. Died after 11 min.				
Control			150	A
7	00		50	A
10	30		50	BB
10	45		40	BBB
Pig 871 (9.1 kgm.) 70–73° C. Died after 12 min.				
Control			100	
5	30		74	A
6	10		74	BB
9	30		54	BBB
12	00	44.5	24	BBB

* Skin temperature lowered by exposure to cool water between two episodes of cutaneous hyperthermia.
** Occasional ventricular extrasystole.

ner that most of the anterior thorax remained above the water level. This was sufficient to abolish artefacts produced by the increased resistance to the inflow of air.

Temperatures were recorded with a thermocouple introduced to a depth of 7 to 9 cm. into the rectum, which had been cleaned by repeated enemas. The anus was closed around the couple. In 3 experiments, heart temperatures were also recorded by means of a thermocouple introduced through the external jugular vein into the right auricle. In some experiments only initial and final rectal and final heart temperatures were measured with a sensitive thermometer. In a considerable number of animals blood was withdrawn from the jugular vein both before and during exposure for the determination of the hematocrit and of hemoglobin and potassium content of red cells and plasma. In most instances, immersion was continued until death. In some experiments exposure was temporarily interrupted, and in a few cases, immersion was terminated at a time when the animal was still living.

In addition to these observations, 3 pigs were infused with an isotonic (1.12 per cent) solution of KCl. Frequent electrocardiograms (lead I or II) were taken. In one of these pigs, the arterial and right auricular pressure and respirations were also recorded. The latter ani-

TABLE II

Rectal temperature, arterial pressure, electrocardiogram, and potassium content of plasma of 15 pigs immersed in hot water

A—Normal sinus rhythm (normal rate, tachycardia or bradycardia). Normal duration of QRS complex.
A′—First or second degree A-V block. Normal duration of QRS complex.
A″—Complete A-V block. Normal duration of QRS complex.
B—Slight, BB—Moderate, BBB—Pronounced } Widening of QRS complex without P wave.
BBB—Can often be interpreted as ventricular fibrillation.

Time		Rectal temp.	Arterial pressure	ECG	K plasma
min.	*sec.*	° *C.*			*meq. per L.*
Pig 877 (7.0 kgm.) 47° C. Died after 26 min.					
Control		34.3	96	A	3.8
10	20	41.6	136	A	6.2
14	05	42.5	112	A″	6.9
24	10	44.3	56	A″	8.2
Pig 923 (13.6 kgm.) 47° C. Died after 50 min.					
Control			116	A	3.8
13	15		146	A	5.5
22	30		148	A	5.5
34	15		102	A	6.2
42	00		56	A	6.5
46	33		66	A	7.5
Pig 1057 (8.0 kgm.) 47° C. Died after 36.5 min.					
Control		37.0		A	4.4
19	50			A	7.0
36	15			A	10.2
36	30	45.5		0	
Pig 1056 (7.0 kgm.) 47° C. Died after 44.5 min.					
Control		37.8		A	4.7
9	30			A	5.9
15	07			A	7.2
34	00			A	7.1
44	30	45.5		0	

Time		Rectal temp.	Arterial pressure	ECG	K plasma
min.	*sec.*	° *C.*			*meq. per L.*
Pig 910 (9.5 kgm.) 72–75° C. Died after 12.5 min.					
Control		36.8	148	A	3.0
2	15	40.7	100	A	19.1
4	40	40.7	86	BB	18.1
7	20	41.5	74	BBB	24.0
13	52	43.7	10	0	17.3
Pig 912 (10.0 kgm.) 72–75° C. Died after 14 min.					
Control		36.0	88	A	4.1
1	20	35.4	154	A	16.7
3	35	37.0	98	BB	
5	07	37.1	74	BB	16.4
9	45	40.8	74	BBB	16.4
13	40	43.1	30	BBB	
Pig 908 (9.1 kgm.) 75° C. Died after 13.5 min.					
Control			96	A	3.8
3	40		96	BB	16.7
8	55		60	BBB	18.5
11	10		52	BBB	17.1
Pig 907 (10.4 kgm.) 75° C. Died after 10 min.					
Control		37.1	116	A	3.5
		37.3*			
6	00	39.0	48	BBB	
		42.7*			
7	30	39.2	32	BBB	17.4
		42.5*			

* Right heart temperature.

TABLE II—*Continued*

Time		Rectal temp.	Arterial pressure	ECG	K plasma
min.	*sec.*	° *C.*			*meq. per L.*
Pig 905 (12.7 kgm.) 75° C. Curare. Died after 23 min.					
Control			94	A	4.8
16	30	41.6	78	BB	
22	40	42.1	32	BBB	17.3
Pig 921 (16.8 kgm.) 75° C. Curare. Died after 27 min.					
Control			122	A	3.2
3	30		66	A	5.1
8	00		58	BB	11.6
18	00		36	B	11.9
26	45		28	B	10.2
Pig 906 (13.0 kgm.) 70–75° C. Curare. Died after 70 min.					
Control		38.6	102	A	4.0
10	50	41.4	112	BBB	
16	35	42.3	62	BB	17.4
25	20	43.0	92	BBB	15.2
44	35	44.6	72	BB	13.3
46	40	44.8	46	A	
48	29	45.0	46	BB	
65	00	46.8	46	BBB	
Pig 913 (8.2 kgm.) 75° C. for 6.5 min. Died after 7.5 min.					
Control		38.6	100	A	3.5
2	25	37.9	100	B	14.2
6	15	40.5	50	BBB	17.7
7	45	40.8	15	0	17.4

Time		Rectal temp.	Arterial pressure	ECG	K plasma
min.	*sec.*	° *C.*			*meq. per L.*
Pig 919 (9.1 kgm.) 75° C. for 5 min. Died after 18 min.					
Control		37.1	138	A	4.2
4	15	41.1	78	BB	25.5
7	45	42.3	28	A	21.4
10	10	43.2	26	A	18.3
14	00	44.2	30	B	17.0
16	45	44.3	14	B	17.5
Pig 918 (8.7 kgm.) 75° C. for 3 min. Died after 55 min.					
Control		36.6	70	A	3.7
4	25	38.7	56	A	11.0
11	00	39.7	62	A	9.5
17	05	40.3	70	A	9.5
37	00	40.6	70	A	9.4
Pig 899 (13.6 kgm.) 75° C. for 1 min. Sacrificed after 77 min.					
Control		37.4	142	A	3.6
5	15	40.5	30	A	10.2
16	05	40.5	76	A	6.9
45	45	40.3	76	A	4.2
76	00	39.2	76	A	7.4

mal received the solution in the subclavian vein, the other two in the jugular vein. Blood samples for the determination of potassium were taken from the carotid artery.

