ON THE SO-CALLED HEAT-DYSPNOEA.

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In the *Arbeiten aus dem Physiologischen Laboratorium der Würzburger Hochschule*, 1872, is contained an article by L. Goldstein, entitled "Ueber Wärmedyspnoe." In it the writer, after discussing the various ways by which the changes in the respiration-rhythm may be brought about (he assumes that the resistance-theory of Rosenthal is correct) and pointing out the various causes, chemical, mechanical, and thermal, which may act on the respiratory mechanism, takes up the thermal; referring especially to a paper by Ackermann, published five years before in the *Deutsche Archiv für Klinische Medicin*. Ackermann found, that if the temperature of an animal be increased by prohibiting the loss of heat from skin and lungs, the frequency of respirations increases, and came to the conclusion that the nervous centres were stimulated to increased action in order to ventilate and cool down the animal through the instrumentality of the lungs.

Goldstein goes on to ask: Is the increased temperature of the blood a new cause adding itself on to the stimulus for the respiratory-centre normally present in the blood; or is it an influence diminishing the resistance? He points out that this question is not decided by the experiment of Ackermann, who showed that an animal which had its body-temperature raised could not be made apnœic; for the persistent activity of the respiratory-centre might be due either to an increased or a new stimulus, or to a diminution of the normal resistance. Goldstein does not enter into this question in his paper, and it must be left still undecided. There is another question which he undertakes to answer. He asks: Where are the points of attack ("Angriffspuncte") for the increased temperature? Does it act on the cerebral convolutions primarily and through these on the respiratory-centres; or does it act on the skin first or on the pulmonary endings of the vagus first; or finally, does it act directly on the nerve-centres which govern the respiratory movements?

To answer these questions Goldstein adduces five sets of experiments, which I will briefly recapitulate, since my work was undertaken in consequence of the fact that they seemed not to justify all the conclusions he had drawn from them.

Experiment I. The animal (dog) is placed in a box and heated, its nose being exposed; the frequency of the respirations increases as the temperature goes up. The animal is taken out when its temperature has reached 41·2° C. Affusions of cold water have no effect in reducing the rate of respirations, except momentarily.

Goldstein thinks that this experiment proves that the increased temperature did not act by way of the skin, because cold affusions did not at once destroy its effects. If, however, we look at the Table given by him[1] we see that there is a fall from 110 to 92 respirations per minute, where we read in the notes: "From time to time cold affusions," and I would further suggest that the heated blood bathing the cutaneous nerves directly is certainly as strong a factor as the cold water poured on the skin, covered as it is with hair. I think, therefore, that this experiment does prove satisfactorily what Goldstein claims for it, and still leaves it undecided whether the increase of the number of respirations is brought about by way of the nerves of the skin, or otherwise.

Experiment II. A cat which had been made apnœic when at the normal temperature is placed in the apparatus, and after the temperature has risen from 37·4° to 39·5°, artificial respiration is again tried, but in vain, no apnœa is produced; the respirations going on at the same frequency. This experiment agrees altogether with those of Ackermann, and, as I shall point out later on, with my own.

Experiment III. A dog, into the veins of which 0·06 grm. morphine was injected, was placed in the apparatus, as in Experiment I. The temperature of the animal rises from 38° to 40°, while the respirations go up from 16 to 366 per minute. This experiment was made to show that it is not the cerebrum, or any feeling of uneasiness, which produces the increase in the rate of respiration. There are, however, some figures in the Table[2] belonging to this experiment which call for notice here. Goldstein, as we shall see further on, comes to the conclusion that the stimulation of the nerves of the skin is not the first cause of the increased rate of respiration; but a closer examination

[1] *Op. cit.* p. 82. [2] *Op. cit.* p. 84.

of this Table would seem to contradict such a conclusion. We see there that the temperature of the animal is falling before and after being in the apparatus. At 10 h. it is 39·6°, at 10.30 when the animal was placed in the apparatus it had fallen to 38·8°. At 10.42 it has fallen to 38·6°. When the animal was placed in the apparatus the respirations were 16 per minute; 12 minutes afterwards, while the temperature of the animal has been falling 0·20 degrees, the respirations have gone up from 16 to 44 per minute. This seems to make it probable that the warm air acting on the skin causes the increase in the respiratory rhythm.

