

REPORT OF A VISIT TO FOREIGN LABORATORIES

MARCH TO JULY, 1910.

By

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Boston, Massachusetts,

1910.

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INTRODUCTION.

1.

The importance of keeping in close touch with as many investigators as possible in the field of metabolism in Europe as well as in America cannot be too greatly emphasized. A certain number of individuals can become familiar with the work of the Nutrition Laboratory through personal inspection and the conduct of researches therein, and a larger number can read the reports. There still remains, however, a large number of individuals who cannot obtain an adequate idea of the work of the Nutrition Laboratory, or, indeed, of the opportunities offered there for work, without personal association with some member of the laboratory staff. This is particularly true of foreign investigators.

The periodic tours in Europe which have been made by members of the Laboratory staff serve a number of well-defined purposes. First, they enable the representative of the Nutrition Laboratory to find out all that is new in the equipment and design of foreign laboratories and apparatus. This point was especially emphasized during my tour in 1907. Innummerable points in connection with the construction and equipment of foreign laboratories and apparatus were found invaluable in the final arrangement of the Nutrition Laboratory.

Second, while a scientific investigator may write a description of his apparatus in the most beautiful language, he will, without fail, inadvertently overlook certain important minor details, which, though they may not affect the principle of the apparatus, nevertheless play a very important rôle in the successful conduct of experiments with it. Hence, a personal inspection and an examination of the methods used by its originator are often of very great

value.

Third, no two men work on exactly the same line, although working in the same field, and a consultation between those working on the same general plan often gives opportunity for an interchange of ideas that is productive of great results in economy of time, since one learns what not to do, and important suggestions and advice are received regarding the possibility of the conduct of more carefully guarded experiments.

To these three suggestions of the value of a visit to European laboratories, there may be added a large number of minor points, such as the infusion of the personal element into the interpretation of reported results; the development of a spirit of scientific activity rather than of polemical discussion; and the equal extension of academic courtesies, together with the establishment of a spirit of fellowship and cooperation.

The foreign correspondence of the Nutrition Laboratory is large; the interchange of minor reprints, etc., is also extensive; but with the delay incidental to the publishing of scientific articles in many journals, it frequently happens that experimental work may be duplicated unwittingly and hence one cannot be in too intimate touch with workers both here and abroad. With the establishment of the annual meetings of the different scientific associations and scientific societies in this country, there is ample opportunity for mutual intercourse and exchange of ideas among American investigators. Furthermore, while the travel required to attend these meetings is greater than in Europe, so far as the number of miles is concerned, nevertheless, the American habit of travel is such that an interchange of visits between members of American scientific societies is much more frequent than is the case on the older continent.

It is gratifying to relate that each year brings an increased number of visitors from foreign shores. It is also of interest to note that it is very clear that the reports of these visitors on returning home have always resulted to the credit of American research, but it neverthless remains a fact that for free and intimate intercourse between American and foreign investigators, periodic visits to Europe by American workers are also necessary.

Three years ago when inaugurating this system of periodic tours in Europe, my primary object was to study the equipment of laboratory buildings, laboratory rooms, and the designs of apparatus, with a view to introducing many of these ideas into the construction and equipment of the Nutrition Laboratory. As has been said before, this has been highly beneficial.

On my tour in the spring of 1910, my object was quite different, namely, for consultation with European investigators in regard to the planning of experiments, securing more detailed opinions and instructions in regard to many published researches both from the Nutrition Laboratory and from other laboratories, and particularly to consult with the eminent clinicians of Europe with regard to the research on diabetes now in progress in the laboratory. The uniform courtesy and consideration with which I was received in all laboratories is a new testimonial to the appreciation of the Nutrition Laboratory by foreign investigators.

While these were primarily the reasons for taking this trip, other material of value to the Laboratory was simultaneously accumulated. Thus, approximately 80 to 100 photographs were taken of new or modified apparatus which had been developed since my last visit of three years ago, and a collection of reprints, supplied by the different investigators, was obtained for the Laboratory, these reprints being frequently accompanied by notes made by the investigator or myself with regard to particular points in the publication. Opportunity was also afforded to purchase a number of pieces of apparatus of different types, which seemed to me advantageous and desirable for use in the Nutrition Laboratory.

The tour covered very much the same ground as that taken three years ago, somewhat more time being given to Scotland and England than previously. A list of cities and institutions visited, as well as the investigators personally seen and consulted, is given on the page following the title page. Before leaving for Europe a letter was sent to each one of the physiologists and chemists

that I planned to visit, requesting specific statements with regard to the possibility of their being absent from their laboratories during the period from March 1 to July 15. From the replies to these letters, a schedule was arranged which enabled me to make connections with every investigator originally written to. It is of interest to note that the schedule was rigidly adhered to and throughout the whole trip I failed to see but two of the men I had planned to visit, Professor Kronecker of Berne and Professor Landergren of Stockholm. Both of these were ill at the time of my visit and were unable to receive me. Obviously a large number of individuals who were not in the original programm were met and consulted with while on the trip.

BRUSSELS, BELGIUM.

Solvay Institute.

Professor Heger, and Dr. Phillipson.

As I was unable to see Professor Heger on my trip to Europe three years ago, I was especially desirous of including the Solvay Institute in my tour for this year, and so arranged to go to Brussels first. The Solvay Institute was established and is supported by Mr. Solvay of the Solvay Chemical Works. It is located in a beautiful building, especially erected for the purpose, which forms an impressive decorative feature of Parc Leopold. The building is very ornate, almost too much so for a scientific laboratory, but in this the architect followed the donator's wish. (See Fig. 1.)

The history of the building is very interesting. As the University at that time was not empowered to hold property and, indeed, has but recently been granted this power, there was considerable difficulty about building the laboratory. The laboratory was built upon land belonging to the city and practically given to Professor Heger. Ultimately, of course, it passes to the control of the University.

For a long time considerable difficulty was experienced, also, in finding a suitable director. Professor Héger, who was Mr. Solvay's physician, was called upon and suggested a good many men, but for one reason or other, they were not chosen. Finally, at the urgent request of Mr. Solvay and others, Professor Héger gave up his private practice at a great sacrifice and accepted the directorship of the laboratory. Mr. Solvay allows 50,000 francs a year for the institution, of which Professor Héger receives 10,000 francs for his services as Director. This sum of 50,000 francs is given to Professor Héger direct each year by Mr. Solvay himself, but without doubt, there will be a provision made for its continuance, certainly as long as Professor Héger lives, and, indeed longer, as Professor Solvay's son is also interested in the institution. Professor Heger is not now actively engaged with the University. He was made an Honorary Professor two years ago, which is probably equivalent to our Professor Emeritus. Although still the Director of the Solvay Institute, he is not, I think, actively engaged in research,

The building is divided into two parts, one part being used for the Solvay Institute of Physiology, and the other for the University Laboratory of Physiology. In the University laboratory, medical students are engaged in practical work, while the research is carried out in the Solvay Institute.

The large windows of the building were designed by the architect under protest from Professor Heger, and have since been found impracticable. As the rooms are very high, Professor Heger finds that they are difficult to heat, but this height was also insisted upon by the architect. At first double windows were used, but they were difficult to clean and were removed as it was found that the heating problem was not insuperable. The convection currents from the windows are, however, very annoying to the workers. When I was there, a large stove was placed in the middle of the room and the stove pipe running the air out through the window certainly looked very incongruous in its elegant surroundings. In two of the larger laboratories a gallery helps to increase the available floor space. Figs. 2-8 give views of the interior of the Solvay Institute, and also of the Stas collection which is located here.

<u>Mr. Solvay</u>.- The Solvay Institute was not at first, I think, a true philanthropic idea on Mr. Solvay's part. Mr. Solvay is a most interesting man with innumerable ideas, and much interested in science. He has, however, many fantasies, particularly with regard to the rôle which electricity and phenomena of that nature play in life. In fact, he thinks that all action in life can be explained by chemical action and electrical properties. In an article recently published in the Rev. gen. sci. pur. app., 20, 982-5, Mr. Solvay enunciates three fundamental hypotheses to serve as a basis for the consideration of



Fig. 1. Institut Solvay au Parc Leopold.



Fig. 2. Photograph of the lecture room in the Solvay Institute.

The arrangement for darkening the room with sliding curtains is shown around the wall, and also the tablets bearing the names of eminent scientists, particularly of chemists and physiologists. These tablets, which keep the memory of these men constantly before the students, are certainly worthy of imitation.



Fig. 3. <u>A view of Professor Héger's private office</u>.



Fig. 4. <u>Tablet presented to the Solvay Institute by Professor</u> <u>Heger's former pupils, in celebration of his</u>

25th anniversary as professor.



Fig. 5. Collection of medals belonging to Stas.

Professor Heger, at the request of Madame Stas, looked over and arranged the scientific material left by Stas, and found this most interesting collection of medals in a large box marked "Samples without value". They represented decorations and medals given to Stas for eminence in scientific investigations. The whole thing is typical of the modesty of this marvelous scientist.



Fig. 6. Photograph of chemicals, apparatus, etc., employed by Stas in many of his fundamental researches.

Of special interest is the small platinum crucible in the right side of the case. This was handed down from Lavoisier to Thenard, from Thenard to Dumas, and from Dumas to Stas. Beneath this case is shown a part of a balance constructed by Stas himself when a boy of ten years.



Fig. 7. Photograph showing more in detail the balance constructed by Stas.



Fig. 8. <u>Balance employed by Stas in many of his determinations of</u> atomic weights.

On a table at the right is a bottle which bears the interesting label "Eau pure, 1852". This was prepared by Stas and the water today is absolutely unclouded, and looks as clear as crystal. physiological processes from the physico-chemical standpoint, these hypotheses constituting a program of research covering certain problems. These are to discover: Methods of identification for, and analysis of, the various catalytic agents; methods of differentiating races, species, and individuals by the characteristics of their respective catalysts; methods of attack on the questions raised in the other two hypotheses. In the hope of stimulating research along these lines, he has offered 50,000 francs as prizes to the authors of the best articles on any of these problems sent to the Solvay Institute before Jan. 1, 1914. (See abstract of article in Chemical Abstracts, 4, 10, p. 1251).

The work of the Solvay Institute.

In the Solvay Institute there have been no experiments on man, and practically all the researches have been carried out with animals. There is a fine operating room, with adjoining rooms for washing, disinfection, etc.,-- all intended for experiments with animals. As a part of this equipment I noticed a small Saarbruck chamber for thoracic operations on small animals.

<u>Toxicity of urine</u>.--A number of experiments have been made in Heger's laboratory on the toxicity of the urine of an epilectic son of one of the laboratory dieners. These experiments, which were made on rabbits, seem to show that there were no toxic properties in the urine itself. As far as I know, a report of the experiments has not been published.

<u>Glandular secretions</u>.--Considerable work has been done on glandular secretions and a number of papers have been published. Demoor and Van Leut published a paper from the laboratory of the Solvay Institute about 1907, and the conclusion was than when the thyroid body of a dog was injected into a rabbit, the serum of the rabbit became thyroid-toxic to the dog. Another paper, published by De Meyer about 1909, showed that when the pancreas of a dog is injected into a rabbit, the serum of this rabbit was insulo-toxic to the dog, and the dog became diabetic. Another paper by Maséay showed that when the hypophyse of a dog was injected into a rabbit, the serum of the rabbit became hypophysiotoxic to the dog. These experiments were repeated, and the dogs

died, but as Héger says, there is also a lethal material in the serum. Evidently the investigators simply tried to see if the dogs would die and the serum was given intraperitoneally. One dose was given and then it was repeated a week later. They found that the Islands of Langerhans decreased greatly and while they were not wholly gone, most of them were destroyed; there was no evidence of a regeneration. The investigators did not study the effect of a small dose to see if the Islands of Langerhans would be regenerated.

Discussion with Dr. Heger.

Discussion of Dr. Meltzer's insufflation scheme.- I called Professor Héger's attention to the insufflation scheme of Dr. Meltzer and he was very much opposed to it. First, he thinks it is necessary to perform tracheotomy and this in itself is dangerous, since there are then two wounds, one of the injury and the other produced by the tracheotomy. Second, the natural filling of the alveoli through expansion and dilatation of the chest wall under these conditions gives the best flow of blood, that is, we dilate it from without. If we dilate it from within, then the capillaries between the epithelium and the walls of the alveoli are choked, more work is put upon the heart, and the subject dies. Professor Héger considers any pressure on the lungs harmful, or any resistance in the breathing. Even with adenoids, there is a decreased pressure and it is bad for the lungs. Personally I cannot see why it is so bad, for if there is a resistance in the nasal passage, there will be a greater dilatation of the chest wall, and this will tend to distend the alveoli.

<u>High versus low protein</u>.- Heger thinks that we have an enormous reserve in the blood which is but slowly brought into circulation and hence can be of great assistance when needed. He says that if we breathe carbon monoxide, we get a great deal of carbon monoxide in the lungs, some in the liver, but very little in the spleen and other organs. This shows, therefore, that not all the blood is brought into circulation. With some men there is unquestionably

a larger amount brought into circulation than in others; by bleeding and putting in a Ringer or physiological salt solution, however, the blood can be brought into circulation. This is the reason why in so many cases of carbonmonoxide poisoning, it is of no use to tranfuse blood, but if the subject is bled and salt solution introduced, the other good blood can be brought into circulation. This is really a development, or another phase, of the idea of "factors of safety" brought out by Dr. Meltzer in his lecture in New York. Heger referred to the fact that if a man loses one arm, the other arm does the work of both and in many similar cases, the great reserve in the body is utilized to make good a loss. He believes that 125 grams of protein represents. perhaps, the higher limit and about 75 grams the lower limit, but the 125 grams may not be needed every day. I suggested the "Baustein" idea and he agreed with it fully. He spoke of building a house and needing a piece of wood for a door-jamb, and said that while a great deal of wood of various kinds is brought into the house during its construction, the one piece for this jamb is especially selected. He believes that most people get about 125 grams of protein a day, and that a student of his in the Congo District found about this amount among the natives. Another of his students working in the interior of China, also found this amount. They made no analyses unfortunately but weighed and calculated from the probable composition. Professor Heger thinks, however, that it is a fact that all individuals take about 125 grams of protein a day. After I spoke about the "Baustein" idea, he thought that we may get the particular fragment needed in one piece of meat rather than in half a ton of vegetables. All animals are first raised on animal protein, mammals on milk, birds on eggs, etc., and thus man naturally needs it. The greatest rapidity in growth is during the period when human beings or animals are feeding on animal protein. When they live on vegetables, their growth is usually less, and practically all vegetarians are small. Heger said he knew beforehand that Chittenden must be small and he was most interested when I

told him that he was. He says he never knew of a man who advocated eating little who was not small, and consequently did not feel the need of eating much.

Heger pointed out that between chemical energy and heat there may be a great many intermediate steps. He said that perhaps in the next 500 years we shall learn something about these steps and be able to identify them and to develop a technique so that we can measure them, particularly the possibilities of energy changes in intellectual activity. Heger remarked that Dr. Higgins weighed 110 kilos, and was suffering from gout, and he also believed that Mr. Fletcher was not mentally active, that is, he was rather quiet and doubtless did not need much protein.

Discussion of respiration apparatus. -- At the time of my visit, Professor Héger had just received a reprint describing our small respiration apparatus and spoke very kindly of its possibilities, as he believes thoroughly in the principle of nose-breathing. I reported that we were making a study of the kind of respiration before and after the valve is thrown. As a result of this talk with him, it appears to me very advantageous that we should get more pneumograph curves before the experiments begin, and while the subject is breathing with and without the nosepieces. The subject should be required to lie still and unknown to him, tracings should be made before the nosepieces are inserted in place. We should also get tracings after the nosepieces are inspected and inserted before the actual experiment begins.

In commenting on the work of Albertoni in Italy, he said that he considered it very good and extremely interesting. He is strongly opposed to the Zuntz mouthpieve and nose-clip, and he believes that they are liable to do harm. He also mentioned an apparatus designed by Ludwig which determines the carbon dioxide and oxygen in the respiration of muscles, on which our new apparatus is an improvement.

Dr. Phillipson.

Among the workers in the Solvay Institute is Dr. Phillipson, who is an especially keen, interesting and clever man. His specific line of work at this time is animal physiology and he has an extremely well equipped laboratory on the top floor of the Solvay Institute. At the time of my first visit he was working on the "Calendar effect". I do not know what that is. He is much interested in finding out whether or not the temperature on the inside of the muscle rises during contraction. He wants to build a small calorimeter on the principle of a Dewar flask, with a resistance thermometer. and after stimulating the contractions of a muscle, to measure the rise in temperature of the surrounding air. I suggested that he should use thermal junction needles thrust directly inside the muscle. He has an Einthoven galvanometer but says he does not like it very well, as the strings are easily burned out. I first saw here the very good photographic registration apparatus of Frank, a view of which is given in Fig. 9. This apparatus registers electric currents, etc., and it is necessary to use a prism to turn the light 90°. He uses the Blix-Sandstrom electrically-driven kymograph as a motor for rotating the photographic registering apparatus. This combination I saw in a number of laboratories. Dr. Phillipson is evidently a man of many interests and a very enthusiastic scientific worker.

General criticism of researches at the Solvay Institute.

Evidently many of the experiments connected with the researches in the Solvay Institute are incomplete and lack adequate verification. The investigators are too often easily satisfied with results and too frequently arrive at conclusions that one always fears may be disproved by subsequent experimentation. This is a point of much interest, especially as it is evident that the same is true, to a certain extent, of many Belgian researches.

These researches tend toward the superficiality and, at times, brilliancy of much French work. Indeed, the general impression received is that the work

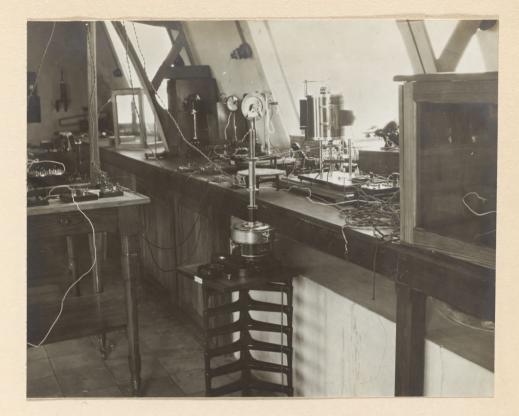


Fig. 9. View in the laboratory of Dr. Phillipson.

The Blix-Sandstrom kymograph is in the immediate foreground on a small table. At the right on the laboratory table is the Frank photographic registration apparatus, and the galvanometer is in the box in the rear of the room in front of the iron girders. Various resistances and potentiometers are on the table at the left and on the table with the photographic registration apparatus. is far from fundamental in character. The haste of the clinician to get results and the unwillingness to make a deep thorough investigation of any one point is so constantly in mind that one wonders if Professor Héger's long experience as a clinician has not to a certain extent unfitted him for the direction of research in a laboratory devoted to scientific research.

The personal charm, brilliancy of speech, and remarkably extensive knowledge of science in general possessed by Professor Heger, to a degree envied by all who know him, do not, however, contribute to his capacity for the direction of assistants in the field of pure research. Even an inspection of his earlier work does not materially alter the general theses here laid down, i.e., that years of clinical experience do not make for ability in abstract research.

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BONN, GERMANY.

Tier-physiologisches Institut.

Professor Oscar Hagemann.

In the past three years Professor Hagemann has made considerable progress with the development of his apparatus but he is still woefully floundering in a maze of details and irregularities. The general installation of the apparatus in the Institute seems to have been very costly, and indeed, it was. On close examination, it is seen that there is a lack of uniformity in all of the investigations, a spirit of disinterestedness on the part of the assistants, and a general feeling on the part of the visitor that the apparatus is altogether too large and too complicated to be thoroughly understood and properly manipulated under the present conditions.

Assistants used in the researches .- Three years ago one great difficulty was with the assistants. The men employed at that time were German students who drank a great deal and as a consequence were wholly incapacitated for scientific work the morning following their indulgence, although they were able to be around, of course. More recently Professor Hagemann has adopted a plan that I used in Middletown, of employing ladies for short periods as needed. These young ladies live in Bonn and while they are comparatively well-to-do, and not obliged to support themselves, they are, nevertheless, glad to get the extra income. They are paid 20 cents per hour for day work and 25 cents per hour for night work, and come when needed. As they are not otherwise employed, they are always available. These assistants are very versatile, and not only compute, but work at the observer's table, and make the physical observations, also. Each woman works 4 hours at a time at the table, and stands the whole period. Others make the calculations but adhere to the regular hours per day, while still other assistants weigh U-tubes



Fig. 10. Professor Hagemann in his laboratory.

In the foreground may be seen a large coil immersed in very cold alcohol, which is used for conducting water out of the current of air. A large balance for weighing these coils is behind the curtains in the closet at the right. and carry out the minor chemical operations. Professor Hagemann finds that the women give much better service than men.