RESULTS OF EXPERIMENTS

In Table I are shown the results of 12 experiments in which pigs were exposed for varying periods of time at temperatures ranging between 44° and 73° C. Changes in rectal temperature, arterial pressure, and electrocardiogram are indicated.

In Table II are shown the results of 15 experiments in which pigs were exposed at temperatures ranging between 47° and 75° C. The changes that occurred in the potassium concentration of the plasma are indicated in relation to changes in rectal temperature, arterial pressure, and electrocardiogram.

In Table III are shown the results of 5 experiments in which dogs were exposed for varying periods of time at temperatures ranging between 55° and 75° C. The changes that occurred in the potassium concentration of the plasma are indicated in relation to changes in rectal temperature, arterial pressure, and electrocardiogram.

In Table IV are shown the results of 3 experiments in which pigs received intravenous infusions of isotonic potassium chloride. The changes in the potassium concentration of the plasma and the erythrocytes are indicated in relation to changes in hematocrit, arterial pressure, and electrocardiogram.

Arterial blood pressure: The immediate effect of immersion in water of 60° to 75° C. upon the mean arterial pressure of pigs was a rise which

TABLE III

Rectal temperature, arterial pressure, electrocardiogram, and potassium content of plasma of 5 dogs immersed in hot water

A—Normal sinus rhythm (normal rate, tachycardia, or bradycardia). Normal duration of QRS complex.
B—Slight widening of QRS complex without P wave.

Time		Rectal temp.	Arterial pressure	ECG	K plasma
min.	*sec.*	*° C.*	*mm. Hg*		*meq. per L.*
Dog 931 (7.4 kgm.) 55° C. Died after 23 min.					
Control		35.4	112	A	2.8
5	10	37.0	92	A	5.2
13	15	40.6	58	A	4.7
20	45	41.4	18	A	6.9
Dog 930 (7:5 kgm.) 60° C. Died after 16.5 min.					
Control		36.9	100	A	4.0
4	45	37.4	86	A	3.3
7	55	38.0	64	A	4.7
10	40	39.1	66	A	5.3
Dog 922 (8.5 kgm.) 75° C. Died after 15 min.					
Control		37.9	118	A	3.1
2	55	37.6	90	A	5.8
6	30	38.4	68	A	6.4
10	20	39.0	76	A	5.8
15	00	39.3	30	A	6.8
Dog 929 (8.2 kgm.) 75° C. Died after 13.5 min.					
Control		37.2	130	A	3.9
3	10	38.5	130	A	4.8
8	30	42.1	120	A	6.1
12	45	44.1	74	B	8.2
Dog 934 (7.6 kgm.) 75° C. Died after 25 min.					
Control		34.6*	148	A	3.1
15	16	41.7*	100	A	
24	45	43.5*	72	A	6.9

* Right heart temperature.

sometimes amounted to as much as 140 mm. Hg. This rise also occurred in curarized animals or when hot water was splashed on the skin. It was absent at immersion temperatures of 45° to 47° C.

At temperatures of 44° to 59° C. the blood pressure was maintained at or above pre-immersion level for 16 to 26 minutes. It began to fall at variable times during exposure and reached half of the original value in 17.5 to 41 minutes. The rectal temperature at this time had risen from 34.3° to 40.1° C. to 42° to 44° C. These animals

TABLE IV.

Physiological and chemical changes in three pigs intravenously infused with an isotonic (1.12 per cent) solution of KCL

A—Normal sinus rhythm (normal rate, tachycardia or bradycardia). Normal duration of QRS complex.
B—Slight
BB—Moderate } Widening of QRS complex without P
BBB—Pronounced } wave.
BBB—Can often be interpreted as ventricular fibrillation.

Time		Arterial pressure	ECG	Hematocrit	K plasma	K cells
min.	*sec.*	*mm. Hg*			*meq. per L.*	*meq. per L.*
Pig 901 (14.8 kgm.). Rate of infusion *0.6 ml. per kgm. per min.* Died after 50 min.						
Control			A[1] (lead I)	36	4.3	123
11	00		A[1]	36	9.0	125
16	00		A[1]	37	9.5	124
18	00		BB	38	11.2	121
26	00		BBB	37	15.5	132
			Infusion stopped			
26	10		0			
35	00		0			
36	00		A			
41	00		A	38	8.7	139
41	30		Infusion started again. Rate *0.7 ml. per kgm. per min.*			
50	00		BBB	35	17.7	136
Pig 911 (8.7 kgm.). Rate of infusion *0.9 ml. per kgm. per min.* Died after 22.5 min.						
Control			A (lead II)	35	3.2	127
11	00		A[2]	34	8.7	122
14	00		B	35	10.6	122
16	00		BBB	35	12.7	125
20	00		BBB	31	27.0	
22	00		0	28	38.0	127
Pig 925 (15.9 kgm.). Rate of infusion *0.6 ml. per kgm. per min.* Died after 39 min.						
Control		76	A (lead II)	33	3.5	112
6	08	76	A	33	5.7	117
12	40	76	A	32	10.6	114
19	37	76	A[3]	34	12.7	110
24	50	76	B	37	15.7	109
35	18	24	BBB	37	26.1	111

1—P wave not clearly shown.
2—P wave getting blunt.
3—P wave very flat.

died after 25.5 to 50 minutes with rectal temperatures of 43.9° to 45.8° C., the heavier pigs surviving somewhat longer than the lighter ones. Heart temperatures were within a few tenths of a degree of these values (Figure 1).