Goldstein has indeed himself seen the difficulty; but gives the following explanation: "That in this case a distinct increase in the number of respirations can be observed with a bodily temperature of 38·6° and 38·8° may be explained by the circumstance, that the temperature of the body has risen considerably, before the thermometer in the vagina has indicated this." If Goldstein cannot trust the indications of his thermometer here, why should he trust the instrument on any other occasion?

Experiment IV. The vagi are cut, the animal is heated up, as before, the respirations per minute rise from 5 to 310, while the temperature of the animal changes from 37·3° to 40·2°: an experiment performed to show, and as I think, showing, that it is not the terminal pulmonary expansion of the vagus upon which the increased temperature acts primarily.

To show that the heated blood would and could influence the medullary centre directly without action upon the peripheral nerves, Goldstein devised the following experiment.

Experiment V. Two tubes 3·7 cm. long, 1·2 thick, provided with tubules at both ends, so that hot water could be passed through them, were employed. These tubes were provided with a groove running lengthwise deep enough to place the carotid of a dog into it comfortably. The artery could thus be exposed to an increased temperature by the heated water running through the tubes. Water of 54°, 59°, and 71° was employed with the object of heating up the blood as it passed through the artery resting on the heated tube.

But can the blood really be heated by this method? Let us look at the figures. At 10.45 the animal respires 26 times per minute; water at 54° C. is made to pass through the tubes; at 10.47 the respirations have risen to 50 per minute. Again at 11.10 the respirations are

16; water of 59° passes through the tubes; the respirations have increased to 62 per minute. Now have we any good reasons to think that in the short time of one or two minutes the blood running rapidly through the carotids and not directly over the heated brass at all, could be appreciably heated? Certainly Goldstein should have brought forward evidence on this point.

I have repeated all the experiments of Goldstein, and have found with him and Ackermann, (1) that by increasing the temperature of the surrounding air one can increase the respirations and the temperature of the animal; (2) that in such a condition the animal cannot be made apnœic; (3) that cutting the pneumogastrics does not prevent the increase in the respiratory rhythm; (4) that opium does not prevent it either. I have also repeated Experiment V. and found, it is true, that passing hot water through the tubes carrying the carotids, as described above, would increase the number of respirations. But I found also that the same increase in the number of respirations took place, when the arteries were clamped so that no blood could pass through them to the medulla. The increase is really, as one cannot fail to observe, brought about by pain; for it must be remembered that water at 54°, to say nothing of 71°, is decidedly painful to the hand. That it was pain that called forth these rapid respirations is shown by the fact that when I let water of the same (54°) temperature run into wounds made in the thighs, the same increase in the respiratory rate occurred.

I give a few figures. The number of respirations without water running through the tubes was 17 per minute; water of 54° was allowed to run through, the respirations went up to 46 per minute. The flow of the water was stopped and the arteries clamped above, on the cranial side of the tubes. The respirations were then 17 per minute when no water was running through the tubes, and went up to 45 per minute when water of 54° was passed through the tubes. We see, therefore, the same increase, whether the blood in the heated arteries was allowed to run up into the cranium or not. Again in the same dog, after the pneumogastrics had been cut and some chloral given, the respirations went up from 5 to 16 only when the hot water was passed through the tubes around the carotids, and went up similarly from 6 to 12 per minute when water of the same temperature was allowed to flow into wounds made in the thighs of the animal. If further corroboration of the view that pain mainly caused the increased respirations be necessary, we might add, that in other animals when

well under the influence of opium the changes were less marked or altogether absent.

Goldstein's crucial experiment does not then prove, as he maintains, that the heated surrounding medium caused the increased respiratory rhythm by causing a rise in the blood-temperature, which hotter blood acting directly on the respiratory centre was the immediate cause of the increase; and the question remains still undecided in what way the changes in the respiratory-centre, causing the increased rate of breathing, are brought about when the animal is heated, by exposure to air of a temperature higher than its own.