In using this kind of assistance, however, he is evidently firmly impressed with the belief that there may be a falsifying of records and he has therefore attempted in every way to make all manipulations automatic and self-controlling. In so far as it is desirable to make manipulations and computations in connection with metabolism experiments self-controlling and automatic, I agree with him fully, but it is almost amusing to see his firm belief that if given an opportunity his assistants would combine to cheat him.

One striking reason for the lack of coordination is the fact that no one is in charge of an experiment. Each individual is given a certain part to do and does his or her part utterly independent of anyone else, and no one has entire charge, or supervises. Even when the experiment is made at night, Professor Hagemann goes home and a girl with an assistant is left there with no trained man in charge. Hagemann maintains that nothing can happen, the only danger being that the assistant may get lazy and not properly regulate the heat supply. He has accordingly installed an automatic apparatus to show when the temperature changes are improperly handled, that is, a thermometer recording the temperature of the ingoing air.

Automatic temperature recorders.- He has a thermal junction system for measuring the differences in temperature between the ingoing and outcoming air and maintains that if the thermal junctions are kept constant, and the inside temperature changes, then the outcoming air will change. Obviously, this temperature difference will be shown on his recording apparatus. In other words, if the thermal junctions are kept at zero, and the inside temperature changes, the absolute temperature of the ingoing air must then be changed and the recorder will show when this has been done. There is also a thermometer in the outcoming air. This registers from 14 to 20° in 0.1, but can be read to 0.01, as each 0.1 equals about 1 mm. Professor Hagemann's reasoning that this

thermometer actually can control a rise in temperature inside the calorimeter is based on the fact that the thermal junction system should always be kept at zero. If the temperature of the outcoming air rises as shown on this thermometer, obviously there has been a lack of attention on the part of the assistant.

The recorder, which was made by Hartmann and Braun of Frankfort, is locked up in a case, and the paper last 24 hours. Great emphasis was laid upon the fact that the case is locked, and the records therefore inaccessible. Professor Hagemann opens this case with considerable impressiveness every morning, removes the paper record and is thereby provided with evidence as to whether or not his assistants have been faithful.

There are thermo-elements, also, for the ingoing and outcoming water currents, and a Hartmann and Braun recorder registers the temperature differ-For the water circuit, there are two recorders, one running from ences. a temperature difference of 0° to 7°, the other from 5° to 12°. The instruments are apparently automatically cut-out when beyond these scales. The contact is made every 30 seconds, and the paper moves at the rate of about 20 mm. per hour. The scale of each instrument is divided into tenths of a degree, each 0.1 being equal to about 1 mm. on the scale. Estimation can also be made to 0.01°. I noticed some of the girls used a magnifying glass for this estimation while others did not. These recorders were calibrated by Hartmann and Braun, and Hagemann says he himself has not recalibrated them. They do not agree with his mercury thermometers but he says he knows why, and that the mercury thermometers are wrong. The calibrations have never yet been satisfactorily made. In further conversation with Professor Hagemann, it appeared that he had made some slight changes in the installation of the thermometers after they were received from Hartmann and Braun and I do not see why these changes should not affect the whole calibration, and thus vitiate all his results. Professor Hagemann's point was that he could make his calibrations as well after an experiment with a

horse, or when the experiment was in progress, as before. This he intends to do subsequently.

I could not see these recorders as well as I wanted to for they were in use, an experiment being in progress. They were apparently constructed on a principle similar to the thread recorder of Sir Horace Drawin, that is, a pointer moves over a paper and is drawn down by a magnet with every contact. This set of three instruments, with resistance the rmometers and thermal junctions, cost about \$500, and are shown in Fig. 11. Professor Hagemann told me that Hartmann and Braun had these instruments for medical use, which would give a control or record of body temperature. He could not find the catalogue in which that form of instrument was shown but gave me sufficient information regarding it to enable us to obtain the catalogue from the manufacturers.

The day before I arrived in Bonn, Professor Hagemann had received a copy of Publication No. 123, which showed that we also had a temperature recorder already in use. This disappointed him very much, as he had hoped to have something new to show me.

Hagemann is rather in favor of using a large amount of water and a small temperature difference, a point on which we did not agree. The only objection to the use of a small amount of water is that the water in the absorbing system is sluggish and large temperature differences are slow in recording and it is therefore difficult in short periods to get sharply-cut results.

<u>Water-meter</u>.- The small water meter that I noticed attached directly to the ingoing water pipe in his calorimeter when I was there three years ago was found to be very inaccurate at a slow rate. This coincided with an experience that we had had with a meter of American make. Professor Hagemann also told me that there was much sediment in the water in Bonn during the spring and this probably vitiated the readings on the meter.

Automatic register for water meter. - Hagemann has devised a very ingenious scheme for recording automatically the flow of water into the large

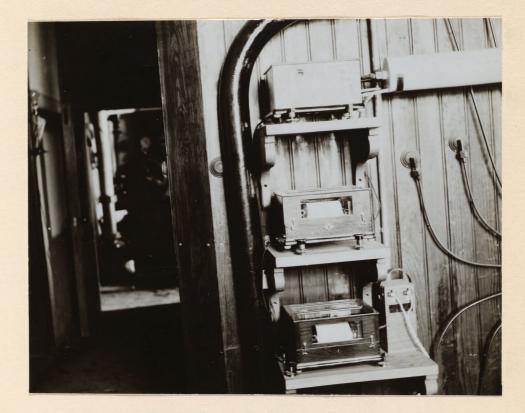


Fig. 11. The three electrical registering thermometers of Hartmann & Braun in Professor Hagemann's laboratory.

The two lower ones are for the temperature differences of the ingoing and outcoming water, and the temperature of the outcoming air is recorded by the top one.

copper cans used as water meters. The old type of water meter, formerly employed in Middletown, in which the water is measured by volume and not weighed, is still used by him. Attached to the lower end of the water gauge levelling tube is a stiff-walled, metal-reinforced tube which connects the levelling tube with a cylindrical steel box, partly filled with mercury. In this box is a float connected with a stylus and by this means, the rise and fall of the mercury is recorded on paper rotating on a drum. As the hydrostatic pressure in the copper can becomes greater, obviously, the pressure on the mercury is increased and the float is raised. When the can is emptied, there is a sudden fall of pressure, and the pointer goes back to the original level. The operation is very ingenious but is not "fool proof", for one of the assistants, or as Professor Hagemann said "Von tam fool", turned it up partly on edge and considerable mercury ran into the pipe leading to the meter can. There is one such apparatus for each can and a separate clockwork for each. Fig. 12 shows this apparatus very clearly.

Inside of the calorimeter at Bonn, there is a combined registering barometer, thermometer, and hygrometer. Also in the outcoming air pipe there is a precision hygrometer, (see Fig. 13) which, though I could not inspect it carefully, appeared to be a hair hygrometer.

Electric alarm contact. An ingenious electric alarm contact is used to indicate when the air sample pans are too full or too low. In this apparatus, which may be seen in Fig. 14, a weighted brass cylinder slides on a hard rubber skidway until it comes to a brass section or wire standing upright and an electric contact is thus made, the skidway being inclined so as to insure a perfect contact. As this contact is purely mechanical, there are none of the disadvantages following the use of mercury. The scheme is a good one but calls for a considerable weight or brass and unless the pans are large, the weight of the brass counterpoise would cause a noticeable difference in pressure. One ingenious point worthy of

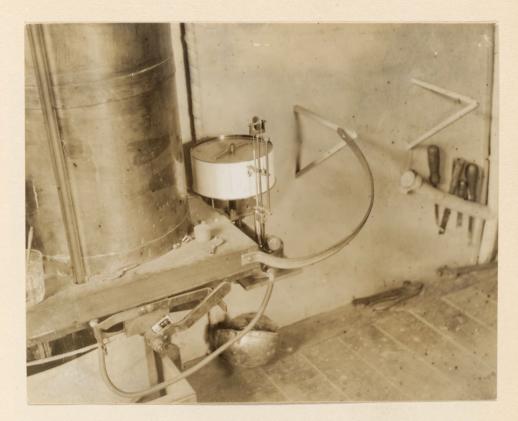


Fig. 12. Drum for graphically recording the number of times that the water meter is filled.

The water meter is at the left and communication is made to the metal tube near the bottom with a mercury recording apparatus. This pen travels up and down over this white paper on a rotating drum actuated by a clockwork.

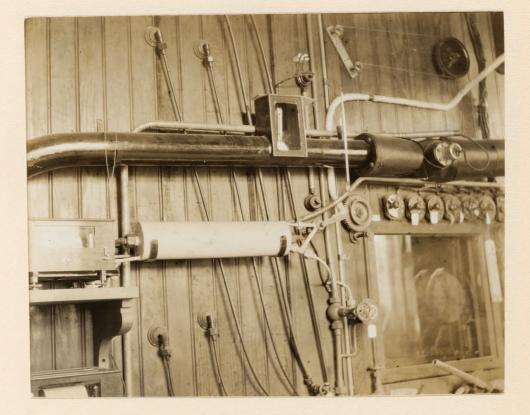


Fig. 13. <u>View showing the hair hygrometer in the ingoing air-pipe</u> of Professor Hagemann's respiration apparatus.

This is shown encased in glass in the upper part of the picture. At the left is the registering thermometer for the outcoming air.



Fig. 14. Photograph of electrical contact device applying the weight of metal against metal and avoiding mercury contact.

The slides are of hard rubber and the contact pieces are strips of brass. Violin strings are used in place of wire or cord.

comment is the use of violin or cello strings in place of cord or wire.

<u>Differential manometer on the water-circuit.</u> There are two side branch tubes near the bulb of the thermometer on the water circuit. These lead to a rubber hose on each side of a mercury manometer. The pressure is read directly and measured in millimeters of mercury. At the time I heard of these I suggested the possibility of using this plan as a check on the record of the rate of flow of water passing through the system, this being somewnat on the idea of a manometer devised by Professor Brodie, now of Toronto. When I returned from Europe, however, I found that our mechanician, Mr. Collins, had already worked out a manometer on this plan which bids fair to be of great service to us.

Professor Hagemann uses the pressure as measured on this manometer to correct the pressure on the bulbs of mercury thermometers. The necessity for this correction was first pointed out by Professor Armsby. I did not understand how Professor Hagemann could calculate from this measurement the error due to the pressure on the bulbs, but he attempts it nevertheless.

<u>Calorimeter experiments.</u>- While I was in Bonn, there was an experiment that had been running for several days without interruption with a horse for a subject. The horse stood most of the time and was very quiet, shifting his position only slightly during the time that I looked into the window. Usually oxen lie down during an experiment but some horses never lie down in the calorimeter.

Determination of carbon dioxide.-In a train of U-tubes for absorbing the carbon dioxide of samples from the ingoing and outcoming air, Professor Hagemann uses a strong caustic potash solution in U-tube through which the air passes just before it enters the sulphuric acid U-tube. These U-tubes are of his own design and cost 5 or 6 marks each, and a great many of them are used in an experiment, as may be seen in Fig. 15. Part of these tubes are filled with soda lime, part with sulphuric acid, and part with caustic soda solution. The balance used for weighing these tubes and the method of weighing several tubes at once may be seen in Fig. 16. By weighing all of these tubes at one time, he obtains the total amount of carbon dioxide absorbed, but as his purifying train consists of caustic potash, soda lime, and sulphuric acid in in different vessels, he is unable to differentiate between the amount of carbon dioxide absorbed by the caustic potash and that absorbed by the soda lime. The air passes through these U-tubes at the rate of about 3 liters per minute. A small mechanical suction pump in the basement is used for mixing the air current. The Geryk vacuum pump formerly employed is now used in connection with a large vacuum drying oven for drying feces.

Determination of carbon dioxide in the bomb. After a combustion in the bomb calorimeter, the gas is allowed to escape and pass through a gas meter where it is measured. The carbon dioxide is absorbed by passing the gas through a train of purifiers and in this way the carbon in food, feces, and urine is determined. The bomb, which was made by Julius Peters of Berlin, is very large and appeared to be about three times the size of the one used in this laboratory, but of exactly the same design.

<u>Thermobarometer.</u> In the basement of his laboratory, Professor Hagemann has installed a new form of thermobarometer, and uses it in direct connection with an Elster dry gas meter. I could not get the details of this thermobarometer or even a photograph of it as the room was so dark. Professor Hagemann is very enthusiastic about it. He reads the meter, corrects the ingoing air meter by this, and then corrects the meters taking air from the two pans, and thus has a double check on the reduced volume of ventilation as given by the meter pump. He showed me some figures which seemed to agree very well but I did not follow the calculations.

<u>Sheep experiments</u>.-I found that Professor Hagemann had made digestion experiments with sheep, using the harness and urine tubes. Some of the experiments covered a period as long as two and a half months. The sheep lie down and seem in every way comfortable.

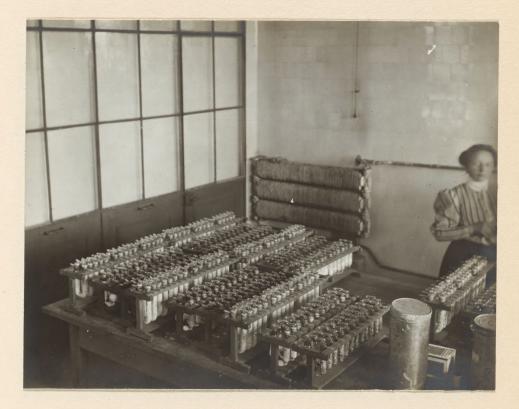


Fig. 15. <u>U-tubes containing caustic-potash or soda lime or sulphuric</u> <u>acid used in connection with residual analyses in</u> <u>Professor Hagemann's laboratory.</u>



Fig. 16. <u>Assistant in Professor Hagemann's laboratory weighing several</u> <u>U-tubes at once on a balance. The general type and shape</u> <u>of the tubes are also shown</u>. <u>Publications</u>.- There is now in process of writing a publication describing the whole apparatus in detail. A most marvellous series of drawings has been made by a skilled artist and the whole thing will probably appear in the Landw. Jahrbücher.

<u>Cost of maintenance</u>.- Aside from his own salary, Professor Hagemann has 40,000 M. for the Institute, but personally handles none of this, and all is paid out by the Government direct. Even if a sum of money is saved on the salary of an assistant, it reverts to the Government and cannot be used for apparatus, etc. The whole institution is subject to the Ministers of Agriculture; not long ago a change in the administration prevented the making of calorimeter experiments for several months.

He deplored with me the character of the assistants Professor Zuntz is obliged to use in his laboratory at Berlin, and said that he is the only one of Professor Zuntz' assistants who has ever done anything independently. According to him Magnus-Levy, Durig, and Loewy were never assistants of Zuntz.

HEIDELBERG, GERMANY.

Physiological Laboratory of the University of Heidelberg.

Professors Kossel and Cohnheim.

The laboratory is in charge of Professor Kossel, and Professor Cohnheim is his associate. Professor Cohnheim is much interested in animal physiology, but Kossel, whose speciality is pure physiological chemistry, does not like or approve of animal experiments. He allows Cohnheim considerable latitude in his experiments, however, but the animals cannot be kept over the summer recess as it costs so much to keep and feed them. As the appropriation for the Department is not sufficient for this, the animals are killed by injecting chloroform into the heart. Thus it is seen that there is no opportunity for Cohnheim to carry out metabolism experiments covering a long period.

Quite recently a Dr. Best has opened a private laboratory in Heidelberg for experimental research. He is a practitioner interested in internal medicine, particularly stomach diseases. In this laboratory, he has small rooms fitted with tables for operating, and also a yard in the rear where animals can be kept in very good condition. In a visit I paid to this laboratory, I found the equipment very simple and practical.

Operation on dog for duodenal fistula.-On the first day of my visit to the laboratory of Dr. Best, I saw an operation for duodenal fistula made by Professor Cohnheim on a large St. Bernard bitch. The animal was first given an injection of morphine between the shoulder blades, and in fifteen minutes became somewhat stupid. She could then be handled and placed on the table without offering any resistance. The animal was next etherized, the morphine making a minimum amount of ether effective. As a large amount of ether is necessary when it is used alone, Cohnheim prefers the morphine-ether narcosis. In spite of the shabbiness of the room and general absence of hospital equipment, the disinfection process is carried out with greatest care. The animals are shaved thoroughly, washed with water, ether, alcohol, and a corrosive sublimate solution. The cloths used were sterilized by boiling for a long time in water vapor, the hands were cleaned, and the coats worn by the two men were also sterilized. A large piece of cloth which had been boiled and sterilized had a hole in it and this hole was placed over the place operated upon. The edge of the cloth was sewed around the hole to the shaved skin, and other cloths were placed around to avoid any possible infection. After the opening had been made, Professor Cohnheim placed his hands in the abdomen and literally "fished around" for the desired portion of the intestine. After he had performed the operation, he placed a cannula just behind the pylorus and as near to it as possible. A rubber tube, connecting with a tube inside the cannula, carried into the small intestine the digestive fluid passing out of it. Cohnheim believes that this injection is extremely important as otherwise, when the digestive fluid reaches the opening of the cannula, it is diverted and flows out, and is therefore lost instead of passing on beyond. This tends to give abnormal results, as the fluid is needed at the pyloric end of the stomach to stimulate the movement at the proper time, since the food passes through too rapidly without the churning motion. By means of the rubber tube connection, however, he has overcome this difficulty.

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Commenting on research of this nature in St. Petersburg, Cohnheim told me that the stands for supporting the dogs having fistulas did not originate with Pawlow but were used for years by Ludwig. He also said that E. S. London, who formerly worked with Pawlow, has left that laboratory and not only claims the originality of all the work, but tries to eliminate Professor Pawlow's connection with it. Professor Cohnheim believes that London's work is all wrong and that it is absolutely unjust to publish it, as he does not inject the digestive fluid into the small intestine. This should be injected as otherwise normal peristalsis and subsequent digestion cannot be obtained. Especially is this true when there are one or more fistulas in the intestinal tract. Cohnheim uses a syringe and injects 25 c.c. of the fluid falling out of the fistula at one time. This is done periodically, sometimes 14 or more successive times. Great care is necessary to see that the rubber does not become clogged.

Cohnheim seems to be very fortunate for he loses very few dogs and can keep them several years if the rubber tube does not give out. He prefers female to male dogs because they are cleaner and gentler and after the operation they stand better for the juice to flow. On the other hand, in operating there is often danger of striking very large vessels connected with the breast and mammary glands that are not found in male dogs. In female dogs it is necessary to cut and the the large blood vessels leading to the breasts before going too deep into the abdomen. A serious objection to the use of male dogs is that the penis is in the way of inserting certain important fistulas. The whole abdomen is clear in the female.

Cohnheim says that many operators do not mind the loss of blood, but rush the operation so as to get through as soon as possible. He prefers to save the blood and has very good results. The morphine action lasts two or more days after injection, the action is very characteristic. On dogs, it acts as a narcotic, but it is very stimulating in its effect on some animals. In an experiment made on a goat the following day Professor Conheim used no morphine as he did not know what effect it would have on a goat.

<u>Operation on a goat</u>.-No experiments have ever been made on the digestive action of the ruminants, and consequently he made a stomach fistula on a goat. Only ether was used but there was a good deal of saliya and the animal was hard to etherize. The preliminaries of the operation were exactly like those with the dog. After the abdomen was opened, Cohnheim hunted around with his arms up to the elbows in the cavity for about 15 minutes for the "Druese Magen". He found everything else and had them out several times on the operating table. When he finally found it, he made a stomach fistula, but as

in goats the stomach walls are thinner than in dogs, very careful work was necessary. After the cannula was inserted, it was necessary to cover the wound with "Netz" as this aids materially in healing. The side opening suggested by Dastre keeps the fistula out of the wound. The cannula is of nickel-plated brass, and has a screw ring on the end to screw it down to hold it to the skin. As the wound heals, the flesh has a tendency to cover it, so it is necessary to unscrew it a little each day as the flesh heals. The cannula when not in use is protected by a cap to prevent the dogs from licking it and unscrewing the ring, thereby allowing the cannula to slip back into the abdominal intestine. Cotton is placed in the cannula to keep out particles of dirt.

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These stomach and intestinal fistulas are often made in Germany. Bickel in Berlin makes them but they are not made much elsewhere. Cohnheim told me that he had tried to impress upon Professor Cannon the importance of making these fistulas in order to carry further some of his research.

<u>Professor Kossel</u>.- Professor Kossel, the well-known physiologist, has been so occupied with his numerous academic duties for the last three years that it interferes seriously with his research. He reports that it is very hard to get and keep an assistant as there is but little call for professors in pure physiological chemistry. This particular line is not of importance to the practising physician and hence is not taken up by many men. When he has a large number of assistants he finds it difficult to carry on so many researches and therefore prefers to have but one or two men. He approves highly of the method employed in the Nutrition Laboratory of having a large number of trained assistants who can serve as extra pairs of hands when necessary although not capable of independent scientific research. The teaching side of Professor Kossel's work is evidently very important, and he is very much in earnest about it. He told me that it required a great deal of time to keep up his lectures, and when anything interfered with such preparation he feels very bad about it and thinks that he has not kept up with the times. <u>Chemistry of the protein molecule.</u>-In speaking of protein and the amount required in the food, Professor Kossel considers that the protein fragments may be used even more as a stimulus than as constructive material or "Baustein", and certain particular fragments are necessary. He cited the classic work of Hopkins on tryptophane.