In pigs exposed to water of 60° to 75° C., the arterial pressure was maintained for 1 to 6 minutes, and reached half of its original value in 5.5 to 11 minutes. The animals died after 8 to 15 minutes with rectal temperatures varying from 39.4° to 46.0° C. However, the discrepancy between heart and rectal temperature often was considerable (Figure 1).

The possible reversibility of the fall in arterial pressure was investigated. Immersion of a pig at 47° C. for 33 minutes produced a fall in blood pressure from 104 to 40 mm. Hg (Figure 2). Exposure to cool water brought the pressure back to its original level and lowered the rectal temperature from 43.3° to 42.0° C. Re-exposure to 47° C. again resulted in a fall in blood pressure, and death occurred at a rectal temperature of 44.5° C. In another instance exposure to water of 75° C. for 1 minute reduced the pressure from 140 to 20 mm. Hg in 5 minutes. During subsequent exposure to room air the pressure recovered, and reached 130 mm. Hg after 73 minutes. The animal was still alive after more than 2 hours. Exposure of one animal to water of 75° C. for 5 minutes resulted in a fall in blood pressure from 138 to 75 immediately after immersion. The pressure continued to fall, and the animal died after 18 minutes.

The arterial pressure in dogs behaved in a way comparable to that in pigs at the same temperature. Animals immersed at 60° to 75° C. survived for 13.5 to 25 minutes (Table III).

Right auricular pressure: Intra-auricular pressures of pigs before immersion varied from 32 to − 66 mm. H_2O (average − 23 mm. H_2O). In only 3 out of 15 animals was the pressure in the right auricle higher than atmospheric (+ 13, 20, and 32 mm. H_2O). In most instances, a slight rise occurred following immersion, the control level

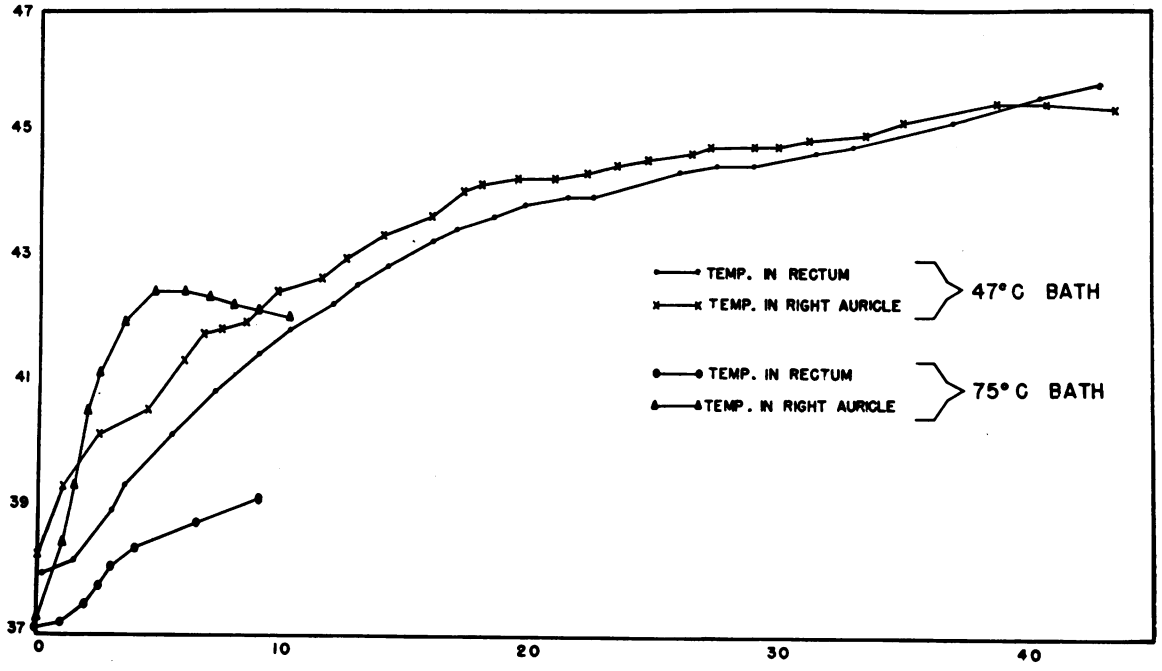

FIG. 1. PLOT OF THERMOCOUPLE RECORDINGS SHOWING RATE OF CHANGE IN RECTAL AND RIGHT AURICULAR BLOOD TEMPERATURES DURING IMMERSION IN LOW (47° C.) AND HIGH (75° C.) TEMPERATURE WATER BATHS

47° C.—Pig No. 882 (13.2 kgm.)
75° C.—Pig No. 907 (10.5 kgm.)

It may be seen that although the right auricular blood temperature rises rapidly after immersion there is considerable lag in the temperature rise in the rectum. The higher the temperature of the bath, the greater the lag.