I hope that by the following experiments, which are given in more detail, some light may be thrown upon this point.

The first experiment, Table I., which coincides with No. I. of Goldstein, is inserted mainly to have something to compare the others with, and for the sake of clearness and completeness.

As far as the method of observation and the apparatus is concerned both are very simple. The apparatus consists of a piece of sheet iron large enough to place the dog-board on it, and of a case or box of wood of corresponding size, open at both ends, with windows and other openings on the side. These and the ends are closed by cloths, which can be removed or lifted aside when necessary. A thermometer reaching down into the apparatus, through a cork, gives the temperature in the interior. The apparatus was readily heated by one or two gas flames, beneath the sheet-iron. The temperature of the animal was taken from a thermometer placed in anus or vagina and remaining there during the experiment. The respirations were counted with the eye, an assistant giving the time, generally for a whole minute, excepting when the respirations became frequent, when fractions of a minute only were taken. The very high numbers cannot be expected to be absolutely correct. (Table I.)

In this experiment the dog was placed in the apparatus in such a way that its mouth was within, so that it had to breathe a warmed atmosphere.

To take a correct view of these experiments one must remember that under circumstances in which a man perspires a dog's respirations increase in number. While we sweat to keep cool the dog pants to keep cool.

Upon an inspection of this table one cannot fail to be struck by the rapid and great increase in the respirations, with but a trifling increase in the temperature of the blood; *e.g.* increase in body-tempera-

Table I.

April 23, 1879. Male dog. Small dose of morphia.

Time.	Surrounding temp.	Respirations.	Temp. of animal.	
7·06	22	53	39·5	
7·08	53			Animal placed in apparatus.
7·14	48	66	39·7	
7·17			39·8	Can be heard panting.
7·22	43	180	39·8	
7·29	43	220	39·8	
7·40	51	280	40·3	
7·48	55	310	40·5	
7·59	55		40·8	Respiration cannot be counted.
8·00	12·5			Taken out of apparatus, on an exposed, cool place.
8·05	12·5	180	40·6	
8·13	12·5	166	40	
8·21	12·5	120	39·3	
8·26	12·5	57	38·6	
8·30	12·5	38	38	
8·39	12·5	24 (?)	37·8	
8·40	45			Placed back in warm apparatus.
8·42	45	26	37·8	
8·46	48	27	37·8	
8·50	48	36	37·9	
8·54	50	60	38	
9·00	54	132	38·4	Begins to pant.
9·13	46	200	39·2	
9·22	46	240	39·6	
9·23	12·5			Taken out on an exposed cool place.
9·29	12·5	180	39·4	
9·32	12·5	194	39	
9·39	12·5	112	38·5	
9·49	12·5	24	37·8	

ture 0·3° C.; increase in respirations from 53 to 180. This fact alone would make it very probable, that the nerves of the skin were the active agents in bringing about these changes.

That however the increased frequency in the respirations can be brought about by the heated air surrounding the skin and stimulating the nerves there, without heating the blood at all, can be gathered from Table II., and one can further see it exemplified by watching a dog on a warm summer-day.

Table II.

April 25, 1879. Bitch. No opiate.

Time.	Surr. temp.	Temp. of dog.	Resp.	
7·30	19	39	22	
7·38	19	38·9	22	
7·39				Animal placed in warm apparatus.
7·42	47	38·9	42	
7·45	48	38·9	66	
7·47	49	38·9	214	
7·54	50	38·9	180	
8·09	51	38·9	320	
8·30	43	38·9	340	
8·45	49	38·9	300	Animal taken out and placed on an exposed cool place.
8·50	19	38·9	268	
8·52	19	38·9	220	
8·59	19	38·9	140	
9·06	19	38·9	120	
9·11	19	38·9	50	
9·14	19	38·9	28	
9·18	19	38·9	24	

We see here that the animal being loosely tied and having its nose not far from a large opening in the apparatus so that it could inhale the cooler air of the room, by panting vigorously, or otherwise, managed to keep its blood cool. The body-temperature was not elevated at all, while the respirations were increased from 16 to over 300 per minute. The enormous frequency of respiration prevented its blood from becoming warmer, and clearly had some cause apart from heated blood as its stimulus.