<u>Alcohol</u>.- Professor Kossel feels sure that the effect of wine is not due largely to the alcohol but to the ethers, esters, and higher alcohols, perhaps. Some act on lower centres and affect locomotion, but others on the higher centres. He cited the instance of a wine served in a certain locality where all who were in the room were talking but no one listening, the wine evidently stimulating the speech. The only hexone base from which alcohol can be derived as a chain of 6 carbon atoms is leucin, he said, although there is always a possibility of a molecular rearrangement.

Professor Kossel plans to be in America in the fall of 1911, as he is to deliver lectures in Baltimore and New York, and has promised to visit the Nutrition Laboratory.

Laboratory of the I Medical Clinic.

Drs. Krehl, Siebeck, and Grafe.

<u>Dr. Krehl</u>.-Dr. Krehl is the head of the Clinic and is extremely busy, not having much personal time for research. The Clinic laboratory is well equipped, with many pieces of apparatus in it, including a Jaquet respiration apparatus, recently built by Dr. Grafe, and an old Rubner respiration calorimeter for small animals with a volumeter. This latter apparatus was used by Krehl a number of years ago. The laboratory is especially well fitted for the chemical, pathological, and bacteriological side of the clinical work.

Krehl does not believe in Rubner's idea of body surface, but says that one must go very cautiously in criticizing Rubner, for the professors in the outlying cities have a very great respect and feeling for the Berlin professors. This seemed to me an interesting sidelight upon the professors in the small university towns and in the large university towns. Evidently the professors in Berlin are the most prominent and most important men in professional lines in Germany, and Krehl seemed to think that they are well aware of that fact themselves. He thinks that Professor Rubner is very sensitive to criticism of his idea that metabolism is proportional to body surface, but Krehl thinks that the idea is wrong. Krehl's brother-in-law, Schwenkenbecher, has worked with Rubner and is now at work himself on a method for getting the body surface. Later, I found out from Jaquet that both Krehl and Schwenkenbecher had been in Basel to inspect Jaquet's apparatus. Krehl thinks that all the older formulas, such as the formula of Meeh, etc., are wrong, and has promised to write to Schwenkenbecher for me and ask him to send me material on the subject.

Krehl believes that there is an individuality in metabolism, and that all people are not alike. Well-nourished women who are not working have, according to him, a lower metabolism than that of normal individuals. Speaking of diabetes, he said that he had thought for a long time that Weintraud's ideas

were not right, and that his experiments were too short. Dr. Krehl had planned to take up this problem with Dr. Grafe using their respiration apparatus, but now that we have entered the field, he has decided to drop it. Krehl's opinion of the Zuntz apparatus is that it is good but only for very short experiments. It is certainly remarkable to see the activity exhibited in this Clinic for a small university town. Such men as Krehl, Grafe, and Siebeck have certainly made possible a great deal of research.

Dr. Siebeck.

Dr. Siebeck formerly studied with Bohr and knew Krogh, and says that Krehl has the highest opinion of Krogh. When in Copenhagen, Dr. Siebeck worked on blood gases, especially in anaemia, and is now interested in studying alveolar air. He uses Haldane's apparatus, but with an improvement.

<u>Slide valve for use in determination of alveolar air by Haldane method</u>.-As he believes that a psychical effect is produced by using the tongue to hold the opening over the wide tube into which the expired air is passed, he has had to make a new slide valve. This valve is slid to one side after the expiration and thus the subject immediately begins to breathe in the free air and at the same time holds the expired air in the tube intact. The apparatus (see Fig.17) is very simple and evidently very tight. I ordered two and they are now in use in the Nutrition Laboratory. With his apparatus he has also had a mouthpiece with a mica valve, which apparently presented no advantages over the Zuntz, the Tissot, or the Durig valve.

Dr. Siebeck is interested in experiments in which air relatively rich in carbon dioxide is inhaled and a study made of its effect upon the composition of the alveolar air. He has found it difficult, however, to get a constant mixture of carbon dioxide in the air. I suggested that he weigh a bomb and make an artificial atmosphere by introducing carbon dioxide into compressed air.



Fig. 17. Photograph of various nose and mouth pieces and masks used by Dr. Siebeck.

Of particular interest is the slide valve in front of the stand near the edge of the table. Two of these valves have been made and are now in use in the laboratory. <u>Spirometer.</u> Dr. Siebeck has just completed a very ingenious spirometer. As he is very anxious to eliminate, so far as practicable, the dead air space after the air leaves the lungs, the tubes connected with the spinometer are made as small as possible, and the air enters from the side instead of through the long upright central tube so commonly used. The spirometer is hung and counterbalanced by a weight and the volume is read over the graduated arc of a circle. Each division on the circle corresponds to 10 c.c. and the whole apparatus holds three liters, - a maximum expiration. Unfortunately I could not get a photograph of it as there was a very bad light and the apparatus could not be removed, and furthermore, I was too much pressed for time.

Dr. Siebeck plans to analyze the gas of the expired air, say, after the first 100 c.c. is expired, then again after 200 c.c., up to the maximum amount. This seems to be a very important study and should be well done by him, although he has an enormous amount of routine work in the Clinic to do.

Dr. Siebeck has a Bohr blood gas pump with the water arrangement for raising and lowering the mercury. He said that there was always so much excess mercury that the water never gets down low enough in the bulb to reach the place where the mercury comes back from the vacuum vessel, so that no water vapor ever gets over into the pump. It had held wonderfully well with the recipients all on for several weeks. It had not been touched for several weeks before I came and the vacuum was still less than 1 mm. of mercury. He reports that Krogh's tonometer is very good but it is very difficult to handle it without breaking the capillary column. They had a great many of these tonometers in the laboratory down stairs but Siebeck said they found them hard to use.

Fig. 18 gives a view of the new type of Pettersson gas analysis apparatus in this laboratory. Some extra cocks had been added to it to aid in getting a sample. Instead of using pyrogallic acid, Dr. Siebeck glows the oxygen in hydrogen and gets very good results in this way, without an explosion. When there is an excess of gas, nitric-oxide must be looked out for, but by simply glowing with a platinum wire, this is avoided. He uses compressed hydrogen

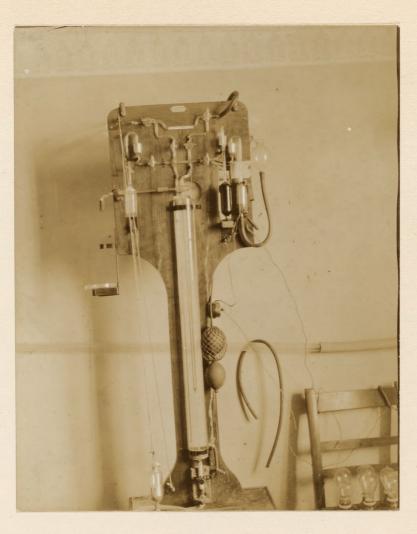


Fig. 18. <u>Gas analysis apparatus used by Dr. Siebeck in Heidelberg for</u> <u>his study of blood gases</u>.

This is on the Pettersson principle and was built by Geissler in Bonn, the mercury seals making the different parts of the apparatus removable, as well as the small chamber for glowing the hydrogen and oxygen mixtures. One or two supernumerary stopcocks are added to facilitate in taking a sample. which is very pure but has a constant error which he has previously determined.

Dr. Grafe.

One of the important reasons for my going to Heidelberg was to see the respiration apparatus described by Dr. Grafe a year or two ago, in which he used a headpiece with a rubber band around the neck, thus minimizing the volume of the respiration chamber. To my utter astonishment when I went into the laboratory, there sto od a Jaquet respiration apparatus complete. I had not known of its existence but it seems that while I was en route, an article had appeared in the Zeitschrift f. Phayiol. Chemie, together with an article describing a series of experiments made with this apparatus on a fasting woman.

Grafe head respiration apparatus .- As a result of the illness of Dr. Grafe, I was unable to see him except for a moment at his bedside one morning before leaving. Dr. Siebeck kindly showed me the laboratory, and the method of using the apparatus. I was informed that Dr. Grafe had practically abandoned the use of the head apparatus. It was found in an adjoining room and Dr. Siebeck put it on while I took several photographs of it. (See Figs. 19, 20, and 21). I was especially interested in the rubber neckband. (See Figs. 22 and 23). The apparatus is simple and the closure between the metal wall and the rubber of the neck band is pneumatic, a method used in many instances in our calorimeter. The especial feature in this apparatus regarding which I wished for information is the closure between the skin of the neck and the rubber neckband. I had previously attempted to find out about this point by correspondence with Dr. Grafe but he did not understand my query. He supposed I referred to the pneumatic tube, which of course I knew from our own experiments could easily be made tight. The method employed by Grafe to make a perfect closure between the skin of the neck and the rubber collar is as follows: First, a roll of thin rubber bandage is wet and passed around the neck several times, the wet rubber clinging tightly to the neck. A rubber sleeve is then pulled down over the head (a very tight fit it must be for a great many persons) and the ends laid upon the rubber bandage



Fig. 19. <u>View of the Grafe head chamber in which the head alone is</u> placed.

A rubber collar fits about the neck of the subject and the opening in this chamber. Dr. Siebeck is lying on the couch while the photograph is being taken. The apparatus has been replaced by the large Jaquet respiration apparatus.



Fig. 20. Another view of the Grafe head chamber and also, at the right, the bed which is used inside the respiration chamber.



Fig. 21. <u>A view of the Grafe head apparatus showing the opening</u> through which the head is placed and the cushions for <u>supporting the back and neck</u>.



Fig. 22. Rubber collar used to connect the neck of the subject with the head apparatus of Grafe.

At the right, in the basket, are two small glass vessels containing sulphuric acid and pumice stone for weighing the water absorbed in the aliquot samples.



Fig. 23. The rubber neckpiece used for the Grafe head apparatus, somewhat extended so as to show the general conformation. At the right are the small glass vessels with sulphuric acid and pumice stone, removed from the basket so as to show their shape better. which is still wet. This bandage is then further wound around the ends of the neckpiece and around the neck, the moistened portions being carefully laid against each other. After repeated windings, it is finished and Grafe and Siebeck believe that the closure is tight. He has tested the closure once on himself by breathing through a special mouth tube and blowing air into the head piece and could see no leak around the neck. He did not do this, however, with a patient and only once on himself. I can see how for his purpose this method of closure would be tight enough, as there is never any pressure inside the chamber. The only criticisms to be made of it are that it must be very trying for a patient and also, as Professor Jaquet said later, this great pressure around the throat must alter the character of the respirations. Dr. Grafe said that he finally used surgeon's plaster to cover the joint.

<u>Jaquet respiration apparatus</u>.-In his description of the respiration apparatus built on the Jaquet principle, Dr. Grafe used no sketches or pictures. This apparatus is very well built and modern in every way and contains a number of new points worthy of special attention.

First, the apparatus is so well counterpoised by means of a heavy weight on the end of a rope passing through the ceiling that it can be easily tipped up on edge and a patient rolled out of the box on the bed and the box then lowered, the idea being to provide for experiments with nervous patients who may want to get out of the apparatus very quickly. Krehl, Grafe, and Siebeck extelled the desirability of this feature. Figs. 24 and 25 show the apparatus when lifted and Fig. 26 when closed. As the box is lowered, it rests on an oil seal at the bottom formed by a wooden rim all around the edge of the box partly filled with thick oil, in which the mowble part of the chamber rests. The part of the food aperture which opens outward is also closed with an oil seal, but inside the chamber, the food hole door slides and is pressed up against a rubber gasket and fastened with two screw clamps. These may be clearly seen in Figs. 24 and 25. The air current enters at the top of the chamber in the the rear (see Fig. 27) and goes out at the bottom beneath one of the tracks on which the bed rolls, i.e., the track nearest the gas meter. (See Figs. 24 and 25). The bed is shown in Fig. 28. There are four glass windows in the apparatus, and the glass is well fastened into the frames, apparently with putty, being heavily and deeply set. It appears to be a good, tight joint, with no possibility of leakage. A sketch of the respiration apparatus, with measurements, is given in Fig. A.

Alcohol lamp.-For the purpose of testing this apparatus, Grafe has made use of hurning alcohol. The lamp used is shown in Fig. 29. The alcohol is placed in a bottle which is very wide at the place where the height of the alcohol is measured, the measurement being made by a small capillary tube at the side of the bottle. The alcohol is highly colored with methylene blue and I could easily see where the dye had dried on the wick. The outside diameter of the vessel at the point where the alcohol was measured was 39 mm. The glass is very thin so probably the inside diameter was not far from 35 mm. Using the formula, volume equals height times $T r^2$, I find <u>r</u> equals 23 mm., then 23 x 23 x 3.1416 = 2.4 c.c. for each millimeter in height. As only 10 to 15 grams are burned in one hour, this would make a very large error for this period, but the experiments are always of several hours' duration and the error is thus distributed over several hours. On the other hand, in his description of the apparatus, Dr. Grafe leads us to think that this is an extraordinarily accurate way of burning the alcohol.

<u>Gas-measuring apparatus.</u>-This apparatus differs from Jaquet's in that Dr. Grafe rotates a meter so as to draw the air like a pump. The same principle applies, also, to his use of four small meters for determining the water content of the ingoing air. (See Figs. 30 and 31). The place where the sample of the ingoing air is taken for the water determination may be seen in Fig. 32. The water is absorbed in small glass vessels containing sulphuric acid and pumice stone, like those I saw in Rubner's laboratory a number of years ago. These glass vessels in a wire basket are shown in

Fig. 22. The apparatus for lowering the mercury pipette which allows the mercury to escape as a sample is taken is essentially on Jaquet's principle, that is, a kind of gear with a pulley and wire running over it. A good point is the use of gas stove tubing, i.e., heavily covered tubing, for the mercury. Over the end of the middle pipette, where the mercury drops off, is a somewhat larger rubber tube which conducts the mercury flowing out into a vessel below without loss. The tube is so large in diameter that there is no danger of its acting as a siphon. The plan seems to be a very good one.

<u>Dog respiration apparatus.</u> In the same room with the large respiration apparatus was a respiration chamber for dogs. This is shown in Figs. 25, 26, and 33. In Fig. 33 the cover is propped up with a small graduate. In size and shape the apparatus looks not unlike that used by Staehelin in Basel, and described in the report of my tour in 1907.

<u>Gas analysis apparatus</u>.- The gas analysis apparatus used in these experiments is remarkable in that it is of an enormous size, the pipette holding 100 c.c. of a gas sample. Figs. 34 and 35 show the apparatus and a sketch with measurements is also given in Fig. B. The important thing is that the carbon dioxide part is not water-jacketed as it is below, and is of but small volume. The oxygen absorption portion is jacketed, even around the absorption pipettes,which are outside the main tank, and very large. Oil is used on the surface and Haldane's solution of pyrogallol. The apparatus was made in Bonn by Geissler's Nachfolger. The carbon dioxide can be read from 0 per cent to 1,2 per cent and each division is 0.01 per cent. The oxygen can be read from 19.0 to 21.0 per cent, each division corresponding to 0.01 per cent.



Fig. 24. The respiration apparatus in Heidelberg showing the chamber partly tilted on a counterpoise weight, with the oil seal into which the edges of the chamber rest when in proper position.

The iron tracks permitting the bed to be rolled on the incline into the interior of the chamber are shown.

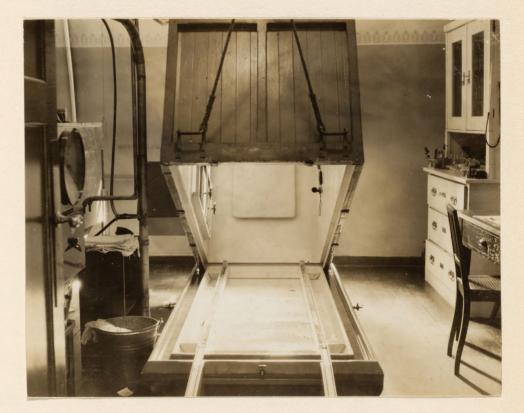


Fig. 25. <u>A nearer view of the same apparatus, showing the position</u> of the gas meter at the left and immediately back of the

gas meter, the outlines of the dog chamber.

In this view is seen the telephone hanging to the interior wall and on the left hand side of the wall, the food aperture with two handwheels which press the door firmly against the rubber gasket.

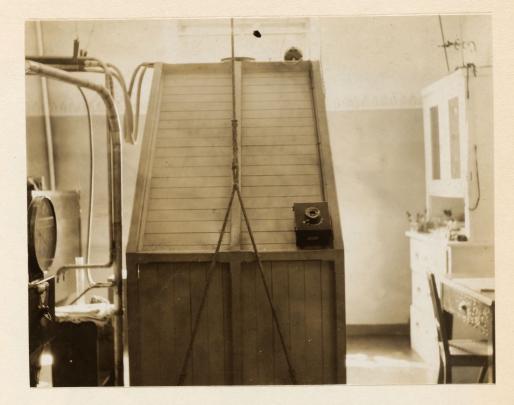


Fig. 26. The respiration apparatus at Heidelberg with the top closed down in place in the oil seal.

The rope to which the counterpoise is suspended is shown in the immediate foreground. The electrical controller is for controlling the fan on top which ventilates the interior of the system. The rubber tubes for the air pipe are at the left, as well as the gas meter.

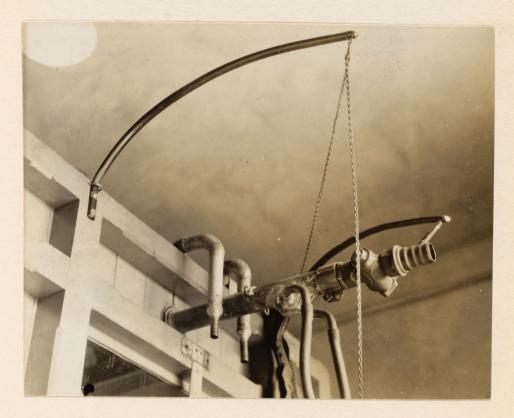


Fig. 27. <u>Rear view of the Heidelberg respiration chamber, showing the</u> <u>opening through which ingoing air is taken.</u>

The two pipes leading to the sampling apparatus for measuring the amount of water vapor entering with the ingoing air are also shown.



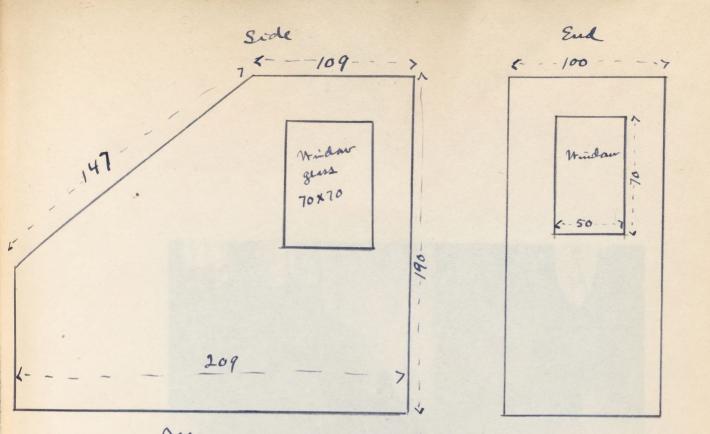
Fig. 28. Bed used inside the Heidelberg respiration chamber.

In the description of this chamber, Dr. Grafe lays great stress on the composition of the mattress, and the oilcloth covering. At the foot of the bed is seen, folded over, an oilcoth or oilcotton blanket. There was also on the bed at this time a regular blanket and pillow. The bed is rolled on the tracks into the chamber.



Fig. 29. View of the alcohol lamp used by Dr. Grafe.

At the left is shown very indistinctly the small capillary tube used for measuring the level. About one-third up this capillary tube may be noted a mark which indicates the level to which the alcohol is always filled. The upper part of the wick is stained with methylene blue, and the chimneys are at the right.



All maswemente in centimeters Also under in top 50 × 50

Fig. A .- Sketch, with measurements, of Heidelberg respiration chamber.