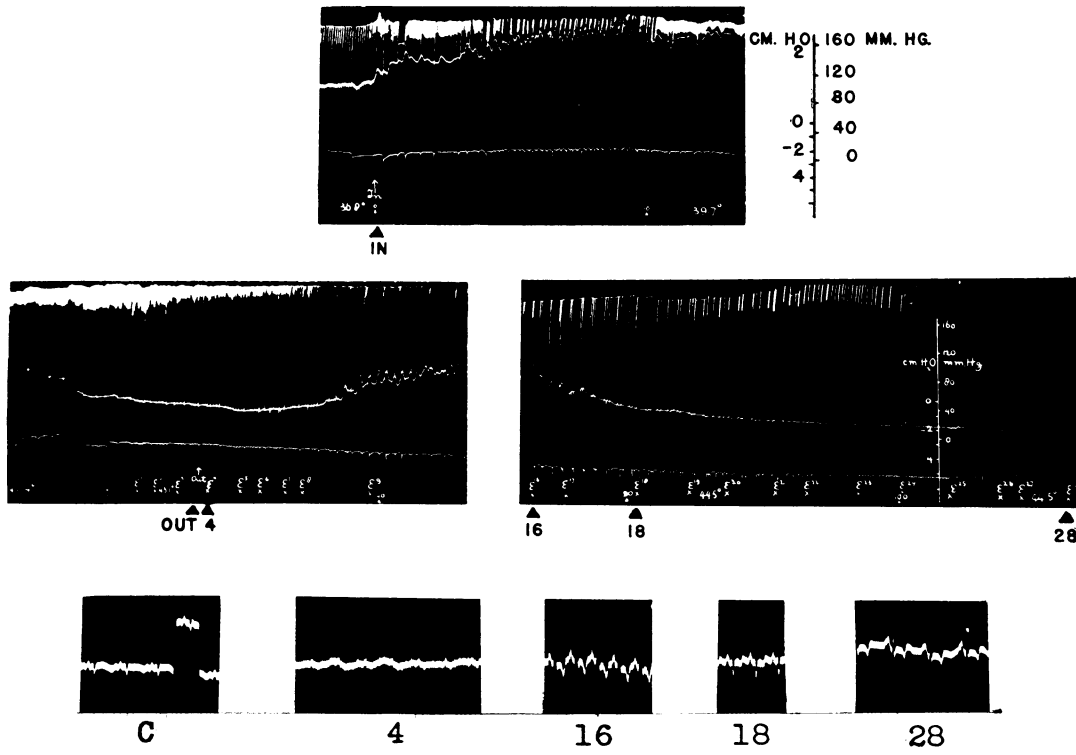

FIG. 2. EFFECT OF 2 EPISODES OF CUTANEOUS HYPERTHERMIA ON PIG NO. 879 (11.8 KGM.) CAUSED BY IMMERSION IN WATER AT 47° C.

The first period of immersion lasted for 33.5 minutes and is indicated by the words "in" and "out" on the first and second segments of the kymograph record. Fifteen minutes after the end of the first period of hot water immersion and between the second and third segments of the record the animal was immersed again at 47° C. and allowed to remain in the bath until dead (56.5 minutes). Between the 2 episodes of hot water immersion the skin temperature was lowered by exposure to cool water. Total duration of experiment was 105 minutes. The upper, middle and lower tracings on the kymograph record represent respectively the pneumogram, the carotid pressure, and the right auricular pressure. The times at which the electrocardiograms were taken are indicated in minutes.

being regained in 0.5 to 3 minutes. In 5 of the 6 animals immersed at 44° to 49° C., this was followed by a gradual drop of 4 to 20 mm. H_2O. There was no rise in venous pressure until 1 or 2 minutes before death. In the sixth pig, immersion did not influence the auricular pressure (Figure 2).

In 7 of the 9 pigs exposed to water of 60° to 75° C., a gradual rise of the right auricular pressure was observed, beginning in the middle of, or even early in exposure, and continuing until death. This rise amounted to 15 to 45 mm. H_2O and occurred at a time when both arterial pressure and respiration were still adequate (Figure 3). In some instances, it was preceded by a fall of 20 to 30 mm. H_2O which rapidly developed 1 to 3 minutes after the exposure had started. In 2 animals, this fall was the only change in auricular pressure that was observed until 1 minute before death when it rapidly rose.

One pig, exposed for only 1 minute to water of 75° C., showed an abrupt fall of 40 mm. H_2O. During the following 70 minutes the auricular pressure gradually returned to the pre-immersion level, coincidentally with recovery of the arterial pressure.

The auricular pressure of 4 dogs was lower than that of the pigs. It ranged from -77 to -108 mm. H_2O. Because of hydrostatic effects the auricular pressures before and during immersion could not be compared. However, neither in the 2 dogs exposed to 75° C. nor in those exposed to

55° and 60° C. was there observed any change in the recorded auricular pressure during the period of immersion.

Because of the possible contributions of the type or rate of breathing to the observed pressure changes, some experiments were performed on curarized pigs. Artificial respiration was supplied throughout the experiments. The course of the auricular pressure was found to be identical with that of the spontaneously breathing animals. At 47° to 49° C. a slow and moderate fall was observed; exposure at 75° C. resulted in a rise, beginning early during exposure.

Respiration: In agreement with earlier investigators, it was found that a rise in body temperature was associated with a pronounced increase in respiratory rate. In the pig, the immediate effect of immersion was usually a short period of very deep and fairly rapid respirations, followed by a variable episode of only moderately increased breathing (rate 20 to 40). In the animals exposed to the lower temperature range the onset of respiratory rates of 170 to 200 was often sudden, and occurred in the first 10 minutes of exposure, at rectal temperatures of 39° to 41° C. Deep gasps interrupted this shallow tachypnea. The arterial blood maintained its bright red color. The tachypnea gradually increased, and rates of 300 were not infrequently reached. When the rectal temperature had mounted to 43° to 44° C., breathing abruptly slowed to 10 to 40 per minute and became much deeper. Additional slowing usually continued until death. In the dog, immersion was immediately followed by a tachypnea of 100 to 150 per minute, which gradually increased. Rates over 200 were not encountered.