To investigate the influence which the nerves of the skin have in this, the spinal cord was divided at the bottom of the neck in another dog, and the animal placed in the warm box with its head and neck protruding. By this means afferent nervous impulses from the heated skin were to a very large extent cut off, but the raising of the temperature of the blood was not interfered with.

This experiment, Table III. (since by section of the cord the nerves of the skin that were heated could not act on the medulla, and since those of the head and neck were not exposed to the heat excepting by way of the heated blood circulating in those parts), shows that the blood itself directly, without intervention of the skin-nerves (at least the

Table III.

May 5th, 1879. Young dog. Cord cut about 4.30. Placed in apparatus in such a way, that the paralyzed and anaesthetized parts only were subject to heat directly. The head was free, so that the dog could inhale air at the temperature of the room. Post mortem examination showed the cord to be cut between the fifth and sixth cervical vertebræ.

Time.	Surr. temp.	Temp. of dog.	Resp.	
5·07	26	37·5	15	
				Apparatus is heated up.
5·12	42	37·4	15	
5·20	51	37·6	14	
5·29	56	37·8	15	
5·35	59	38·3	18	
5·40	60	38·8	20	
5·49	62	39·5	29	
5·54	58	40·0	31	
6·00	57	40·8	31	
6·07	56	41·5	79	
6·08				Taken out of apparatus.
6·11	23	41·6	64	
6·17	23	41	41	
6·26	23	40·4	38	
6·30	23	39·9	28	
6·38	23	39·5	26	
6·46	23	39	24	
6·53	23	38·5	22	
6·58	23	38·1	20	
7·06	23	37·6	18	
7·14	23	37·1	18	

great bulk of them), can raise somewhat the number of respirations. But there is a difference between the two modes, as can be seen by comparing Tables I. and II. on the one hand with Table III. on the other. In I. and II. where the skin is heated, either alone as in II. or together with the blood, we see an increase of the respirations from 53 to 310 respirations with an elevation of temperature from 39·5 to 40·8, and in No. II. from 22 to 340 respirations, where we have no increase in the temperature of the dog's blood, while in No. III. the highest figure for the respirations is 79 (the animal beginning with 15), with a change in the temperature of the animal of 3 degrees. There was noticed also a difference in the character of the respirations in the two kinds of experiments. While

in I. and II. the animal soon showed that complex of processes known as panting, this did not occur in III. It is of course possible that this might have set in if the temperature had been raised still higher.

An interesting experiment is the following Table IV. which not only supports No. III. but may help to solve another question.

Table IV.

May 20, 1879. Bitch. Tracheotomized and lower cervical cord cut. When in apparatus, neck and head free and exposed.

Time.	Surr. temp.	Temp. of dog.	Respir.	
7·30				Trachea and cord are cut.
7·39		38·8		Artificial respiration for 2 minutes, producing apnœa lasting 1 minute.
7·51		38·2	32	
7·53	44			Animal placed in apparatus.
8·03	49	37·8	27	
8·09	50	38·2	27	
8·12	51	38·4	32	
8·20	48	39·1	46	
8·23	50	39·5	48	
8·29	50	40·1	56	
8·33	50	40·6	130	
8·36				While the animal is still in apparatus, artificial respiration is kept up for 2 minutes, producing apnœa of about 1 minute.
8·40	49	41	100	
8·41				Animal taken out on an exposed cool place.
8·45	21	41·3		Artificial respiration for 2 minutes, producing apnœa of about $\frac{3}{4}$ min.
8·48	21	41	84	
8·52	21	40·4	60	
8·55	21	40		Artificial respiration of 2 minutes, apnœa of 1 minute.
8·58	21	38·6	36	
9·04	21	38	40	
9·10	21	37·6	36	