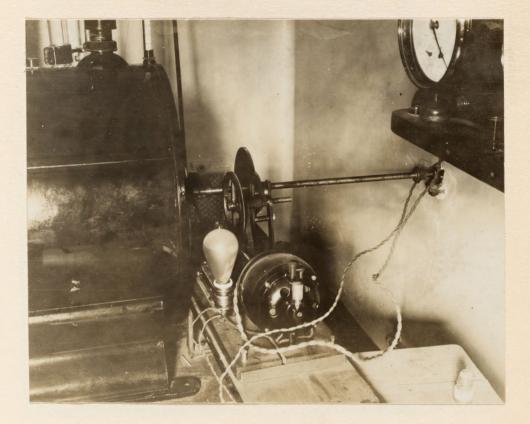


Fig. 30. <u>The electric motor and gearing used to drive the gas</u> <u>meter, which is likewise used as a pump, in the</u> <u>Heidelberg apparatus.</u>

The axle extends toward the rear wall and there a chain, not shown in the photograph, actuates the drum for the four small meters used in taking a proportional sample.



Fig. 31. The four small gas meters used for taking aliquot samples of the incoming and outgoing air.

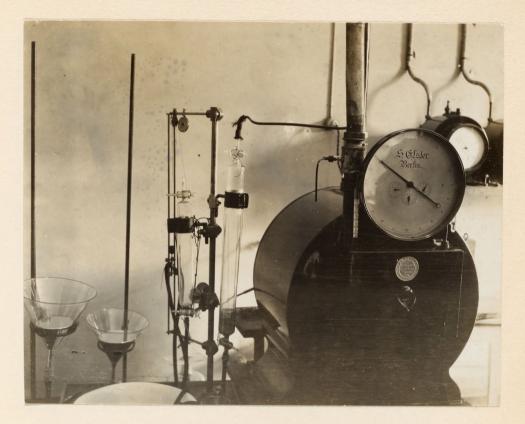


Fig. 32. Details of the main gas meter for measuring the ingoing air current.

The large pipette for collecting the aliquot sample of gas is shown at the left, also one of the smaller Jaquet pipettes for transferring from the larger pipette and for preservation of the sample. The system of pulleys for lowering the mercury pipettes which allows the mercury to flow out gradually is shown at the left.

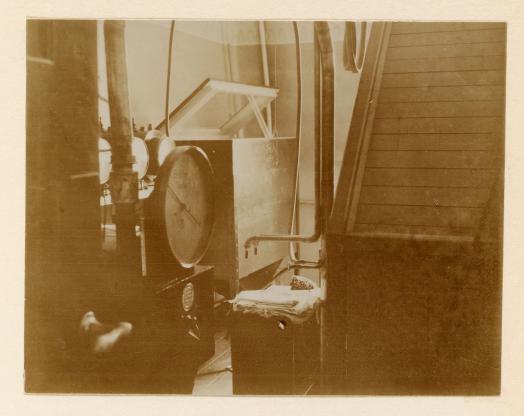


Fig. 33. The gas meter in the foreground at the left, the corner of the respiration chamber at the right, and in the

rear, the chamber used for small animals.

The part of the small respiration chamber which has the glass window is propped up with a small graduate. The four small meters used for taking aliquot samples of the ingoing and outcoming air are shown in part behind the large gas meter at the left.

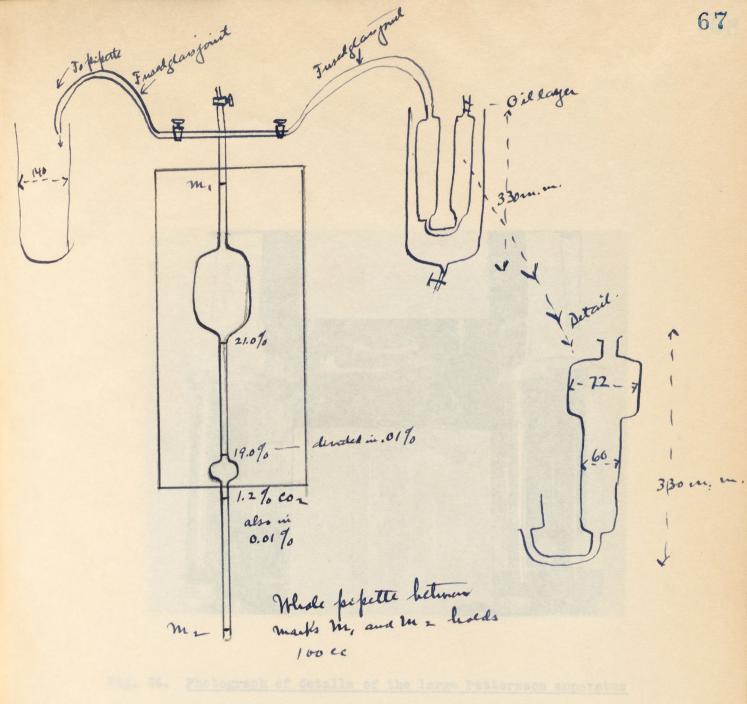


Fig. B. Sketch, with measurements, of the Pettersson gas analysis apparatus.

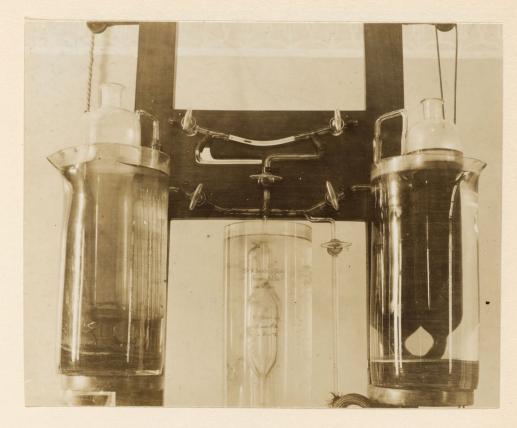


Fig. 34. Photograph of details of the large Pettersson apparatus for analysis of the air in the Heidelberg respiration

chamber.

At the right is the pyrogallic acid pipette and at the left the carbon dioxide pipette. The bulb for measuring the gas is shown in the water jacket in the centre, while a petroleum manometer on the principle of Sondén is shown in the background.



Fig. 35. The lower part of the large analysis apparatus for analyzing the ingoing and outcoming air of the Heidelberg respiration

chamber.

The portion of the apparatus in which oxygen is measured is completely immersed in water; the carbon dioxide portion is below and although jacketed with water, is not easily discerned. The position of a Jaquet sampling tube in relation to the transferring of the sample to the gas analysis apparatus is here well shown.

Professor Jaquet.

Professor Jaquet is now actively engaged in private practice, having a private sanatorium not far from Basel, but he still retains his connection with the pharmacological department of the University. He has no respiration apparatus, but as he has just arranged for an assistant, he hopes to be able to carry out some researches. His interest in mountain experiments still continues and he has plans for many other researches. Seldom have I talked with a man who in so short a time (2 hours) expressed such a multiplicity of ideas on so many subjects, and practically all worthy of note.

Criticism of high altitude experiments .- Professor Jaquet criticises strongly the investigations of Zuntz and his coworkers in the higher Alps, and maintains that there is an after-effect of muscular work which is apparent in experiments in the high mountains. He considers it illogical to climb the mountain previous to investigations, as the muscular work involved makes the observations useless for several days. Jaquet has made a large number of experiments on muscular work and finds that the increased metabolism after work persists for several hours, that there is then a sub-normal result for twenty-four hours or more and the metabolism finally returns to normal only 48 hours after the work is ended. Climbing a mountain involves a large amount of work which affects the resting metabolism which follows. When the after-effect of the work has passed away, the very important transitional period due to the influence of the high altitude has passed and the opportunity is lost. Jaquet said that he had figured out a great many of the "nuchtern" values given in the Zuntz records for days after work and always found them to be abnormal. His theory is that instead of climbing up a mountain, one should use a mountain railway as any climbing on the part of the subject makes the experiment of no value. Since there are now many hotels very high up on mountains reached by railways, this muscular

exertion can be avoided. This is somewhat along the line suggested by Durig, when, in a recent article, he expressed the hope that the Nutrition Laboratory would some time make experiments on Pike's Peak. Jaquet was very free in his criticism of Zuntz and his former coworkers, although his opinion of Durig was of the very highest. He says that Durig's work rings true, and that he considers him to be careful to the last degree and the best of the whole Zuntz school. Jaquet considers that the apparatus of Zuntz is too heavy to be carried on the back and that aside from the mere load, there is a lot of work involved in balancing when carrying it up a mountain.

The mechanical efficiency of the body .- When asked why he thought Zuntz gave figures for the mechanical efficiency of the body somewhat higher than those reported by Carpenter and myself, Jaquet replied, without qualifying his statement in the least, that Zuntz was all wrong, and that there was not sufficient ventilation through the Zuntz mouthpiece for a man carrying a pack on the shoulders. He considered that the ventilation itself was mechanically wrong because it changed the breathing from thoracic to diaphragmmatic, which is abnormal. It appears to me, however, as I pointed out to Jaquet, that if the work of balancing a load is added to the other work, Zuntz should get a lower rather than a higher efficiency than we do. This seems to me a very important and very striking point. I discussed the matter quite freely with Zuntz in his own laboratory but it is by no means explained as yet. Jaquet says that the muscular work involved in bicycling is very effective, and that training consists in having the nervous stimulation, which brings other muscles into play, diminished to the least. Balancing the Zuntz apparatus must call for extra work, and as riding on a stationary bicycle involves no extra work, it is natural to suppose that a lower efficiency would be found by Zuntz than that found by us. Jaquet tried working on a treadmill and found that after 12 experiments the efficiency did not alter, that is, a minimum metabolism per kilogram was found. In all cases, he made some 60 experiments, but there was no change after the twelfth. The training was then complete. Jaquet believes that there are many such operations in life, where, after a short

training, we obtain the minimum metabolism. He still uses the Speck apparatus, with two large spirometers, and carries it up on the mountain on a train, doing no work in transporting it or himself.

Researches on obesity: Jaquet has made some experiments on a girl, 22 years of age, but the respiration experiments were not successful. The girl lost 1800 grams in 24 hours and while in bed, and taking milk lost an additional 1600 grams in 24 hours. At the end of four weeks, she went home but in another four weeks had gained all she lost. Jaquet uses for feeding fat people a diminished volume of liquid, with less carbohydrate, and a fairly protein-rich diet. He emphasises the importance of taking into consideration the water content of the body, and believes that there are different kinds of obesity. For instance, some men eat all day long, breakfasting at 10 a.m., later going to a wine room, dining at noon, in a wine room again in the afternoon at 4 p.m. and then dining at 7 p.m., as well as frequently eating in the evening. This is a clear case of over-eating.

Krehl and Schwenkenbecher have been in Basel and studied Jaquet's apparatus and the latter had worked with it. Staehelin now has a Jaquet apparatus in Berlin, and still another is being built somewhere, but I could not find out where.

<u>Criticism of Rubner's book</u>:- Jaquet says that Rubner's book, Die Gesetze des Energieverbrauchs bei der Ermehrung, is full of errors and he criticises it sharply.

<u>Diabetes:</u>-In discussing experiments with diabetics, Jaquet said that he thought that in diabetes we have a different kind of body to deal with as compared with normal individuals, and that the acidosis of itself might involve the energy loss in the abnormal cleavage. Personally, I cannot see this, for practically all of the minor cleavages in the body are unaccompanied by energy changes of any magnitude. The hydrolysis of the protein molecule for example has been shown previously to be without material energy changes. Another important point that Jaquet made was that there may be retarded digestion in diabetes as he had found this to be the case with fat people. This might cause the increase in metabolism that we found, that is, the supper of the night before might not be digested until quite late in the day. This is an ingenious idea but I personally am inclined to think that it is hardly probable. We should test this on some diabetic, by a fairly long fasting experiment. We have had but one such experiment as yet, that with Mrs. Feehan (Experiment No. B-1 in Publication 136), but she was in fairly good health, nearly sugar-free, when it was made.

Analyses of out-door air.-Jaquet was extremely interested in our work . with the Sonden apparatus for studying the oxygen in the air. I emphasized the fact that we found that there was a continual rise in the percentage of oxygen as the gas was passed into the pyrogallic acid. My explanation of the fact that there was a distillation of water into the concentrated pyrogallic solution interested him extremely, and he said that the same idea had occurred to him several years ago. In using the Sondén apparatus he lowers his mercury so slowly that the water flows down the tube very slowly and regularly and the same amount of water clings to the side; he thus reads the meniscus of the <u>water</u> rather than that of the mercury. This seems to me to be an absolutely wrong procedure. In discussing this point further, he remarked that he made some sort of correction for it, but how he did not explain. Stachelin in Berlin later verified the correctness of my interpretation of Jaquet's procedure but believes it is inaccurate.

<u>Comments on other research work</u>.- Jaquet thinks that results obtained with Grafe's rubber collar are liable to be very inaccurate and personally he would not think of employing it. He thinks, furthermore, that normal respiration is not possible with this collar. He is rather opposed to the use of the Zuntz respiration apparatus, and, as I said above, still adheres to the Speck form of apparatus. When questioned with regard to some recent French work of Robin's he was very emphatic in saying that its printing should not be allowed.

Muchternwert .- Contrary to the opinions of Zuntz and his coworkers, he believes that the nuchternwert cannot be found 12 hours after the last meal. In his experiments he has found that not only the respiratory quotient is changed in a later period but also the total metabolism, as measured by the oxygen consumption and carbon-dioxide output, and that there is a noticeable lowering of of the total metabolism in the later period. Jaquet believes that there are many people with slow digestion, and has tested this point with fat people, but not with normal individuals. He suggested that we might do this to advantage. In still further discussing this question he said that especially erroneous results might be found after severe work, and that he hoped to make experiments in which the respiratory quotient should be determined 12 hours after different kinds of meals, following severe muscular work. He thinks that until the withdrawn glycogen is deposited again, there will be no change, or very little change, in the respiratory quotient. (It would be well for us to look up the researches of Johansson on this point). Jaquet thinks that there is a great disposition on the part of the body to store up the glycogen when it is drawn upon.

Experiments on a horse by Zuntz and Hagemann.- In discussing the experiments on a horse made by Zuntz and Hagemann, Jaquet said that the work was carried out with insufficient ventilation and that the horse had a temperature increase the result of respiratory disturbance.

Prison diet. Jaquet has been appointed by the Swiss Government on a Commission for studying prison diet. One of the first things he observed in the prison diet was the enormous volume of material eaten. By putting into a pan the entire food for one day and measuring it, he found that there was a total volume per day of 4-1/2 to 5 liters. The measurement included the tea, coffee, etc., but not the water consumed and no alcoholic drinks were allowed. With the increased cost of food caused by the rise in prices, this Commission tried to reduce expenses by planning a more economical diet. One important economy was in the use of a good deal of peanut oil, which is relatively cheap, in a fat which contained some lard to give it flavor. This fat is used only

for cooking and is not used to spread on bread, but the prisoners could so use it if they desired. I pointed out the fact that Hindhede of Denmark advocated using cocoanut or palm oil instead of butter for bread. Jaquet, while interested in Hindhede's ideas, said that they had tried palm oil and found that the melting point was too high, and that its use resulted in many gastric disturbances. One explanation of these gastric disturbances might be that the fat may possibly solidify on the lining of the stomach. It also interferes with the secretion of the gastric juice. As a matter of fact, cocoanut or palm oil is used in the manufacture of cocoa, but is not used at all in their prison diet.

The prison diet at present contains 90 grams of protein and 2800 calories of energy for light work and 3600 calories for heavy work. Before the Commission began to modify it, the diet contained about 50 grams of fat and 750 grams of carbohydrates, but now it contains 100 or more grams of fat and a proportionately low amount of carbohydrate. The protein of the diet was reduced because Professor Jaquet thinks that above 100 grams is "luxus", but he could not go much below 100 as the diet was to be used for practical purposes in a prison, and not for scientific experiments.

A very good way to test the diet is to feed it to the prisoners; most of whom are long term men. Each prisoner is given a portion; if he likes the food, it will all be eaten. The feeling of satiety produced by the new diet made all the prisoners complain and at first, they refused to eat. They soon became accustomed to the diet, however, and felt better for its use. This diet is now taken as a standard for prisoners in all Switzerland.

After talking with a man like Jaquet, one can only consider it a very great misfortune that the arrangements at the University are not such as to enable him to carry out scientific research. He is evidently extremely interested in such work but must continue his private practice and hospital in order to provide for himself and family. I consider him one of the brightest men that I have met in Europe. Such a man refutes strikingly the theory that private practice unfits a man for research work, though Jaquet is acknowledged by all in Europe to be a very superior man, both in private practice and in research.

Why famile, the way visiting the School, to the Mutrikies Laboratory. I had a new interesting desversesion with his and found that in his extensive practice in harlet, he had had many rests of diabetes and is thoroughly of the opinion that diabetes is in large part due to sutpintorication. Since he is one of the moment balleyers in this theory regarding diabetes, I was very glad to

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ZURICH, SWTIZERLAND.

Dr. Mende.

A year or more ago Professor Folin of the Harvard Medical School sent Dr. Mende, who was visiting the School, to the Nutrition Laboratory. I had a very interesting conversation with him and found that in his extensive practice in Zurich, he had had many cases of diabetes and is thoroughly of the opinion that diabetes is in large part due to autointoxication. Since he is one of the prominent believers in this theory regarding diabetes, I was very glad to meet and talk with him.

<u>Diabetes.</u> According to his observations, 80 to 90 per cent of the early cases of diabetes show signs of autointoxication with an enlarged colon, gas in the stomach, etc. Later in life there is less autointoxication, and after 60 years of age, none, but whenever there is a high acidosis, there are evidences of intestinal putrefaction. Dr. Mende puts many of his patients to bed, and gives them a diet which contains no meat, but a high proportion of carbohydrate. Oatmeal, potatoes, soup, yolk of egg, macaroni, and milk, or Nessler's milk preparation form a part of the diet, supplying in all, from 100 to 120 grams of protein. The patients remain in bed eight days and then the signs of autointoxication are diminished. This is confirmed by the indol and phenol passed in the urine. With acidosis, indol and also phenol are present in the urine. Later he gives white meats to avoid xanthin, etc. These meats are well-cooked and sterilized. With this treatment, the percentage of sugar falls off in many cases. If there is no tolerance, he uses aleuronat bread containing 50 per cent of aleuronat, -"no bread, naturally". He uses no codein in treatment.

Dr. Mende believes strongly in the nervous origin of diabetes, and cited the instance of a girl who had diabetes after infection in the neck. There was also some albumen, but no casts, and there was no tendency to diabetes by inheritance. As she was approaching coma, she was given some sodium bicarbonate. He has often tried to revive patients when coma was imminent by injecting some high percentage of physiological salt solution; after the injestion, the patient would brighten up.

In regard to fresh air and oxygen he has a peculiar belief. He holds no particular views with regard to the use of oxygen but thinks that an electric fan, with a rapidly moving current of air, is very important. He thought that as the fresh air goes by the nose it is of benefit. I spoke of the possibility of the sound of the fan acting as a suggestion, and also the possibility of its quieting influence due to the effect upon the heat regulation in cooling the face by the air as it passed by.

Electro-magnetic therapy .- While in Boston a year ago, Dr. Mende was very enthusiastic about a new electro-magnetic therapy that he had been using and was very anxious to have me see it. When in Zurich I went with him to the Institute Salus where they treat patients regularly by this method and met the man who had invented the apparatus, Mr. Muller. Evidently Mr. Muller is used to giving demonstrations for the uninitiated. He showed me a number of preliminary experiments, which seemed very striking, but I found that the results were not unusual for a magnetic field for the amount of current used. The magnet was a laminated bar about 7 centimeters square and about 22 centimeters long. made up of sheet iron and paper, through which was passed a heavy current of 40 amperes at 110 volts, with a frequency of 100 per second. Mr. Müller made a number of experiments with iron nails and iron powder and then placed these iron nails and powder in a glass Petri dish and interposed a bar of aluminum between the magnet and nails. This produced a very peculiar effect on the figures formed by the powder. Finally an iron rod, some 6 inches long and 1-1/2 inches in diameter, was placed on top of the magnet, and on top of this rod was put a ring which was a little larger than the rod and perhaps 3/8 of an inch thick. This fell in a rotary spiral rather than straight down. An aluminum ring of the same size did not fall. If placed at the bottom of the iron rod and the current closed, the aluminum ring will be shot up into the air

some three or four feet. He also had an aluminum disc with three cords attached to it and these three cords were attached to a wire circle arrangement. This aluminum disc was held over the magnet and was repulsed, but the three cords held it from flying up into the air. He also had an aluminum ball in an aluminum ring like a globe and this rotated very rapidly.

He only uses one pole of the magnet and it is necessary to pass water about or through it as the heat is very great. He finds it practical not to use the other pole and obviously it is not a horseshoe magnet, for he must have an alternating north and south pole. The physiological effect he found best at 40 amperes. While he has tried other currents, he has reason to believe that a frequency from 100 to 120 per second gives the best results. Above 120, he believes that the physiological effect will cease or at least diminish. Any physiological effect to be noted must be within 12 to 20 centimeters from the end of the magnet.