It is difficult to estimate whether the respiratory or the circulatory system failed first in these animals. If bradypnea is considered as the first manifestation of failing respiration it might be said that the cardiovascular system survived somewhat longer, as judged by the presence of an appreciable arterial blood pressure. However, at least in the beginning of bradypnea, the pulmonary ventilation certainly was as adequate as during the control period. If the onset of prolonged apnea is considered as the end point of adequate respiratory function, both systems failed simultaneously. In 3

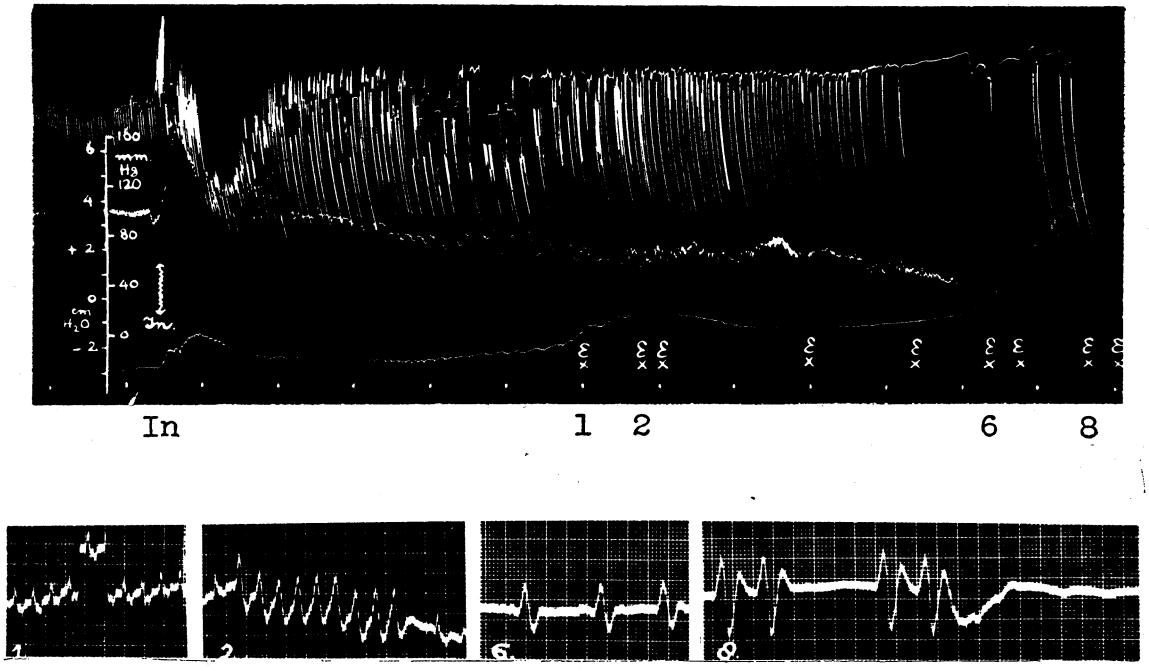

FIG. 3. EFFECT ON PIG NO. 871 (9.1 KGM.) OF IMMERSION IN WATER BATH AT 70° TO 73° C. FOR 12 MINUTES

The upper, middle and lower tracings on the kymograph record represent respectively the pneumogram, the carotid pressure and the right auricular pressure. The sequence in which the electrocardiograms were taken is indicated.

animals, artificial respiration was applied at a time when the arterial pressure was still appreciable (80–90 mm. Hg), without having the slightest effect upon its downward course. Moreover, the final rectal and heart temperatures of the curarized pigs fell well within the range of those of spontaneously breathing animals.

Exposure of pigs to 60° to 75° C. produced an increase in respiratory rate which did not exceed 80 to 90 per minute. The breathing remained deep until the terminal episode of bradypnea, ending in occasional deep gasps. In dogs the respiratory changes were essentially the same as those encountered at the lower temperatures.

Electrocardiographic changes: In both pigs and dogs, the first change, beginning immediately after immersion, consisted of a progressive increase in heart rate to levels of 300 to 350 per minute. Associated with this increase, changes occurred in the QRS complex, consisting of decrease in amplitude of the R wave and deepening of the S wave, or vice versa, with maintenance of the normal QRS interval and inversion of the T wave. The changes in the initial ventricular deflection might, in part at least, be due to variations in type of breathing with resulting changes in the position of the heart (Harris (15)). They occurred only to a minor degree in curarized animals.

In the pig, the abnormalities following this sinus tachycardia varied markedly with the temperature of exposure. Of all animals exposed to water at 44° to 50° C. (Tables I and II) only one showed appreciable widening of the QRS complex and loss of P wave. This occurred 1 minute before death. Another animal showed disappearance of the P waves. The changes in the remaining pigs were limited to sinus bradycardia and sinus arrhythmia that became most pronounced 2 or 3 minutes before death (Figure 2). Occasionally, auriculoventricular block of varying degree was seen during this period.

In contrast, 11 pigs continuously exposed to temperatures of 64° to 75° C. (Tables I and II) all showed the gradual development of exceedingly wide ventricular complexes with very large T waves, and the gradual disappearance of the P wave.[2] The general shape of these complexes resembled that of the original supraventricular ones. Their development was usually associated with definite slowing, although the heart rate remained regular. In some cases, the transitional phase consisted of salvos of fairly rapid and wide ventricular complexes, which interrupted a still-existent sinus bradycardia. In the terminal stage, the initial ventricular deflection could not be separated from the final one. The electrocardiogram consisted either of very slow, extremely wide ventricular waves, separated from each other by isoelectric intervals of 0.2 to 1.0 second, or of more rapid variations at 160 to 240 per minute, in which one wave merged with the next. The latter state might be called ventricular fibrillation (Figures 3 and 4).

In 9 of the 11 pigs, these changes made their first appearance early during immersion, at rectal temperatures of 37.0° to 41.6° C., and at a time when the arterial pressure and respiration were still adequate. In four of these, the blood pressure at the time of onset of the wide complexes was actually equal to, or higher than, that before immersion. In only 2 animals were the abnormalities first noticed when the pressure had fallen to low levels, and it is possible that they would have been demonstrated earlier if more electrocardiograms had been taken. Exposure for 6.5 and 5 minutes similarly resulted in marked widening of the QRS complex, whereas exposure for 3 and 1 minutes did not produce deviations other than those at lower temperatures.