It will be remembered that Ackermann as well as Goldstein and myself did not succeed in producing apnœa in an uninjured heated animal. But when the cord is cut matters are different. Three times without failing in any trial did I succeed in the same animal in bringing about apnœa, once while the animal was yet in the apparatus

and while its temperature was on the increase, and twice after the animal had been taken out of the box. The figures show that this was not due to a diminution of the temperature of the dog itself, for this was even rising while the respirations were in abeyance after artificial respirations. The last two experiments then show that the respiratory centre can be influenced (in these cases stimulated) by changes in the blood brought about by heating the animal.

There arises now however another question which we think is partly answered by these experiments; that is: How does the blood act when it increases the number of respirations, does it stimulate the centres by virtue of its increased temperature, or does it act by virtue of the increased venosity (to use a short phrase)? For we may assume that an increase of the temperature of the tissues will increase also the chemical changes in them.

The last experiment would seem to point in the direction of the chemical changes as the effective causes, and that the increased temperature—at least within certain limits—has none or only a slight direct effect on the respiratory centre. For although the temperature of the blood remained high (40° to 41°), artificial respiration, which charged the blood with oxygen but, as shown by the thermometer, did not reduce its temperature, produced apnœa lasting three-quarters of a minute, while when the animal had been at the normal temperature the same amount of artificial respiration produced apnœa lasting a whole minute; this difference being probably due to the increasing changes proceeding in the body using up the oxygen at a more rapid rate than under normal conditions.

This leads us to consider some statements made by Ackermann in the October number, 1866, of the *Deutsche Archiv für Klinische Medicin*. Ackermann there publishes the results of investigations on animals which he had exposed to increased temperatures in various ways.

One of the conclusions at which he arrives is that not only the skin but also the lungs are used as an apparatus to regulate the body-temperature; the skin acting in a more gross manner, the respiratory mechanism being used in bringing about the minor changes and adaptations.

This sentence my experiments fully confirm, especially that showing the increase of respirations due to exposing the skin of the animal to an elevated temperature, while that of its blood was not affected.

Ackermann makes however another statement (p. 361). He says:

"This increase in the frequency of the respirations has its cause not, as might be expected, in a want of oxygen in the blood or in an excess of carbonic acid but alone in the increase of the temperature of the whole organism. We must recognize a heat-dyspnœa.....At high temperatures of the animal, artificial respirations have no influence on the frequency of its respirations, not even when in consequence of the inflations the blood shows a bright red colour in the veins, while by artificial respirations at a lower temperature the number can be greatly reduced, and at ordinary temperatures even brought to a standstill."

For temperatures not exceeding certain limits, the experiments communicated in this paper would seem to clear up this matter. The attempts to produce apnœa may prove unsuccessful because the respiratory centres, though not stimulated by the venous character of the blood, yet are constantly influenced by powerful peripheral stimulation of the heated final distributions of all the ordinary sensory nerves of the skin and other tissues. When the nerves, or more accurately a large portion of them, were excluded by section of the cord apnœa could be produced, though it seemed not to last quite as long as at normal temperatures.

Conclusions:

1. Goldstein's experiment with the tubes is inconclusive.

2. The increased respiration following exposure of the animal is due to two causes, skin-stimulation and warmed blood.

3. Of these, skin-stimulation is the more powerful.

4. Apnœa can be produced in heated animals if skin stimuli be cut off.

5. The direct action on the respiratory centres of the hotter blood of the heated animal is probably not, or not only, due to its temperature but to its greater venosity.

As regards the influence of the heat of the blood, *per se*, I add this restricting word "probably," because though 40° or 41° may not have acted as direct stimuli in the cases given, higher temperatures in these animals, and these same in other animals, may act differently from lower temperatures. I hope that I may take up this work in the future and discuss the effects of higher temperatures.

In concluding, I express my thanks to Prof. Martin, who not only suggested this interesting topic, but also directed the work and helped in various ways in its execution.