The most remarkable thing that I saw in this connection was the optical experiment. The magnet was placed in a horizontal position and I was told to pass my eye by it and look at a window, but was given no idea of what would happen. I noticed a flickering of the light, and bright flashes of light appeared in the eyeball. After trying this once or twice, I asked a friend who was with me also to try it. He independently, without knowing what I had noted, made the same observation.¹ Dr. Mende and Mr. Muller are both very enthusiastic about this magnetic therapy and maintain that the active haemoglobin is always <u>increased</u> after its use. It is of positive value and many nervous diseases are bettered.

⁽¹⁾ See discussion of this optical effect with an alternating magnetic field in Science, Vol. XXXIII, N.S., No. 837, (Jan. 13, 1911), p.68.

Electrical resistance of the body.- The one feature of the institution which seemed to me the most unscientific and open to question was the fact that in measuring the resistance of the body, this resistance varies with different nervous persons, being greater than normal with some people, while with others it is less. I was told to make the following experiment: Two electrodes (metal) were handed to me and I was told to grip them in my hand and hold them tightly. I was then asked to think of something disagreeable, which I could not do under the circumstances, and so I was told to think of anything I desired. The pressure of the hands on the electrodes fluctuated more or less, obviously, and I found that I unconsciously either diminished or tightened the grip on the handle. I was then told to breathe deeply, which I did, and was pricked with a needle. These results were supposed to be due to changes in nervous conductivity. In actual practice, Mr. Muller uses salt water electrodes and has a glass screen so placed that the patients cannot see the apparatus, nor get into difficulty by short-circuiting, etc.

They had made an experiment with a dog which had trouble with the spinal marrow. The dog was treated by this magnetic field method and rapidly recovered, which proved that the treatment could not be psychical. Mr.Müller also stated that he had taken water from Lake Zurich and held it before this magnetic field and got some remarkable crystals which he thought might possibly be due to the polymerized oxygen. He believes that there is a chemical change in the body fluid as the haemoglobin changes and increases. In some printed matter which he gave me were some curves showing that the conductivity of normal individuals increased slowly but that the maximum is reached in half an hour. He also finds that the maximum effect of the magnetic field treatment is reached in one-half hour. The charge for a half hour treatment for each person is, I believe, 3 francs.

Another combination used is a vibrator and the heat from an electrical current. Of course this is purely mechanical, the vibrating attachment vibrating back and forth and giving the vibrations like any other machine. He

had an ingenious supplementary apparatus to apply to the back of a chair so as to give massage. Both Dr. Mende and Mr. Miller believe that the conductivity through the body is chiefly in the nerves at the ends of the fingers, and as a larger number of nerves end there, the conductivity would be greater at this point than through the elbows. While the distance through the body is less in the elbows, nevertheless, the number of nerve endings is very much less than in the fingers, and consequently the conductivity would be greater in the ends of the fingers. With tables, they say, resistance goes down very rapidly as the nerves get very tired. I notice that they had attempted to interest Dr. Flexner in this matter, but he had failed to see their point. I do not wonder. I asked them about the concentration of the salt solution and whether there was not an ionization of it. I also asked if the temperature of this calt solution was changed as the hand warmed it in a half hour, and suggested that if such were the case, there was a possibility of change in resistance.

On subsequent discussion of this matter with other physiologists on my trip, I became convinced of the point that the idea that the nerves conducted electricity was entirely wrong. The conductivity depends upon the muscles but the nerves are fatty and therefore have a higher resistance than muscles and probably the resistance is in large part due to the skin resistance¹ on the surface of the body. I was so deeply interested in this as to have some tests made at the Nutrition Laboratory, all of which pointed toward the fact that the conductivity was not due to the nerves. Under such conditions, then, if this method is used for testing the efficiency of the electroc-magnetic treatment, one can reasonably call the whole theory into question.

(1) Experiments made recently (1910) at the McLean Hospital for the Insane at Waverly, Massachusetts, have shown that pilocarpine alters this resistance enormously.

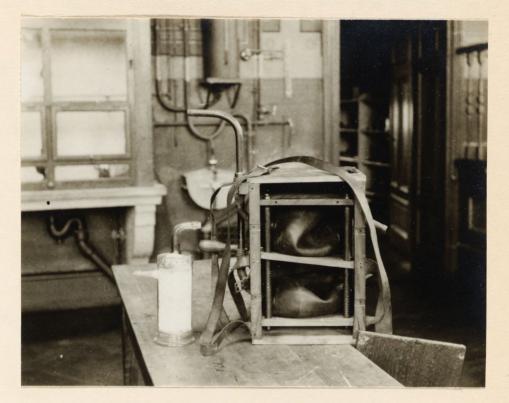


Fig. 36. <u>View of the Burgi respiration apparatus used by Professor</u> <u>Kronecker and his pupils in the experiments on the effect</u> <u>of marching in the mountains.</u>

The bellows and the rubber bags for maintaining the ventilating current of air are shown inside the casing. These bellows are carried by an attendant. The vessel holding soda-lime for absorbing carbon dioxide is at the left.

BERNE, SWITZERLAND.

Physiological Institute, (Hallerianium).

Professor Asher.

I had the misfortune on reaching Berne to find Professor Kronecker too ill to see me, and this was a disappointment as I had corresponded with him a number of times and had hoped to meet him at the time of my visit. His associate, Professor Asher, showed me the laboratory and through his courtesy I was able to secure photographs of two pieces of apparatus that I did not get three years ago. Among these were two photographs (Figs. 36 and 37) of the apparatus used by Burgi in studying the carbon-dioxide output in mountain climbing. These show the apparatus ready for use, the soda-lime absorbers and pump being actuated by an assistant who walks behind the subject. I also obtained a photograph (Fig. 38) of the small mercury thermometers used by Kronecker for studying the maximum temperature in the alimentary tract.

Asher had the highest appreciation of Durig and Gamgee. Asher's investigations have been confined to the enzymes and more recently to the iron metabolism and the question of the spleen in the higher metabolism. His work has been recently substantiated by work on a man and the iron metabolism has been shown to be from haemoglobin or a form of iron in organic combination; I do not recall exactly what it was. Professor Asher was very much occupied in his editing of the Ergebnisse and in this publication he is certainly rendering great assistance to physiologists and physiological chemistry.

MUNICH, GERMANY.

Physiological Institute of the University of Munich.

Professors Frank and Weinland, and Dr. Heilner.

Professor Frank, who is the successor of Professor Carl Voit, is not particularly interested in nutrition or metabolism, and at the present time is so much occupied with making changes in the building that he has not much time for work. The most striking thing that one notices in going into the laboratory is the fact that the classic Pettenkofer-Voit respiration chamber and accessory apparatus have been entirely demolished. Practically nothing is left. I understand that the apparatus is stored, with a possibility of its being installed somewhere later, but it seems to me that it will never be reconstructed. The unfortunate feature about the whole thing is that although the claim was made that it was removed in order to get more room, the space made available by its removal is very small and for some unaccountable reason, in the exact center of the room has been built a dark room used for photographic work. It is very difficult to understand why this is done.

Professor Frank is very much interested in medical pedagogy and is strongly opposed to extending the curriculum in medicine. He believes that it should not be made too broad and that the students should not be over-tired. In his lectures he confines himself to simple experiments and never demonstrates more than one form of apparatus: for example, in giving a description of the tambour, he shows the Marey tambour and no other. He very strongly criticizes some of the American-made apparatus.

Dr. Frank is particularly interested in developing his photographic registration apparatus which I mentioned as having been used by Dr. Phillipson of Brussels, and which I saw in one or two other laboratories. This is made in Giessen and is very good. He has recently arranged to use it in a horizontal

position so that it will not be necessary to use a prism to turn the light, and will require only to be balanced.

Professor Frank was very much inclined to be adversely critical of a good many laboratories and a good many physiologists. He was greatly opposed to the use of the Zuntz mouthpiece and told of a research he saw made by a Russian. Zuntz was there in person, and there was a leak which Zuntz attributed to the carelessness of the assistant, but Professor Frank could not be persuaded that this was the fault.

In discussing the question of the inspiration of oxygen, he reported that animals died under a high pressure of oxygen, and that the oxygen seemed to act as a poison. Why this was so, he could not tell, but he thinks that this question should be studied. This fact has been known for a long time. It is not a matter of decompression but a toxic effect of the oxygen itself.

I was very much interested in talking with Professor Frank and regretted exceedingly that so bright a man was not interested in metabolism and could not contribute to its literature.

Professor Weinland.

With the same seriousness and intensity of purpose that has characterized his work for a good many years, Professor Weinland still maintains an interest in glycogen in diabetes. The importance of recognizing the fact that there are many steps in the oxidation is well known, and he questions the wisdom of attempting to conclude from the respiratory quotient alone whether or not there is a defective oxidation. He believes that the heat determination is the vital thing. He finds glycogen in the lower animals always, even after a very long fast. In studying this point, he believes, that experiments with animals can be made to supplement experiments with human beings with excellent results. In discussing the use of oxygen, he finds that when shaking a paste of the animal tissue and pure oxygen in a warm chamber, there is a larger absorption when pure oxygen is used than when air is used. He does not think it possible to make these experiments when the mixture is only allowed to <u>stand</u> in air, or all oxygen; it must be shaken. This is a very important point and suggestive as indicating the possibility of the utilization by the tissue of pure oxygen in preference to air.

Dr. Heilner.

Dr. Heilner is very enthusiastic about Dr. Neubauer of Munich and says that his work is wonderful. Dr. Heilner is now interested in a study of the anaphylaxis serum of rabbits with fever. This serum loses its activity against infection through a fever, either by over-heating in a heat chamber or by infection. He is writing a book of selected chapters on pathological chemistry. He finds that if urea is injected, much nitrogen is excreted, even more than the nitrogen in the urea, and that the injection of a few centimeters of oil increases the nitrogen excretion. All his experiments are made on rabbits. Evidently Heilner is rapidly losing his interest in metabolism and the clinical features of metabolism appeal to him more than the physiological features.

Institute for Animal Physiology.

Professors Erwin Voit and Krummacher.

Professor Voit has a very well arranged respiration apparatus for animals, on the Carl Voit principle. In this he uses small Munich gas meters which he calibrates both for rapidity of the passage of gas, and for the changes in water level, and maintains that they are accurate to 0.1 of a per cent. When filling with water and reading the level on the side tube, he leaves the drum pointing at zero on the scale.

The large gas meter which is used for the main ventilating current of air is shown in Fig. 39. At the back of it, at one side, is the respiration chamber and near this, a small respiration chamber entirely of glass. On the table in the rear are the tubes connecting with the sampling apparatus. This large gas meter was evidently just being calibrated or being prepared for a subsequent experiment.

The main gas meter used with the respiration calorimeter itself is driven by water power and provided with an air-moistening device in front of it. This may be seen in Fig. 40. As a matter of fact, this photograph is almost an exact duplicate of Fig. 102 in Mr. Carpenter's report of 1908, on page 252 of his report. The connection between the meter and the apparatus itself, however, can be seen a little petter in the photograph given herewith, as the pipe, together with some of the mercury valves, are shown at the right. On the wall at the rear are hanging a large number of Pettenkofer tubes for use with barium-hydroxide. Any one of several chambers can be used with this main apparatus. Fig. 41 shows the rear of the meter with the 4-way valve, which, when thrown by a lever, connects any one of the chambers with the main apparatus. This valve was devised by the diener in the laboratory, and is extremely ingenious, enabling the four tubes to be deflected at will from one apparatus to

another.

An improvement over the original system of Pettenkofer and Voit is a mercury valve which checks the rate of working of the valve. By means of a screw at the bottom, the level of the mercury can be rasied somewhat and in this way a greater resistance to the passage of the air current made. These screws and the valve arrangement are shown in Fig. 42. A small sketch of this regulator is given in Fig. C.

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The small mercury pump, with the Voit valve used for carrying the air current through the small sampling meters, may be seen in Fig. 43, at the extreme right of the mercury valve regulator just mentioned. An ingenious clamp is also used by Voit to hold the barium-hydroxide tubes, and if one were to employ this method, Voit's new clamp should certainly be used.

One of the chambers is completely surrounded by a water mantle (see Figs. 44 and 45) so that experiments can be made at different temperatures, a petroleum regulator in the bath regulating the heating of the water. The same general type of petroleum regulator is used in other places in the laboratory, as, for instance, for holding a bath at a constant temperature of 15°, for keeping the water at a constant temperature in calibrating burettes, and for keeping standard solutions at a constant temperature. This use of a constant temperature is typical of many of Erwin Voit's methods for recording temperatures. He is extremely accurate and extremely precise.

The gas meters are calibrated by means of water, before and after each experiment, and as previously stated, Professor Voit finds them extremely accurate. As a matter of fact, in analyzing the ingoing air, room air is used and Professor Voit sees no reason to think that it might be better to use outdoor air. These gas meters are calibrated and a description of the method of calibrating was given by Voit is a paper in the Zeitschrift f. Biologie, Bd. XXII, p. 281, entitled "Ueber die Aichung der Gasuhren". Professor Voit has sent us a copy of this.

Laboratory construction - I found much to interest me in the laboratory, the construction of the hoods being very good indeed. Structural steel is used and the partitions between different sections of the hoods can be taken down, allowing much greater space. I found that the iron had been painted with a special paint called Bessemer Frabe fuer Eisen Anstrich Grau (Marke Ambos) sold by Rosenzweig and Baumann, who report that they have a branch house in Philadelphia. We have tried to get in touch with them. Voit says that the iron must be well scraped and then a thin coat of the paint put on as fast as possible. He emphasizes the fact that this coat of paint should be thin. The paint should then be allowed to dry and a <u>second</u> thin coat put on. This is the secret of success, he says. The Kjeldahl hood had been painted two years before and it still looked very well. The paint on the outside of the hood lasts for five or more years; on the inside about three years.

Figs. 46 and 47 show very clearly the general type and construction of these hoods, which certainly are very roomy and light. The glass used is from 2 to 3 mm. thick, and not easily broken. The uprights between the door and the hood can be folded up and thus give more room.

<u>Kjeldahl determinations</u>.- Professor Voit introduces caustic soda into the Kjeldahl flask by means of a glass stopcock, and finds that the strong alkali does not cause this stopcock to stick as he keeps it well smeared with fat. He uses a short-necked, round-bottomed flask for distilling, which holds about 400 c.c., and digests with sulphuric acid and phosphorus pentoxide in a pear-shaped flask of about 200 c.c. capacity. Mercury is used as a catalyzer, and later potassium sulphide is added. The standard acid is hydrochloric acid and he titrates with barium-hydroxide, using phenolphthalein. Voit maintains that if one uses sulphuric acid and barium-hydroxide, this forms a compound with the precipitated barium-carbonate (BaC03 + BaS04) and one can easily get false results. The sodium hydroxide is measured out in a graduate, and the acid is collected in a Volhard flask with two bulbs at one side. One ingenious feature is the little glass foot, that is melted to the bulb side of the Volhard flask to support it. A very ingenious drying-oven (Fig. 48) is used in which hot air circulates inside the oven in a coiled pipe and goes out through a chimney. This chimney has an annular space through which the water vapor and gases are withdrawn from the drying chamber itself. Thus, the air enters the chamber preheated. Voit dries materials first at 70°, then at 100°. Some materials it is necessary to dry in a vacuum at 100°. He first makes the vacuum and then heats, using a sulphuric acid vessel between the pump and the chamber; in this way he gets a very high vacuum. There is a check valve of glass on the pump and he reports that the acid never sucks back. By means of a ground glass joint, he can switch the acid vessel into the system or out again at will, and thus by two 3-way stopcocks, short-circuit, so to speak, the air current passage around the sulphuric acid vessel. There is no oxidation under these conditions and the fat is reduced to the minimum weight and stays there, without oxidation.

<u>Covering for table top</u>.- Voit uses the ordinary wood top treated with aniline hydrochlorate and potassium bichromate. He believes he was the first in Germany to use asbestos lumber. Another point of interest is the fact that the ceilings of the laboratory are papered to prevent calcimine, etc., from dropping down. This is especially valuable, as when ash analyses are made they are not spoiled by substances dropping into them.

<u>Discussion of theoretical problems</u>.-Professor Voit said that he does not believe that ordinary body movements play any great role in metabolism. I did not agree with him, however, and spoke of the difference in muscular movement between lying down and sitting up or standing. Voit said that when standing, there was considerably more muscular movement than during sitting, but he was surprised that there was any difference between lying down and sitting. He suggested that in the bed calorimeter the mattress shut off heat radiation, and he suggested that we use not a rubber air mattress but one of woven wire, and thus allow heat to be radiated from all sides. It is of interest to note here that the woven wire mattress suggested by

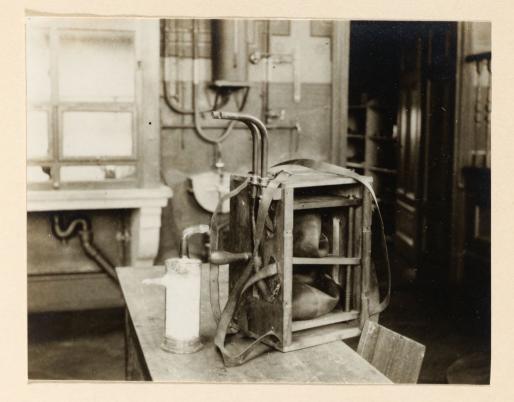


Fig. 37. <u>Another view of the Burgi respiration apparatus</u>. This shows more clearly the handle of the bellows. The mouthpiece and connecting tubes are not shown in either of these figures. as they have not been in use for some time.

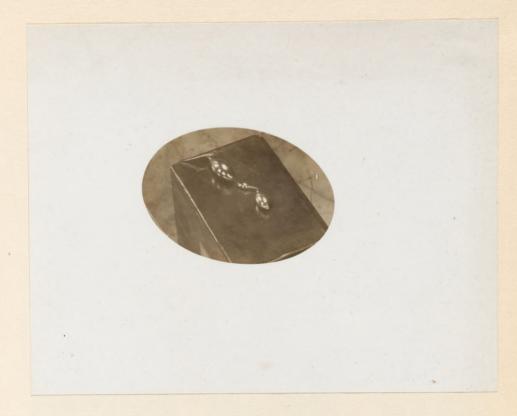


Fig. 38. Two small mercury thermometers used by Kronecker in studying the maximum temperature in the alimentary

tract.

By swallowing these thermometers, and noting their loss in weight at the end of the experiment, the amount of mercury expelled may be determined, the loss in mercury being proportional to the temperature.

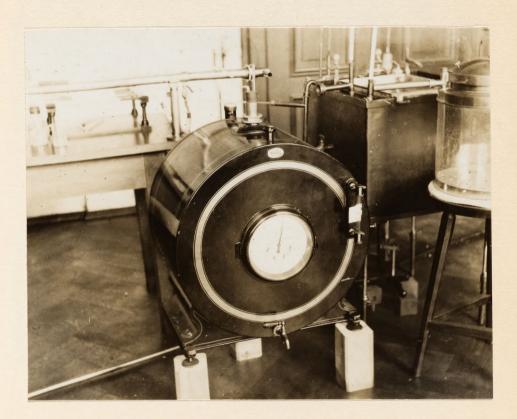


Fig. 39. Large gas meter used in the experiments with animals.

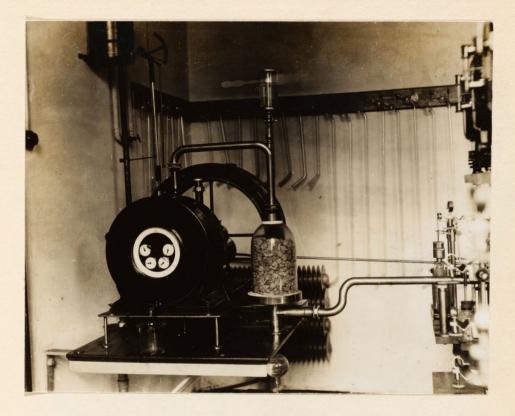


Fig. 40. <u>Gas meter, water wheel for power, and moistening chamber</u> with pumice stone used in connection with a Pettenkofer-Voit respiration apparatus for small animals.

At the rear, and hanging on a wall, are a large number of bariumhydroxide tubes. The connection with the respiration apparatus at the right is clearly shown.

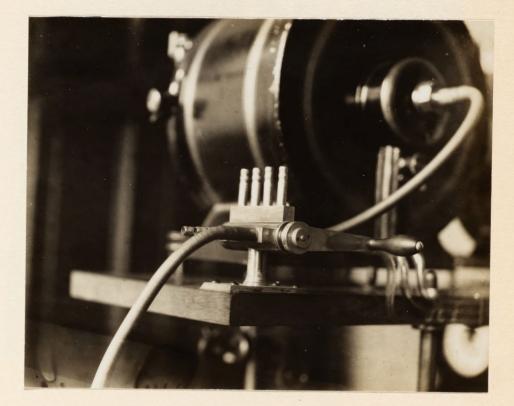


Fig. 41. <u>A 4-way valve devised by the mechanician of the laboratory</u> for shifting from one apparatus to another, using the same meters for both.