In the dog, the electrocardiographic changes at high temperatures were in no way different from those encountered at 44° to 50° C. (Table III). They were limited to an increase in rate and to minor changes in the ventricular complex. No widening occurred and the auricular manifestations remained present until the end.

Chemical changes: A complete discussion of the effect of temperature on the potassium concentration of the plasma has been reported (2). The potassium concentration of the plasma of 15 pigs in which physiological studies were made is shown in Table II. The initial plasma levels ranged be-

[2] During tachycardia, actual observation of this disappearance was impossible because of overlapping of P and preceding T waves. In these instances, it was assumed that the same changes had taken place as in the instances where the P wave could be followed through a stage of decreasing amplitude to disappearance, as subsequent slowing of the beat similarly revealed the absence of auricular complexes.

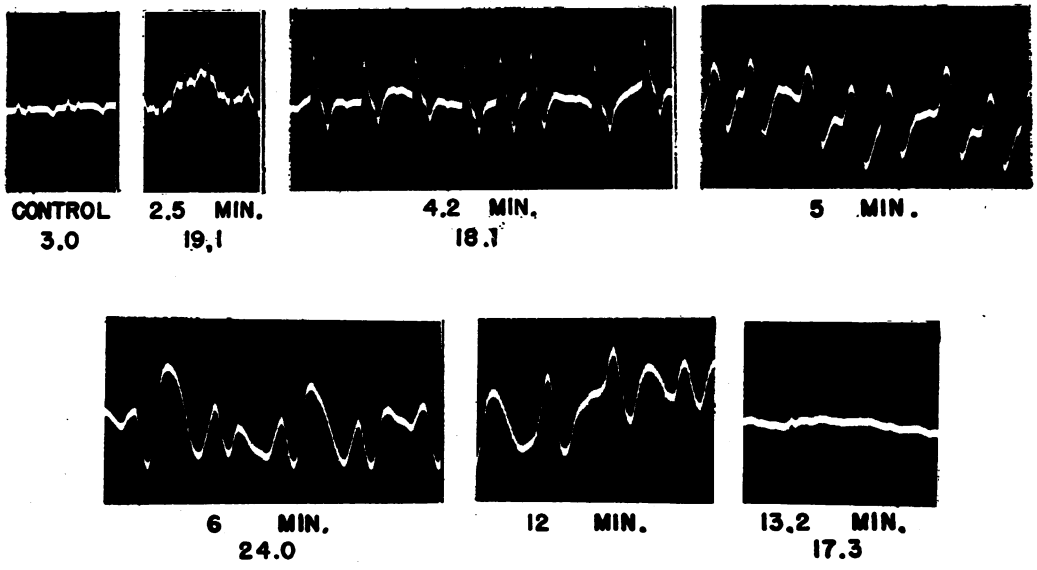

FIG. 4. RELATIONSHIP BETWEEN PLASMA POTASSIUM LEVEL AND CHANGES IN ELECTROCARDIOGRAM (LEAD 1) DURING IMMERSION OF PIG NO. 910 (9.5 KGM.) IN WATER BATH AT 72° TO 75° C.

The plasma potassium values are given in meq. per L. Death occurred 12.5 minutes after beginning of experiment.

tween 3.0 and 4.8 meq. per L. The potassium concentration of the red blood cells ranged from 113 to 145 meq. per L. The course of these concentrations during immersion varied markedly with the temperature.

Immersion of 4 pigs at 47° C. produced a gradual and sustained rise in plasma potassium. Ten minutes exposure resulted in levels of about 6.0 meq. per L. During the rest of the exposure, the level increased by an additional 1 to 4 meq. The highest level was 10.2 meq. per L. obtained 30 seconds before death.

On the other hand, continuous exposure at 70° to 75° C. characteristically resulted in an enormous rise in the plasma potassium level. This increase was found to take place with surprising rapidity. In 5 pigs, the plasma after 1 to 4 minutes of exposure, contained 14.2 to 25.5 meq. per L. of potassium. A sample drawn in this period from one curarized pig was still essentially normal and the peak observed in this animal was only 11.9 meq. Peaks from 16.7 to 25.5 meq. were observed in 6 pigs during exposure. Curare did not prevent rises in this range in 2 pigs; however, no early observations were made on these animals. In some instances, the potassium level fell towards the end. However, it remained markedly elevated.

In some experiments the exposure was terminated before the animal had expired. Immersion for 6.5 and 5 minutes similarly resulted in a tremendous rise of plasma potassium. At the time of death, the level was still very high. Immersion for 3 and 1 minutes produced a less pronounced increase; at the time of death, the level was only 2 to 2.5 times the normal one.

DISCUSSION

These observations show that the physiological disturbances leading to death in pigs exposed to water at 46° to 50° C. are of a different nature from those encountered in animals exposed to temperatures of 60° to 75° C.

In pigs immersed at the lower temperatures, the occurrence of a gradual fall in right auricular pressure followed by a fall in mean arterial pressure, indicates a progressive decrease in venous return to the heart. That this decrease, at least during a major part of the exposure, was due to an increase in capacity of the peripheral vascular bed, rather than to loss of intravascular fluid, is evident from the fact that the changes in circulatory dynamics were found to be reversible to a considerable degree. As the exposure continued, the detrimental effects of the heated blood upon

the heart muscle were added to the peripheral effects, and both factors undoubtedly contributed to the lethal ending. That relatively small increases in plasma potassium may predispose to vagal heart failure without causing the characteristic electrocardiographic disturbances of potassium poisoning is suggested by a recent report by Hoff, Humm, and Winkler (16).

It is difficult to say whether cardiovascular failure or respiratory insufficiency was the immediate cause of death. Profound arterial hypotension and pronounced bradypnea were usually encountered at the same time. It can be said, however, that the mean arterial pressure fell considerably before any impairment in respiratory function was evident. Artificial respiration applied at a time when the arterial pressure was still appreciable had no effect upon its downward course. Moreover, curarized pigs did not survive longer than spontaneously breathing animals; all but one animal died after 25 to 51 minutes of continuous immersion. The plasma potassium level increased by 66 to 250 per cent; the highest level found was 10.2 meq. per L. No profound changes in cardiac function, as judged by the electrocardiogram, occurred. As will be shown, plasma potassium levels up to 10 meq. per L. do not produce significant changes in intraventricular conduction.

At immersion temperatures of 60° to 75° C., the pigs survived for only 8 to 15 minutes. In the middle, or even earlier during exposure, at a time when the respiration was still adequate and the mean arterial pressure was still considerable, pronounced changes in cardiovascular function made their appearance. They consisted of a rise in right auricular pressure, and electrocardiographic changes in the form of disappearance of the P wave and progressive widening of the QRS complex, often terminating in ventricular fibrillation. At the same time, the potassium concentration of the plasma reached values of 16 to 19 meq. per L. This was associated with a striking destruction of red blood cells.

These observations strongly suggest that the hyperpotassemia was responsible for the disturbances in cardiac mechanism and for the subsequent myocardial failure, evidenced by the rise in auricular pressure. That the damaging effects of a rising plasma potassium level first of all manifest themselves in the heart is well known. In rabbits and dogs, the infusion of a solution of a potassium salt produces a sequence of electrocardiographic changes similar to those observed in pigs during exposure to high temperatures [Winkler, Hoff and Smith (17), and Nahum and Hoff (18)]. It was found that an identical sequence of changes takes place in infused pigs (Table IV). In 2 animals, infusion rates were maintained that were likely to produce death in approximately the same time as in the burned pigs. It is evident that potassium levels of less than 10 meq. per L. failed to produce either changes in the P wave or widening of the QRS complex, just as was the case in burned pigs. Higher levels resulted in a succession of changes which were similar in all respects to those observed at high temperatures (Table II). In the one animal (Figure 5) in which arterial and right auricular pressure and respirations were recorded, the auricular pressure began to rise 19 minutes (s) after the infusion had started. The potassium level was 12.7 meq. per L.; the P waves had begun to flatten 3 minutes before and had disappeared. Three minutes later widening of the QRS complex began. The arterial pressure and respiration remained normal for another 10 minutes.[3]

That the cardiac changes due to the potassium ion are reversible to a remarkable degree is clear from experiment 901 (Table IV). The usual succession of electrocardiographic changes was observed until, some seconds after a potassium level of 15.5 meq. per L. had been reached, the string shadow remained resting. The infusion was stopped. No electric or auscultatory evidence of cardiac activity could be demonstrated for the following 10 minutes, although the animal continued to breathe at a very slow rate. Then heart action returned and respiration became more rapid. The electrocardiogram had returned to normal. A plasma sample taken 5 minutes thereafter contained 8.7 meq. per L. of potassium. Infusion was started again, the well-known changes were again observed, and the pig died with a potassium level of 17.7 meq. per L.

The rapidity with which potassium is removed from the plasma makes it imperative that the re-

[3] The rate of infusion was slow enough so that the rise in venous pressure could not be ascribed to the administration of the isotonic salt solution *per se* [Altschule and Gilligan (19)].