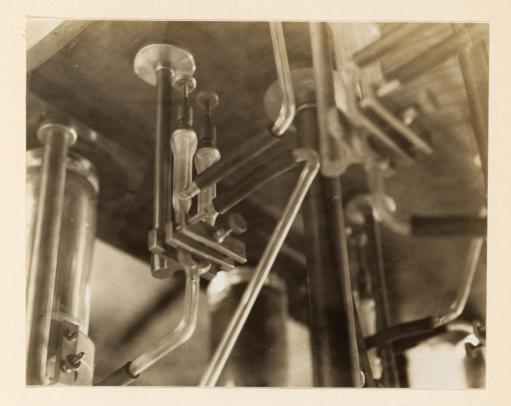


Fig. 42. Mercury regulator for regulating the flow of gas in the sampling pump.

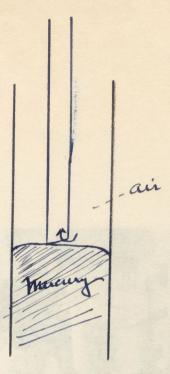


Fig. C. Sketch of mercury regulator.



Fig. 43. Mercury sampling pump after the principle of Voit.

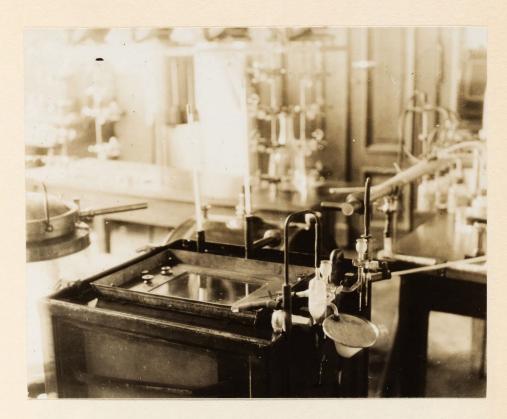


Fig. 44. Tank in which the animal calorimeter is immersed for making experiments at different temperatures.

The surrounding water jacket is kept at a constant temperature by a thermo-regulator, containing petroleum, and the water bath therefore enables a constant temperature.

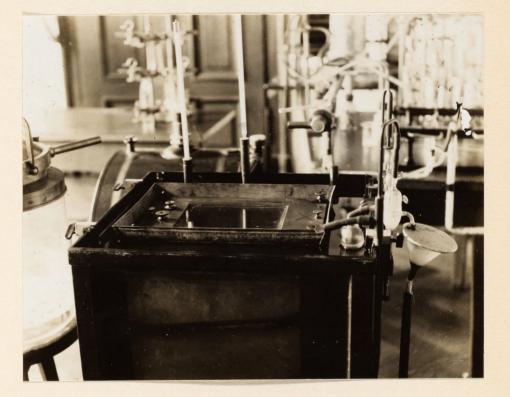


Fig. 45. Another view of this water bath for constant temperature in which the respiration chamber is immersed.

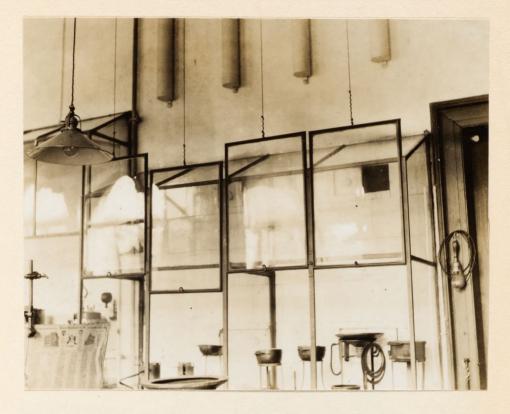


Fig. 46. View of the Kjeldahl hood in Professor Voit's laboratory.

The steel construction of this hood, and its light, airy, and spacious nature, are especially to be commended. The lower portion of the guide on which the door slides can be removed, and thus get a larger space. The one criticism that I had was the fact that the counterweights were exposed to the air and the fumes of the laboratory and the metal columns upon which they were suspended were also exposed.

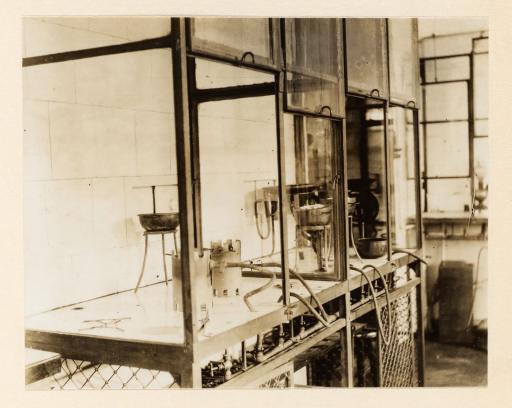


Fig. 47. <u>Closer view of the hood, showing the arrangement of gas</u> cocks beneath and the general spaciousness and open nature of the entire construction.

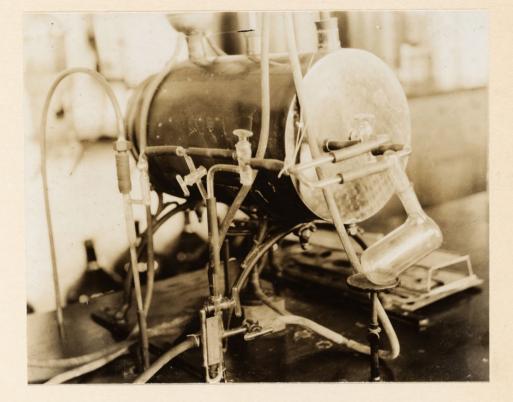


Fig. 48. <u>Drying oven in the laboratory of Professor Voit</u>. The oven is arranged for vacuum drying and has various stopcock arrangements which connect it with the vacuum pump. The sulphuric acid recipient at the rear allows only dry air to enter the chamber, and thus high vacuum is obtained. By means of a system of by-passes, the sulphuric acid vessel can be cut out of the circuit. Professor Voit has been secured and plans made for testing it immediately.

Differentiation in protein.-Voit does not believe that there is any great difference in the nutritive value of the different kinds of protein and has courteously given me a number of reprints setting forth his views on this problem. One interesting point was that if an experiment should be continued for two weeks, he believed that there may be an entirely different body composition and a different need for nitrogen, - not necessarily a difference in the kind of nitrogenous matter but a difference in the amount and therefore in the need. He thought that vegetarian versus meat diet was hardly worth considering. The only trouble with the vegetarian diet is that it requires ballast, but he does not believe that there is any difference in the two sources for the proteid.

The dextrose-nitrogen ratio. - Professor Voit thinks that we should feed a man a long time before determining the dextrose-nitrogen ratio, but I pointed out the impossibility of this in diabetes.

He also believes that it is absolutely <u>impossible</u> to get carbohydrate from fat. In his experiments he uses female dogs and experiments last from 8 to 10 days, taking the dogs out of the chamber only one-half hour each day to catheterize and feed them. He is still actively engaged in working on nitrogen problems.

The impression one gets from Professor Voit's laboratory is that he is extremely accurate and precise in his methods of work. One questions seriously whether or not in searching after this extreme accuracy, he has not lost some of the larger view points. It seems to be a current belief in Munich and in other places in Germany that for the number of years he has been in investigations, he has not made the progress that one would expect. There is no question but that he is a devoted worker with a true belief in the utmost painstaking care and accuracy, but in inspecting his laboratory and in discussiong problems with him, one is led to believe that the larger aspects of the case are not in part properly appreciated.

Professor Voit's associate, Dr. Krummacher, has carried out quite an extensive research with the bomb calorimeter, using the Kröker bomb. His researches also impress one with the idea of painstaking care and accuracy, but without particular reference to the more fundamental problems involved. The whole laboratory is a model of neatness and exactness and in establishing a new laboratory, one should certainly see this first. I regret extremely that I did not include it in my first visit of three years ago.

First Medical Clinic.

Professors Fredrich Mueller, and Q. Neubauer.

Professor Mueller told me the very astounding fact that there was very little diabetes in Munich and it is almost impossible to get cases to show the clinic. There is a great deal of rheumatism and gout, but in Vienna there was a great deal of diabetes and very little gout, although the people in both places were of the same race or stock.

Jaquet respiration apparatus.-Commenting upon the Jaquet respiration apparatus, he says it is but a legitimate outcome of the old chamber of Liebermeister that they used to call the "mail-coach". The oil seal introduced by Grafe in Heidelberg is really very old. When he was in Basel, Mueller told Jaquet that he should get it in order, which he did, using the Swedish gas analysis apparatus. Instead of the wooden wall used by Liebermeister, Jaquet used a metal wall. Jaquet naturally got the credit for the whole apparatus.

<u>Diabetes.</u>- Mueller has found from personal experience that he could not keep diabetics on a low diet. Even taking into consideration the sugar lost in the urine, etc., they must have a rich diet. He was somewhat like Frank in his strong tendency to criticise adversely a good many other workers. He cited the importance of using a four-legged proof in experiments and said that while almost any stool will stand on three legs, with four legs, if good, it should stand perfectly level, and is a much better stool. Of course the four legs should all be of exactly the same length as otherwise there will be more or less disturbance of the balance.

Dr. Neubauer.

Dr. Neubauer is very serious, very intense, and an indefatigable worker. He uses the Mernst light as a source of monochromatic light, with a saturated solution of potassium bichromate. The results, he says, are very satisfactory, particularly as all the results are compared with one another. He deprecates strongly the use of animal charcoal in filtering solutions containing B-oxybutyric acid for he maintains that the acid is held back by the charcoal. The transition from B-oxybutyric acid to diacetic acid, he believes, is more or less of a reversible reaction, and in normal individuals there is no retardation of these oxidation steps. In diabetics there is probably a retardation after the diacetic acid step. Both B-oxybutyric acid and diacetic acid should be in about the same proportion, if there is equilibrium. As a matter of fact, he has recently found that this is so. Dr. Neubauer has also made a number of important experiments on the syntheses in the living organ with artificial circulation. His theory with regard to the reversible reaction between B-oxybutyric and diacetic acid is certainly very interesting and worthy of further study.

Ser.

VIENNA, AUSTRIA.

Clinic von Noorden.

Dr. Falta.

In discussing the subject of the dextrose-nitrogen ratio, Dr. Falta said that he thinks that the experiments are too short. He lays much weight on the 1-hour periods and the hourly excretions of nitrogen and dextrose. In his experiments he found the dextrose-nitrogen ratio was constant and maintains that he is not interested as to where the dextrose comes from, but only in its constant relation to the nitrogen. This dextrose-nitrogen ratio, in his opinion, is a measure of the intensity of the diabetes. He has also studied the effect of giving diabetics sugar and believes that the sugar is either burned or added as glycogen, possibly as fat; if the latter, there should be a different respiratory quotient.

He holds that Magnus-Levy is right and that the increased metabolism of diabetes is due wholly to a disturbance in the relationship between body surface and body weight. If a diabetic loses fat, obviously this fat does not take on oxygen or give off carbon dioxide. It is not active protoplasmic tissue, therefore, what is left has a greater metabolism. I pointed out to him, however, that I did not see why, under these conditions, one of our patients, Case C, when he began losing weight, did not increase in metabolism per kilogram of body weight.

My chief object in making this visit to Vienna was to clear away the misunderstanding between Dr. Falta, Dr. Joslin, and myself, with regard to the diabetic work. This, I believe, was finally arranged to Dr. Falta's complete satisfaction.

Hochschule f. Bodenkultur.

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Professor A. Durig.

Durig maintains that Jaquet is wrong in his conception that the work of transporting the respiration apparatus to the top of a mountain affects the resting values the next day, and says that his new work on mountaineers shows no change in the "muchtern" value beyond the first few hours after reaching the top. The after-effects may last eight hours, but not longer. He was rather critical of the piece of research on mountain work from Rosenthal's laboratory, a report of which has just appeared. The method of using the Zuntz apparatus is not especially difficult to acquire, he says, but everything must be absolutely right before beginning. He emphasized the fact that in the recent Teneriffe expedition with Zuntz, Barcroft and Douglas, he spent many hours fitting up and testing his apparatus before he undertook any analyses.

BERLIN, GERMANY.

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Physikalisch-Technische Reichsanstalt.

Dr. Hagen, Director.

My visit to this laboratory was unfortunately made when Professor Lindeck was away. I was especially interested to find that they were regularly calibrating bombs by the method of Steinwehr and von Jaeger and used their method, also for finding the hydrothermal equivalent. In discussing resistance thermometers, they told me that the quartz thermometers are not much more sluggish in taking the temperature than those with platinum wound on mica in a glass tube, but when a current is passing through, they give up the heat a great deal more quickly.

University of Berlin.

Physiological Institute.

Professor Rubner.

Since my last visit, Professor Rubner has changed his line of work, inasmuch as he has accepted the professorship of physiology in the Institute of Berlin as the successor of Professor Engelmann. This change was made on the express condition that he should retain his Hygiene Laboratory, as it had been built only a few years before, and he did not wish to erect a new building. In his laboratory he has retained the respiration chamber but does not do much work with it. A dog calorimeter will, however, soon be in operation.

Experiments have been made here in the hope of combining the Regnault-Reiset principle with the Pettenkofer-Voit principle by absorbing most of the carbon dioxide in the air circuit and determining the amount unabsorbed by barium hydroxide. This apparatus, I believe, was still in the experimental state.

Professor Rubner believes as firmly as ever that the Zuntz experiments of only 20 minutes are of no avail. He is also strongly of the belief that we can never get accurate results for calorimeter periods as short as one hour on account of the change in body temperature. In discussing body temperature, he was very enthusiastic regarding a recording body temperature apparatus, made by Siemens & Halske. I spent a good part of the day hunting this up and found that the apparatus was sensitive only to about 0.1°C and was not at all adapted for our purpose.

Professor Rubner informed me that Professor Pettenkofer was a transitory diabetic and found in his own case that the sugar increased always after mental work, but his results were never published. Rubner thinks that we should study

diabetics at times with glycosuria and at other times when sugar-free. Under these conditions he thinks the disease is apt to show more and prove more advantageous for study than in well established cases. With older people he thinks that diabetes plays a very small role, that is, it does not do a great amount of harm. He regrets, as do most physiologists, that the old Pettenkofer-Voit respiration chamber in Munich has been torn down. 12

His criticism of Professor Zuntz' new respiration apparatus for oxen was that it was too complicated and it seemed to him that every year it was getting more and more complex. I discussed with him the conductivity of the body in light of the experiments that I found in Zurich and he thinks that with protein and water, there will be the best conductivity, but where there is bone and fat or nerve, there will be less conductivity. He firmly believes that the nerves are much poorer conductors than muscles.

I was shown every possible courtesy by Professor Rubner and through him came into touch with many prominent clinicians in Berlin. His interest in the Nutrition Laboratory is very great. Professor Rubner is coming to America in 1912 as the Hygienic Congress meets then and he is the president of it.

Agricultural High School.

Institute of Zootechny.

Professor Curt Lehmann.

Unfortunately when I visited this laboratory, I found Professor Lehmann was busy on one of his "four-consecutive-hour-lecture" days, a pedagogic curiosity that is characteristic of Professor Lehmann. In talking with his assistant, I found that it seemed to be a mania among the younger assistants in Berlin to write books or articles on the bomb calorimeter, and one or two of Lehmann's assistants were engaged on this subject. They use 3987.8 calories for their standard value for the heat of combustion of sugar, taking it from Landolt and Bornstein, who, in turn, quote from Fischer and Wrede. I called their attention to the fact that this value was unquestionably somewhat too high.

In the catheterization of dogs (see foreign report of 1907, p.332), they have found that a 2 per cent boracic acid solution was preferable to the permanganate of potash for disinfecting the catheters. For preserving urine they use hydrochloric acid and thymol, and when the urine is dried in vacuum on filter blocks at room temperature, there is no loss of nitrogen.

The calorimeter that I was so much interested in three years ago, designed by Professor Lehmann, had not made much progress. His assistant told me that he had decided to substitute a potassium-hydroxide pump with a tall tower, that is, a small modification of the Zuntz-Oppenheimer apparatus. The electrical anodes and balance had been partially installed for giving a constant current or for measuring the current, but the apparatus was about as I found it three years ago. One of the assistants informed that Dr. Abderhalden had planned to do a great deal of work on animal feeding experiments.

First Medical Clinic.

Professors His and Stachelin, and Dr. Fleischmann.

Professor His is much interested in Robin's idea of a constitutional tendency towards different diseases. For instance, tall, thin people often die of tuberculosis. Such people can eat a great deal, the excess of food causing a watery, fat deposition in the body, but they always are thin, and are of the quick-growing, tall type. He thinks that men of this class have a greater metabolism and oxygen consumption than normal.

Professor His was very friendly in speaking of Dr. Falta and thought he was a very promising man with a great many ideas. He said that when Falta and Stachelin worked together, Stachelin was a very good control, but now that Falta is alone, he is either enthusiastic or depressed.

In speaking about rheumatism, he said he had written a book about it but now he knows nothing about the subject, - the book being something like von Noorden's diabetic book.

In studying the influence of potassium iodide, he found that the results in Berne were different from those in Berlin, and it was through his influence that Dr. Fleischmann was sent to Berne to study this point. Professor His has a very high opinion of Fleischmann and referred to his work on atropine. In speaking of Jaquet he remarked that when Jaquet was in private practice, he coquetted with research, and when he was in research, he coquetted with pharmacology, and now again in private practice he coquettes with research, but on account of his large family he must get money.

Professor His is coming to America in the fall of 1911 and will doubt= less visit the laboratory. In discussing the question of diabetes, he said he had found that catmeal differs very much from starch, although each contains the same amount of carbohydrates. He thinks there is either a different kind of starch or an active principle in oats. He made extracts of oats and began to study the effect. Apparently the oat extract had the same effect as the oats. The experiments are not yet finished but he plans to continue them.

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Professor Stachelin.

Experiments with respiration apparatus .- I had the misfortune not to see Professor Stachelin when I was in Europe three years ago, and so made a special effort to get in touch with him during this tour. I found him in the First Medical Clinic using a Jaquet respiration apparatus that he had had constructed there and which had been described a few months before in one of the bulletins of the Charite. With this apparatus they were studying the effect of radium on a woman, with one preliminary hour and then four 2-hour periods. The radium was taken before and after the experiment. The work was done by a Japanese. In giving the radium treatment, they used radium emanation water which was given to a healthy woman and the effect on the digestion, etc., was studied. As a matter of fact they had found presumably but a 5 per cent increase as a result of the radium. I was much interested in the room in which these radium emanations were given. It was a small, hastily constructed room, with walls of heavy paper. To my utter astonishment the air was passed through a small wash bottle containing potassium hydroxide; and it was supposed that the carbon dioxide in the air of the room would be absorbed by this. It was almost amusing.

Stachelin had also made a series of experiment on a fasting woman who was to live 10 days without food and water, and 30 days with no food, but on the twenty-second day he have glutaminic acid as a preventative of acidosis. The woman was very, very sick, and vomited, and Stachelin was very anxious about her. Unfortunately they did not get as much out of the experiment as they should have, only the individual days being reliable, and all the results should be taken with some degree of reserve. The nitrogen of the urine fell to a little over 2 grams per day, but the B-oxybutyric acid and diacetic acid rose to 14 grams per day. The sodium chloride balance was also determined. They are perfectly sure that no food was taken as the room was sealed and the woman stayed in the hospital all of the time. The subject was a professional woman faster, not "Schenk". There was only a small amount of fasting feces, the total for the whole time being but a few grams.

Professor Stachelin gave me a reprint regarding his respiration apparatus and since I made a great many marginal notes on this reprint, it is unnecessary to go into further detail here. Several views of the chamber, with accessory apparatus, are given in Figs. 49 to 56. The glass tube conducting the air into the chamber had an internal diameter of 25 millimeters. The gas analysis burette had a very fine calibre, 0.01 per cent being equal to about 2 millimeters in length. The ventilation is ordinarily 80 liters per minute. The most interesting part of the apparatus was the method of taking a sample, which is described in detail by Professor Staehelin in the reprint. As shown in Figs. 53, 54, and 55, two vessels filled with mercury are lowered into two fixed inverted cylinders, then gradually withdrawn, the air being sucked in behind them. The criticism I should make of this method would be that there is no opportunity to stir the air in these cylinders and there may easily be stratification. Professor Zuntz agreed with me in this. Furthermore, it is not possible for any one using the method to fill the vessels completely with mercury; as about 25 c.c. of air sample is left in the top of the sample pipette at the beginning, that is, the pipette is not completely filled with mercury. There is no manometer on the top of the chamber now. The temperature of the air pipe leading to the chamber is always within 0.2° to 0.3° of the temperature of the meter, but the temperature of the ingoing air may be from 0.5° to 1.3° lower. Stachelin leaves the sample for analysis

in the tube until the next day, without pressure inside, but relying upon the tightness of the cocks.

An ingenious water seal was attached to the connection above the meter in which the end of a glass tube was brought directly against the end of a metal tube on the meter, a rubber hose fastened over the ends and the whole thing immersed in water. As a matter of fact, this was not in use at the time I was there, and is more theoretical than practical.

The Pettersson gas analysis apparatus which Professor Staehelin uses was made in Berlin and a more miserably set up apparatus I never saw. I wondered how any experiments could be made with it.

<u>Analysis of outdoor air</u>.- Staehelin in Basel had also found a difference in the oxygen content of outdoor air, but he had always feared that it was the fault of the method, as Hempel's research showed constancy. He was extremely glad to hear of our results which confirmed his.

Dr. Fleischmann.

Dr. Fleischmann, working in the clinic of Professor His, has been much interested in studying the effect of iodide injection. He found that the rabbits in Berne all had goiter and their reaction to iodides was different from that of the rabbits in Berlin without goiter. When animals react differently in two localities, it would seem as though there may be a great opportunity here for error in pharmacological and pathological studies. The fact that all animals and many human beings in Berne are subject to goiter is well known.

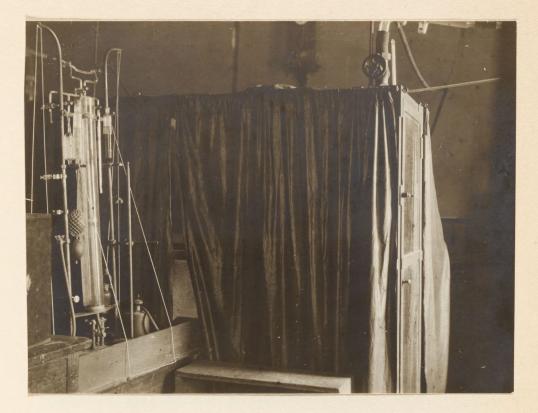


Fig. 49. <u>General view of Staehelin's Jaquet respiration apparatus</u> with curtains over it to make it dark for the subject.

At the time this was taken, the subject was in the darkand an experiment was in progress. The walls of the chamber are practically all of glass which is more or less translucent. At the left is shown the very poor Pettersson gas analysis apparatus, constructed in Berlin for Staehelin. The wires running to the board show the method in which it must be tied up and raised to keep it from falling over.

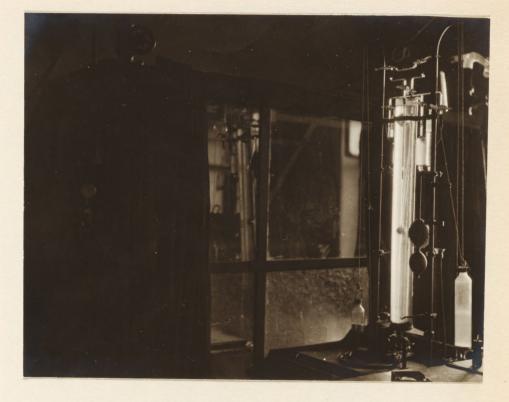


Fig. 50. Another view of Staehelin's respiration apparatus, showing curtains partially pulled to one side, and the gas analysis apparatus used for the analysis of the ingoing and outcoming air.



Fig. 51. <u>View of food aperture of Staehelin's respiration apparatus</u>. Rough glass is used and thoroughly cemented into an iron frame. This is supposed to be absolutely air-tight.

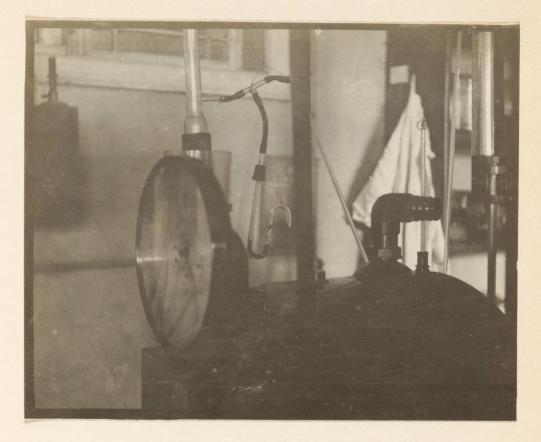


Fig. 52. <u>View of the gas meter used by Staehelin in his respiration</u> apparatus.

The small manometer indicates the pressure on the meter.



Fig. 53. <u>Gas meter with details of sample-taking device of Staehelin's</u> respiration apparatus.

As the gas meter revolves, the upright is made to slowly revolve and thus lower automatically the two vessels containing mercury. As they lower, air is drawn into the two sampling vessels.



Fig. 54. <u>Rear view of gas meter and sampling device of Staehelin's</u> respiration apparatus.

The train of gears containing the sampling device with the motor is shown here as being separated, the light background of the wall behind being visible between them. At the right are two of the Jaquet sampling pipettes, in which the air is taken from the collection pipette at the end of each period.

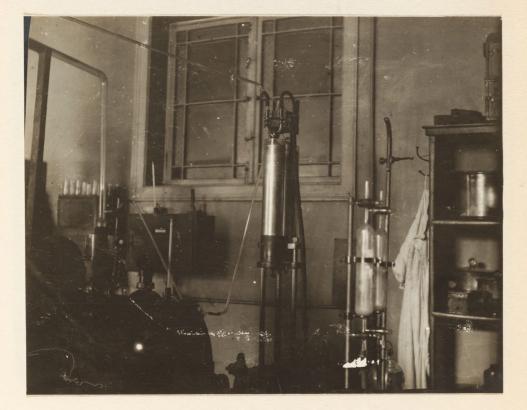


Fig. 55. Another view of Staehelin's gas meter and sampling device.

This shows the connections between the air sampling device and the incoming pipe to the left, and the outcoming pipe near the meter. The Jaquet sampling pipettes are shown at the right.

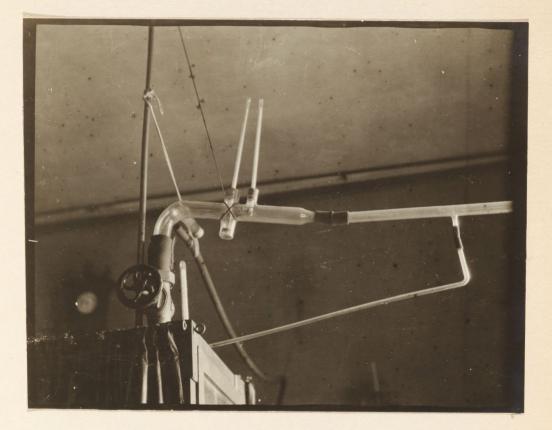


Fig. 56. Details of wet and dry bulb hygrometer used by Staehelin in ingoing air.

The glass tubing is shown where the samples of the ingoing air are taken across the room to the sampling device.

Second Medical Clinic, Charite.

Professor Kraus, Dr. Brugsch, and Professor von Bergmann, Dr. Plesch.

This new Medical Clinic is in a marvellous building, as elegant as the new Rockefeller Institute Hospital in New York, all of the fittings being of the finest and most expensive character. The chemical laboratory is beautifully equipped with a special room for ether extractions, Kjeldahl digestions, sand-baths heated with gas, and a drying apparatus after the principle of Faust. Below is the Roentgen ray room, with lead glass windows, and electro-cardiogram apparatus with a string galvanometer, the vibrations being deadened by means of a sand mattress (Nikolai).

The respiration calorimeter, which is a Rubner apparatus intended for experiments with dogs and children, is very perfect. Professor Heubner of the Children's Clinic was in the room when they were explaining it to me and when they made the statement that it could be used for either dogs or children, he shock his head. It is now modified so that determinations of the oxygen may be made. There is a large soda line chamber, but the carbon dioxide is still determined by barium hydroxide. The oxygen is supplied from a bomb and the bomb is weighed. Professor Kraus said that he anticipated great results from this chamber.

There was also a large Rubner respiration apparatus or Pettenkofer-Voit chamber for man, and a Zuntz-Geppert apparatus, and they had planned to use the latter apparatus inside the large chamber. Dr. Plesch, who made a great many gas analyses in the laboratory, said that he had used both the Zuntz-Geppert apparatus and also Haldane's, but thinks it all depends upon who uses it. He also believes that the Zuntz circulating scheme for oxygen will never work with these large respiration chambers. In discussing the mercury pump in which water is used to raise and lower the mercury, Plesch

remarked that Professor Bohr was not the first to employ this method as Fredericq had used it much earlier.

Dr. Brugsch has worked on diabetics and also with depancreatized dogs, and has special ideas on the origin of diabetes; all his experiments agree. He said he did not see why determinations of the oxygen consumption are important in diabetes. His belief is that the metabolism is not increased, but that diabetics act differently when under special conditions, that is, with a large diet, etc. Dr. Brugsch is to continue working on diabetes, determining only the carbon dioxide.

Of interest in the equipment of the laboratory was a room for drying photographic plates at 45°C. Also, in the balance room, there was a small box compartment for each worker with a desiccator. Fraulein Dr. Rahel Hirsch, an assistant, showed me the bomb calorimeter and the apparatus for the determination of carbon dioxide, according to Kröker. While Professor Kraus is very enthusiastic over the Rubner apparatus, Fraulein Hirsch thinks that they ought to have our apparatus.

Konig. Tierärztliche Hochschule.

Professor Abderhalden.

Abderhalden remarked that he can now buy hydrolyzed protein from Schering, and one gets the specific dynamic action even when hydrolyzed. He told me that Professor Tangl has made the extirpation experiments with no kidneys and gets the same results, disproving the idea that there is kidney work. In his laboratory there is only his own personal library, and none belonging to the Institute. He considers his feeding experiments as now concluded, and that it has been proved that the body can synthesize protein from hydrolytic products.

Agricultural High School.

Institute of Animal Physiology.

Professors Zuntz, Loewy, and Drs. Caspari, and Cronheim.

Professor Zuntz' new laboratory is in the Tier-Physiologische Institut of the Landw. Hochschule. It is equipped with two respiration chambers, one, a small Zuntz-Oppenheimer respiration chamber for experiments with animals, and the other, a much larger chamber for experiments with large animals, such as the horse, etc. Views of these chambers, and accessory apparatus, are given in Figs. 57 to 68.

Respiration chambers.- The small chamber is constructed on the Regnault-Reiset, or closed-circuit principle, while the large chamber is operated on the Pettenkofer-Voit, or open-circuit principle. Professor Zuntz hopes, however, to change the latter to a closed-circuit apparatus, but he is very far from it as yet. I did not see the results of his experiments with the Pettenkofer-Voit chamber but he reports them as being very satisfactory. When asked why he made his Pettenkofer-Voit chamber so large, he said that since by means of a Pettersson apparatus excellent results had been obtained with a man in the Sonden-Tigerstedt chamber which contained 100 cubic meters, he believed that he ought to get very good results in his chamber with a horse. His reasoning, I believe, is correct so far as the carbon dioxide production is concerned, but it seems to me a great error to make the apparatus so large if determinations of the oxygen consumption are to be attempted.

For making the carbon dioxide determinations, a Pettersson apparatus is used. This appears to be an exact duplicate of that of Johansson and Tigerstedt, as it is graduated from 0 to 4 on one side and from 4 to 8 on the other. Zuntz says that he can obtain duplicates to 0.032 or 0.033. The efficiency of the apparatus for measuring carbon dioxide is tested by admitting to the chamber pure carbon dioxide from a previously weighed steel cylinder. Professor Zuntz finds that the carbon dioxide which he gets in Berlin is perfectly pure, as all of the gas is absorbed by potassium hydroxide after 50 liters have been let out of the bomb. He contends, and correctly, I think, that until he can more accurately determine the oxygen, there is no necessity of his tosting the apparatus by means of burning alcohol, as he is able to determine carbon dioxide very accurately. In testing the apparatus, he holds it at 50 mm. of water pressure for one hour and finds that it is necessary to allow for the loss of only a few millimeters of water, after taking into consideration, of course, the change in barometric pressure. For determining these changes, he uses a thermobarometer, consisting of a block tin tube wound about inside of the chamber.

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Professor Zuntz said that he did not particularly care for the bariumhydroxide method of determining carbon dioxide as used by Pettenkofer and Voit and that he took the samples of air fractionally by clockwork, and also every two hours. An ingenious method is used for taking a sample by which the bulb of a pipette is lowered and the water allowed to flow out according to a method originally devised, I believe, by Loevy. The lowering of the bulb is accomplished by substituting it for the weight of a Swiss clock, a device first used, I think, by Schaternikoff in Moscow. This method differs See the movement of a gas meter drum and a sample proportional to the volume is obtained. Since, however, the speed of ventilation in Professor Zuntz' apparatus remains constant in practically all of his experiments, the proportioning of the fractional sample by time is as accurate as proportioning it by volume.

In discussing other forms of respiration chambers, Professor Zuntz said that he thought Hagemann was in a better condition for running experiments now than he was two or three years ago. He also believes that the apparatus of

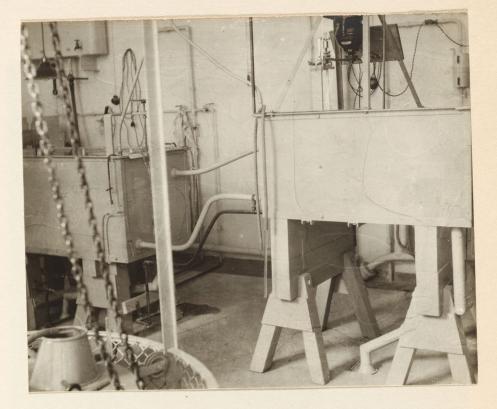


Fig. 57. General view of the Zuntz-Oppenheimer respiration apparatus.

The tank at the right contains motor, ventilating apparatus, and potassium hydroxide absorption tower. At the left is the respiration chamber. The two curved pipes painted white are the ingoing and outcoming air respectively. The black pipe, below the white pipe, and bent to conform to it, is a gas heater for heating the air. The chain and pulley attachment at the left is for the calibration apparatus, for calibrating the spirometers for admitting oxygen.

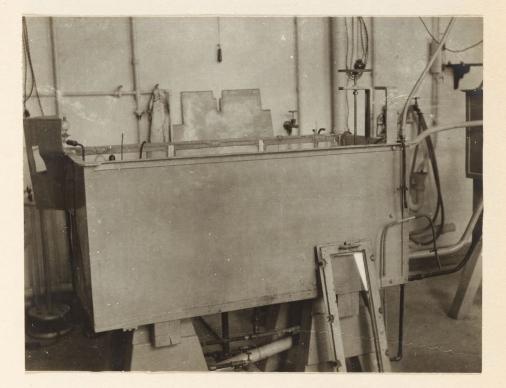


Fig. 58. Outer water bath for the Zuntz-Oppenheimer respiration apparatus. The inner glass lid, which is screwed down by a clamp, is shown resting against the wall of the outer vessel, in the immediate foreground.

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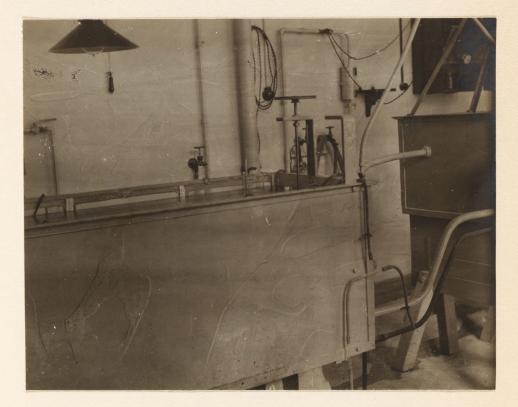


Fig. 59. <u>View of the respiration chamber tank of the Zuntz-Oppenheimer</u> apparatus showing the tank filled with water.



Fig. 60. <u>Another view of glass tank showing the interior chamber of the</u> <u>Zuntz-Oppenheimer respiration apparatus immersed in water</u>.

The opening through which the animal is placed can be indistinctly seen at the top.



Fig. 61. Looking down from the top on the Zuntz-Oppenheimer chamber. The inner chamber is shown with the cover removed and the water all withdrawn from the outer chamber.

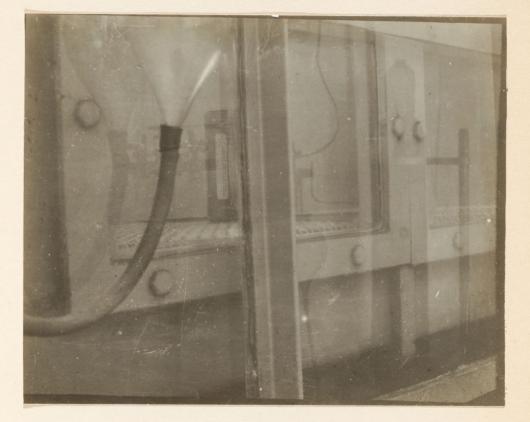


Fig. 62. Imperfect view of the interior of the Zuntz-Oppenheimer small respiration apparatus.

This tank is immersed in water and the photograph is taken through water.



Fig. 63. <u>View of pump and rotary ventilator for the Zuntz-Oppenheimer</u> respiration apparatus.

At the left is the rotary ventilator, actuated by a shaft which extends to a motor above. At the right is the large chamber for freeing the air of carbon dioxide. A small pump actuated by an upright shaft intermittently pumps strong caustic potash into the interior of the dome, and this absorbs the carbon dioxide.

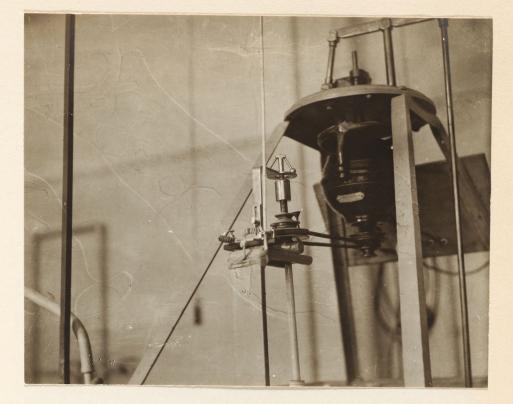


Fig. 64. <u>Electric motor for running the rotary blower and for the pump</u> for the caustic potash in the Zuntz-Oppenheimer respiration apparatus.

The rotary blower is run by a turbine and the pump by a walking beam, connected with a bevelled gear on the end of the armature shaft. An ingenicus feature is the small regulator which shows when the motor shuts down. When the motor is running, the two balls on the governor above are raised in the air by centrifuge force and when the motor stops, they settle back on a metal plate, closing the contact and ringing a bell, thus calling an assistant in any part of the laboratory to the apparatus.

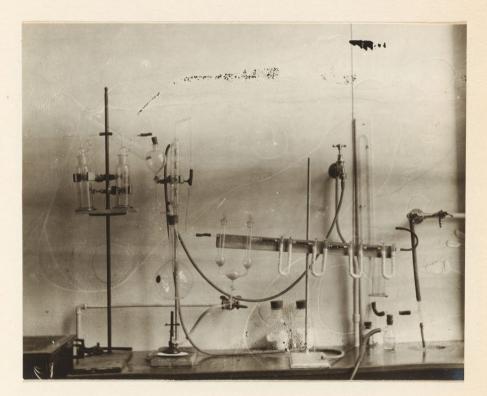


Fig. 65. Apparatus for determining the carbon-dioxide absorbed by the caustic potash in the Zuntz-Oppenheimer respiration chamber.

An aliquot portion of the potash is allowed to flow into the large flask and the carbon dioxide is weighed in soda lime tubes, the gas having been previously thoroughly dried by passing it over sulphuric acid and glass beads.

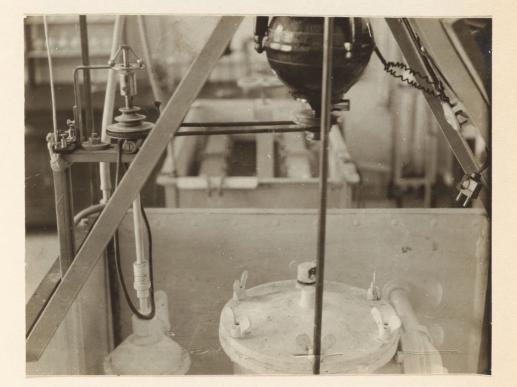


Fig. 66. <u>Another detail of the electric motor, rotary blower, and shaft</u> <u>for the "spitz" pump of the Zuntz-Oppenheimer apparatus</u>. The details of the little centrifugal governor are here well shown.



Fig. 67. Elaborate system of introducing oxygen into the Zuntz-Oppenheimer apparatus, showing large gasometer and water vessel, or levelling bulb, for admitting water into the gasometer.

The amount of water is weighed from time to time and also the amount of oxygen introduced into the chamber.

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Letulle and Pompilian in Paris ought to give satisfactory results as the theory is good. He deplored, as did I, the fact that the Pettenkofer-Voit respiration apparatus in Munich had been removed.