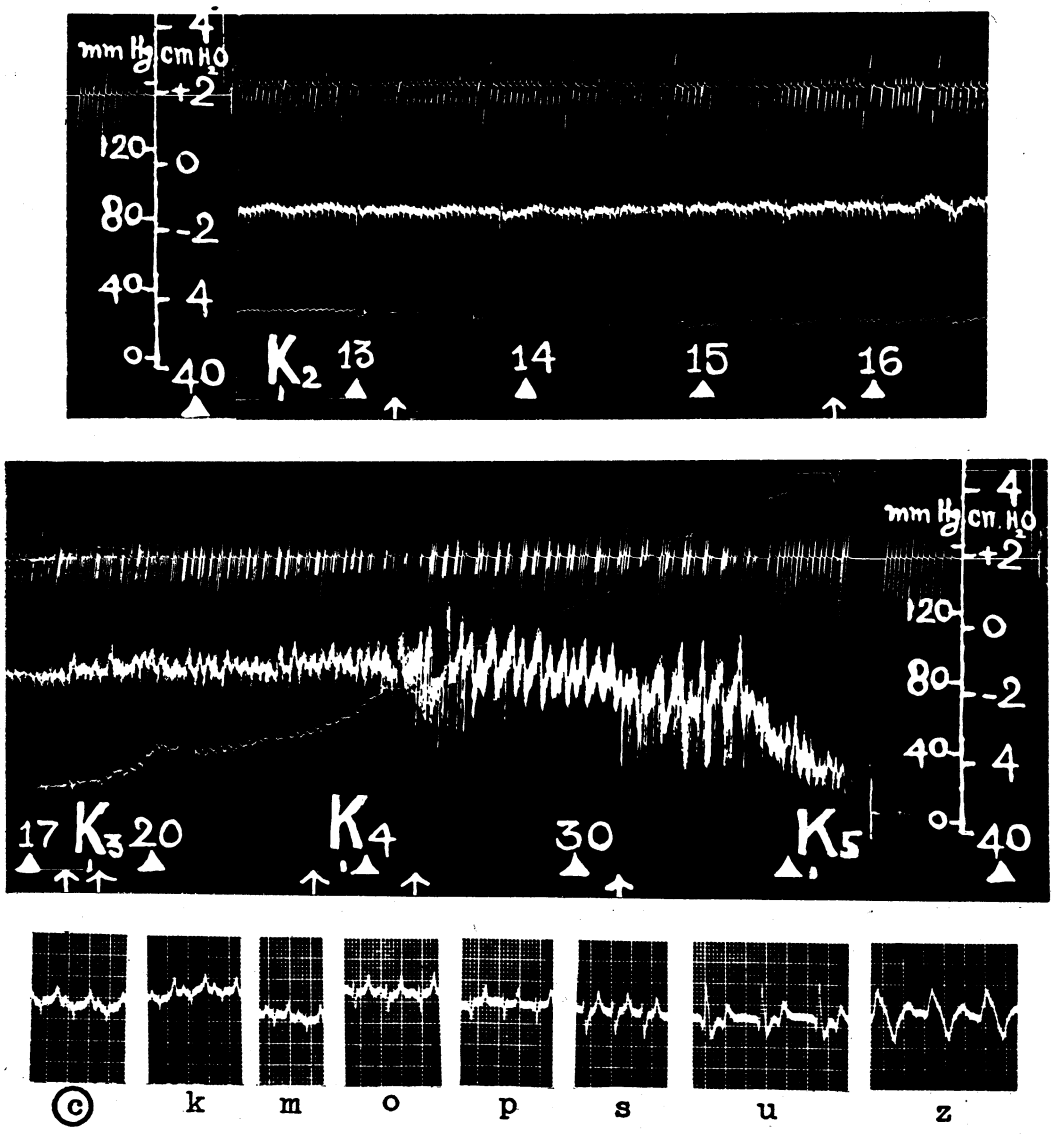

FIG. 5. EFFECT OF CONTINUOUS INTRAVENOUS INFUSION OF 1.12 PER CENT KCL AT THE RATE OF 0.6 ML. PER KGM. PER MIN.

The upper, middle, and lower tracings on the kymograph record represent respectively the pneumogram, the carotid pressure, and the right auricular pressure. The time in minutes is shown at the base of the record. The time at which blood samples were taken is indicated by the symbols K_2, K_3, K_4, and K_5. The times at which the depicted electrocardiograms were taken are indicated by letters from k to z.

lease of the ion into the circulation be intensive enough and be continued for a sufficiently long time to lead to death. This actually occurs in the burned pigs. The liberation of potassium often occurred at so rapid a rate that there was a lag between the rise in potassium and the electric changes. Thus, in pig 910, a level of 19.0 meq. per L. was reached in 2 minutes, whereas more than 4 minutes were required to produce the typical widening. Animals exposed to high temperatures for only 1 or 3 minutes did not release sufficient potassium to produce a characteristic effect on the heart; whereas exposure for 6.5 minutes was adequate in this respect. Exposure to 75° C. for 5 minutes resulted in a tremendous rise in potassium and in electrocardiographic changes, but

even here both manifestations diminished in intensity during the following 14 minutes.

Although it is clear that in pigs exposed to high (60° to 75° C.) temperatures the most striking physiological disturbances are those which result from the release of excessive amounts of potassium, continued exposure results in a progressive and generalized rise in body temperature which undoubtedly causes disturbances other than those due to hyperpotassemia. Thus, the peripheral and central factors that were the cause of death at lower temperatures also come into play at these high temperatures.

In order to evaluate the relative contributions of red blood cells and fixed body cells to the increase in plasma, potassium experiments were performed on dogs (Table III). Whereas the potassium concentration of their fixed cells is similar to that of the pig, their red cells contain only small amounts. Immersion at 75° C. resulted in an intense hemolysis, but the potassium level did not rise above that encountered in pigs at 47° C., and electrocardiographic changes characteristic of hyperpotassemia were not seen.

The distribution of the potassium in human blood is similar to that in pig's blood, the potassium concentration of the red cells being approximately 110 meq. per L., that of the plasma approximately 4 to 5 meq. per L. [Kramer (20), Scudder (21), and others]. High plasma potassium levels should therefore be expected in humans in whom a major part of the body surface has been exposed to high environmental temperatures. Several minutes of exposure would probably be required to result in the very high levels encountered in these experiments. It is also probable that, if the immediate effects of the exposure were survived, a markedly elevated plasma potassium, occurring immediately following the injury, would fall within the next hour. It should be remembered, of course, that a rise in plasma potassium is a normal postmortem phenomenon.

SUMMARY

There are 2 principal mechanisms by which exposure of the surface of the body to excessive heat may cause rapid circulatory failure and death.

In one, the systemic hyperthermia caused by conduction of heat to the interior of the body by way of the blood stream leads to a rapid and progressive decline in blood pressure and failure of circulation due principally to peripheral vascular collapse.

In the other, the circulatory failure is principally central and is due to the effect on the heart of an excessively high concentration of potassium in the plasma. Central circulatory failure is likely to occur when the overheating of the skin and subcutaneous tissue is so intense, prolonged, and generalized that potassium is released from the erythrocytes so rapidly and in such large amounts as to result in maintained plasma levels in excess of 11 meq. per L.

In the case of thermal exposures of low intensity, peripheral circulatory failure may occur without sufficient rise in tissue (and blood) temperature to cause a dangerous rise in plasma potassium. When a thermal exposure has been of sufficient severity to cause fatal hyperpotassemia, the central circulatory effects are likely to be complicated by peripheral vascular collapse.

It is essential to the development of hyperthermic potassium poisoning that the erythrocytes have a high original concentration of this element. Thus, fatal hyperpotassemia, due to hyperthermia, may occur in the pig but not in the dog. Since man and pig have similar potassium concentrations in their erythrocytes, it is inferred that they are probably similarly susceptible to the development of fatal hyperpotassemia following cutaneous exposures to excessive heat.

Although thermally induced disturbances of the respiratory centers may contribute to either type of hyperthermal circulatory failure, maintenance of pulmonary ventilation by artificial respiration does not prevent death or cause significant prolongation of the survival period.

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