<u>Criticism of Professor Zuntz' large respiration chamber</u>.- It seems to me impossible to control the temperature of this large chamber with sufficient accuracy to make practicable the measurement of oxygen on the closed-circuit principle. As has been pointed out in our own work, this temperature regulation of the chamber is of the greatest importance and without calorimetric features, it is difficult to see how Professor Zuntz can possibly maintain an accurate control of the temperature in his chamber.

Furthermore, Professor Zuntz assumes that all the caustic potash solution is in perfect mixture in the chamber in which it is made and that there is no change in the volume or in the dilution of the liquid in different parts of the pump or chamber. This, however, should be fully demonstrated.

My general impression of the apparatus as a whole was that while it suits his purpose admirably as an open-circuit apparatus, and that an extremely ingenious use is made of the Sondén-Pettersson gas analysis apparatus in connection with it, nevertheless any attempt to make it a closed-circuit apparatus would be a failure. I doubt seriously if results can ever be obtained which will give values inside of 5 per cent and if values larger than 5 per cent are to be obtained, the experiments are without avail as computations can be made from well known factors as close as this.

Zuntz' criticism of respiration apparatus at the Nutrition Laboratory.-Professor Zuntz' chief criticism of our small apparatus is that it gives no information regarding the mechanics of respiration, such as the rate or volume of respiration. He thinks these are of great importance, especially in view of the new methods of studying blood gases and tension, with the new ideas about the total amount of blood circulating through the body. He is very conservative about giving up the old method and would rather seek to improve it than to adopt a new method which does not take into consideration the

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volume of respiration. In speaking of the use of this apparatus by different clinicians, he says that Winternitz and, of course, Magnus-Levy, are both excellent technicians, and have used the apparatus with great success, but there is very much of the older work which is not good, and an actual discredit to the apparatus.

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Testing the Zuntz respiration apparatus.- I personally was the subject of a respiration experiment and attempted to find out whether the Zuntz values as used by him, under conditions that he would consider ideal, gave as little resistance to respiration as he maintains that they do. I always found that there was a very noticeable retardation of respiration when the values were in place. In the extensive study of the various types of respiration apparatus which Mr. Carpenter of the laboratory staff is making, it is important that this point be tested carefully. It is possible by means of a Tissot spirometer and a gas meter to measure the volume of air expired in 20 minutes, using first the mouthpiece, then the nosepieces, and note whether a greater volume of air is taken through the nosepiece or through the mouthpiece.

I pointed out to Professor Zuntz that while the calibration of this meter was usually made with a regular flow of water, in actual use the air was passed through the meter by a series of impulses. I suggested that he calibrate his meter under the same conditions as when used, and he told me that he had so calibrated it years ago. I have been unable to find anything that Professor Zuntz did not do years ago. He found at that time that if he used the calibration for a somewhat higher rate than the actual rate of ventilation, the error was fully compensated; thus, with a gas current of 7 liters per minute, he would use the calibration for 10 liters per minute. The error in any case was only a few tenths of a per cent error. The constant water level in the meter is, of course, very important. Professor Zuntz' criticism that the volume of respiration per minute, and per single respiration, cannot be obtained with our respiration apparatus is perfectly good and sound. He says that if the minute value of the respiration is not regular, this shows irregularity in internal muscular exercise. With certain persons he has found that this irregularity is very rhythmical with a period of short, shallow respirations followed by a period of deep respirations, etc., as was the case with Higgins and one or two of our other assistants. Such people, of course, cannot be used and Zuntz says that at his laboratory he tests his subjects for a week or more to find out if the respiration is regular and to train them to the apparatus. Many of them he finds he cannot use at all.

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It is a source of great regret to me that Professor Zuntz has not installed our respiration apparatus in his laboratory. We are studying his apparatus most critically and it seems to me that it would be very helpful if he would study ours most critically, and raise all possible objections to it. I sincerely hope that he will soon have a respiration apparatus like ours in his laboratory.

Experiments at Teneriffe.- Professor Zuntz had recently returned from Teneriffe, where he was a member of a party of four who studied the effect on the respiratory exchange of the muscular work involved in mountain climbing, also on blood gases, the dissociation curve of oxyhaemoglobin, etc. He said that he found a decrease in the alkalinity of the blood at 2000 meters of about 10 per cent, and at 4000 meters 6 to 8 per cent with all the four persons in the party. This decrease was held for 14 days and was not the effect of the work of climbing. Barcroft, who was a member of this expedition found that the tension of the oxyhaemoglobin also changed correspondingly. Barcroft's methods are remarkably accurate. Zuntz has found that the after-effects of work last about one and a half hours' which, he thinks, is longer than at the ordinary sea level. The acidity developed at a high altitude is due, he believes, to lactic acid, there being an incomplete oxidation in the muscles. I cited the statements of Mohr in regard to diabetes, the acidity liberating carbon dioxide, etc., but Professor Zuntz is not particularly impressed with Mohr's technique as he is more especially a clinician, with excellent ideas, but not a particularly good technique.

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Professor Zuntz is very much pleased with the new Durig valves; he used them at Teneriffe, and will doubtless continue to use them in his laboratory. He found that the small, portable Haldane apparatus could not give results for oxygen determinations in the air closer than 0.05 per cent. In discussing the methods of gas analysis, he said that over water it was possible to get results to 0.01 per cent with the apparatus used at his laboratory, but it takes an especially trained man, such as Durig, to do it.

The Haldane apparatus for determining the carbon monoxide in the blood is used in Zuntz' laboratory very satisfactorily. This apparatus, which is known as the Haldane-Barcroft apparatus, is shown in Figs. 69 and 70.

In discussing the question of the effect on metabolism of change in body position, Professor Zuntz said that he found no difference in metabolism between lying down and sitting with a head rest and no muscular tension. He believes that the position oulined by Johansson as <u>vorsatzliche Muskelruhe</u> can be held for 15 minutes, but not as long as Johansson requires, namely, one hour. He deplores Johansson's idea that carbon dioxide alone is an index of metabolism and said that at a Congress in Heidelberg he spent two hours trying to convince him of it.

<u>Criticism of muscular work experiments</u>.- I spent considerable time, in fact, part of several days, discussing with Professor Zuntz most carefully the work that was done by Mr. Carpenter and myself at Middletown on muscular work. Professor Zuntz made a number of criticisms with his usual keenness, but I was able to meet all of these to his satisfaction. It still remains a fact, however, that there is a wide difference between

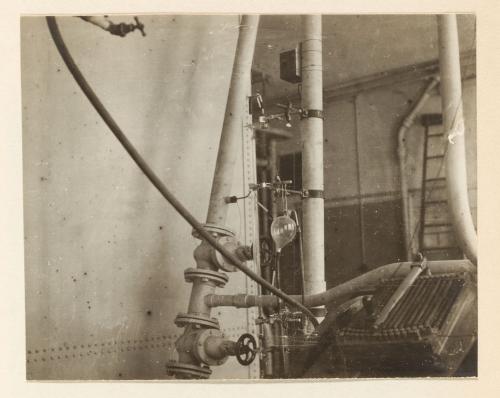


Fig. 68. <u>A corner of the Zuntz respiration chamber for large animals</u>. The sampling is done by lowering a bulb, and allowing it to flow out gradually. This bulb is lowered by means of clockwork, using the bulb as a substitute for the weight on a Swiss clock. The rheostat shown in the photograph is attached to the large gas meter and regulates the speed of the motor used to move the gas meter. The riveted boiler plate of which the chamber is constructed is clearly shown.

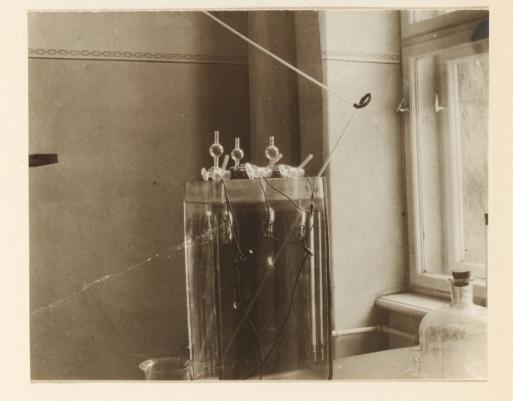


Fig. 69. <u>Gas analysis apparatus of Haldane-Barcroft, somewhat modified</u>, for determining the oxyhaemoglobin in the blood.

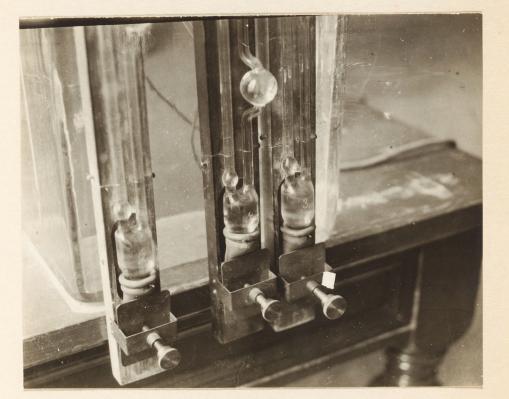


Fig. 70. Lower portion of Haldane-Barcroft gas analysis apparatus in Zuntz' laboratory, showing adjustment for the levels.

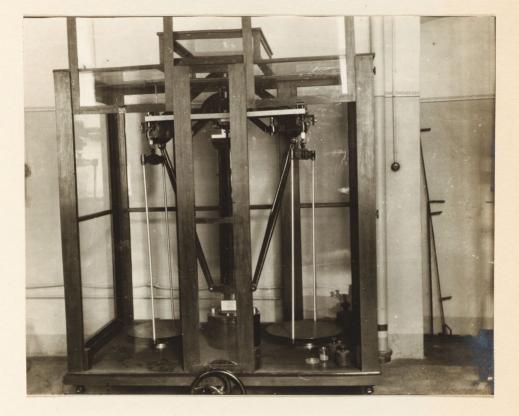


Fig. 71. Very large Sartorius balance in Zuntz' laboratory capable of weighing 50 kilograms, presumably to 1 milligram.

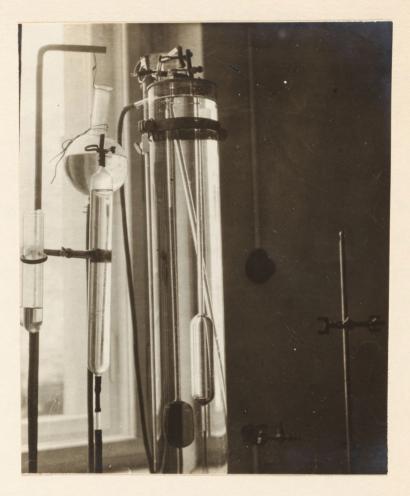


Fig. 72. Zuntz apparatus for analysis of high per cent of oxygen.
Zuntz
This consists of a burette such as the commonly uses, only inverted
with the graduated portion above the bulb rather than below. The absorption pipette is exactly in the rear and of the type commonly used. The gas collecting tube is shown at the left with a levelling bulb.

our results and those of Zuntz, as ours give an efficiency of 24 per cent, while Zuntz obtained 34 per cent. Furthermore, all the arguments made against the Zuntz method seem to contribute toward an even greater efficiency than was found.

In discussing the experiment made with a horse, Professor Zuntz said that he found when there was no increase in body temperature, the aftereffect of work was very short, - less than one hour. With men he thinks it is also very short. I raised the point that with our men we found the periods from 1 a.m. to 7 a.m. were frequently high after severe muscular work, and he thought that although the men appear to be sound asleep, there is muscular tension and consequently his and our results do not conflict.

Experiments on feeding a dog carbohydrate. - Recently a dog who had been fed a fat-meat diet for four days was given 250 grams of sugar and the respiratory exchange studied every hour for eight hours. Not once did the respiratory quotient exceed 0.8, and most of the time it was 0.77. Under these conditions it would seem that the sugar must have been stored as glycogen.

Electro-magnetic therapy.-I reported to Professor Zuntz my experiences with the electro-magnetic therapy in Munich, and found, to my astonishment, that he had also investigated the subject. The only thing he found difficult to explain was the eye movement, shown when moving the eye in front of the magnetic field. Zuntz' explanation for this was that possibly there was a stimulation of the nerves as the result of induced current of some kind. He does not have any higher opinion than I do of the method of measuring the resistance and using that as index of the general nervous condition, and believes that the conduction is much better through muscle than through nerve. He cited the fact that Hermann has shown that the nerves are not as good conductors of electricity as muscles.

The amount of work that Professor Zuntz has done in the field of physiology is certainly remarkable. His new laboratory ought to have been built for him 20 years ago; it is too late for him now.

Professor Loewy.

Professor Loewy is writing a book, or rather, a portion of Oppenheimer's Handbuch. At the time of my visit he was about to make a respiration experiment on a patient in the Virchow Hospital who had no sweat glands and who was therefore easily influenced by temperature changes. At Professor Loewy's invitation, I went to the hospital and watched the experiment in progress, taking four photographs (Figs. 73 to 76).

The disease seemed to be hereditary, as the young man had a cousin with the same disease and also a younger relative. It was at first thought that he was stimulating disease in order to avoid military duty, but this suspicion was proved to be unfounded, as it was noted that he had a body temperature of 39 degrees. He had no teeth, which is characteristic of the disease.

Five experiments had been made with this subject in about 14 days. The patient was in bed during all of the experiments but they were not quite nuchtern as a cup of tea with two cubes of sugar had been given him four hours previous to the experiments.

During the experiment which I saw, the subject slept very soundly most of the time, not even the flies disturbing him. He was surrounded with a number of hot water bottles to artificially raise the temperature and was well covered with a blanket although it was in May and the room was reasonably warm.

The intestine values of Speck, which Loewy personally prefers to the Durig values, were put in position and suspended by a cord as shown in Figs. 73 to 75, so that there should be the least possible strain upon the man. An important addition to the regular Zuntz apparatus was a rubber bandage which was drawn around the back of the head, holding the lips firmly pressed against the ordinary Zuntz rubber mouthpiece. Loewy pointed out that it was very important that the valve for the inspired air should not get dry, and he had to wet it once during the experiment. Professor Loewy has an idea of enlarging the glass parts and putting in a sort of Drechsel wash bottle with cotton for moistening the air. The expired air passed through a large tube into an Elster dry gas meter provided with a chain and gear to lower the pipette and to allow water to flow out and samples to be taken as the air passed through the meter. Two mercury thermometers were carefully read. The respirations were 20 per minute and the pulse was 90. Frequently the subject swallowed saliva every 1¹/₄ to 2 minutes, but apparently there was no undue pressure against the nose as a result.

Professor Loewy made two experiments, simply refilling the sample pipette at the end of each experiment. The man was entirely unaware of what was going on about him during the whole time. At the end of the experiment, Professor Loewy remarked that it had been an "Ideale Versuch".

This was the first time that I had ever seen a careful use of the Zuntz method, and I regret to say that I was not particularly impressed with the accuracy of the technique. It may be that one could expect no better conditions with a hospital patient who was comparatively unaccustomed to this apparatus, although several experiments had been made with him previously. It certainly appeared to me, however, as if the nose clip, for example, did not fit particularly well although Professor Loewy assured me that this patient had a very peculiar nasal formation, with a mucous membrane which was very tenacious, and that the nostrils themselves would hardly separate after the clip was removed. As a matter of fact, at the end of the experiment when the clip was removed, I noticed that the nostrils very slowly relaxed. The subject had no beard and Loewy maintains that the closure between mouth and mouthpiece was ideal.

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Fig. 73. Patient with no sweat glands in the Virchow Hospital, Berlin, as subject of a respiration experiment in which the effect on metabolism of increasing the body temperature was studied.

The Zuntz mouthpiece, with rubber protected covering to hold the lips against the mouthpiece, is particularly noticeable. The valves are made of the intestines of calves.



Fig. 74. Another view of the subject shown in preceding photograph.

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Fig. 75. Another view of Loewy's subject, showing the eyes closed. The patient slept throughout the whole experiment.



Fig. 76. <u>Showing connections between the patient, the respiration</u> <u>apparatus, and the gas meter, which is an Elster dry gas</u>

meter.

The sampling tube filled with water is shown at the left of the meter and the small pipette, which is lowered and allows the water to flow out proportionally, is shown attached to strings running over the pulley. Three sample pipettes were filled and three experiments made at this time.

Dr. Caspari.

Dr. Caspari told me of an experiment he had been making in conjunction with Dr. Rosenthal, on the effect of the inversion of carbohydrates by radium and by the magnetic field. He found that starch could be hydrolyzed, for example, in a magnetic field, and while it is very difficult, nevertheless some positive evidence is obtained. One great difficulty was to get the Wehnelt interrupter to run fast enough. He reported that the material had not been published.

In discussing the question of diet in the tropics, he referred to an experiment made by an assistant who determined his respiratory exchange before going to the German colonies in Africa, and again on his return. There was no difference, but Caspari rightly considers that the results of a single experiment is not conclusive.

In speaking of a vegetarian diet, he said that his Hauptmann H. was <u>wonderfully</u> strong. When he only weighed 44 kilograms, a very large fat man came into the room and rather criticized his small body-weight and appearance of feebleness. They engaged in a wrestling combat and this skeleton, weighing but 44 kilograms, actually threw the other all around the room. Professor Caspari opposes strongly Professor Chittenden's view and does not believe that the protein minimum is by any means the physiological optimum.

Caspari believes that in the higher altitudes, the dissociation between oxy-haemoglobin and oxygen is much looser than under ordinary conditions. This is of great advantage at the start as there is plenty of oxygen for the tissues, but later the tissues become poor in oxygen and as this loose combination is bad for the tissues, mountain sickness results. Barcroft of Oxford anticipated Caspari and Loevy in publishing these results.

Dr. Cronheim.

Dr. Cronheim is working upon the metabolism of fish and found that the oxygen consumption of the German carp was about one-third of that of man at rest per kilogram of body weight. He thinks that the muscular exercise of always keeping constantly in motion, - a characteristic of fishes, - may be very great. The carp grows to a weight of 650 grams in two years. The first year it grows to a weight of 50 grams and then there is a very rapid increase. The carp grows to about 1850 grams and while there is only about 5 per cent of fat when they are young, there is about 40 per cent of fat in the dry substance at the adult age, yet the metabolism per kilogram of body weight is about the same as when they are younger, and have but little fat.

ST. PETERSBURG, RUSSIA.

Institute for Experimental Medicine.

Professor Pawlow.

Professor Pawlow is as intensely interested in his experiments on the psychical influence on the salivary gland as he was at the time of my visit three years ago. Practically all of his experimental work is along this line, and but very little work is done on digestion, or on pancreatic or other fistulas. As the proceeds of the sale of gastric juice forms a considerable proportion of the income of the Institute, the preparation of this material is still carried on and a number of dogs are kept for the $(f_{ac}, \pi_{i,qs}, 78-80.)$ purpose. This gastric juice brings them in an income of 6000 roubles per year. Its sale is chiefly in Russia and while there are many private manufactories of the material, they are all handicapped by the fact that Professor Pawlow has a monoply of the technique and knows all the minor details. In operations, Professor Pawlow uses morphine and then chloroform, and he personally gives the dose.

In the laboratory he prefers to study only the reflex problems, but occasionally there will be a medical man or a foreigner who wishes to study digestive problems. Candidates for a doctor's degree, however, are usually required to work upon reflex problems. These reflex problems are certainly very remarkable, as a brief resume of the method shows.

<u>Method of experiments regarding the psychical influences on the salivary</u> <u>gland</u>.- A series of tones is arranged in the order of do, re, mi, fa, and the subject, a dog, is always fed after hearing the tones in this order, but never when they are blown or sounded in any other order. In a very few days the dog learns the difference between the period when the majority of the tones are in the ascending series and that in which the majority of the tones are given in the descending series. As a result, the sounding of the descending tones does not stimulate the salivary gland sufficiently to have saliva pass through a fistula. A little later the dog learns to distinguish all of the 24 possible combinations, but the saliva is stimulated only when the series of do, re, me, fa (1, 2, 3, 4) are sounded.

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In another method of study, a dog stands before a paper wheel and is always fed immediately after it begins to move. Another series of experiments is also conducted with the same dog in which the paper wheel is moved and simultaneously a very high tone is sounded, amounting to $\frac{1}{2000}$ (*) and simultaneously a very high tone is sounded, amounting to $\frac{1}{2000}$ (*) tions per second, but the dog is not fed. The addition of this tone to the movement of the paper wheel is found to act as a retardation of the stimulus of the wheel. I personally could not hear the tone where I sat but when I put my ear over the box, about 5 or 7 feet away, I could get a very faint tone. The dog is always fed after the wheel moves, but as soon as he hears the high tone, the saliva ceases to flow.

After the dogs have been trained to this point, an operation is performed and a certain portion of the brain is taken out. This operation upsets the whole order of the series. Professor Pawlow proposes to take out additional portions of the brain from time to time and determine the relation between the brain and the flow of saliva.

He is very much in need of a new laboratory as the experiments are of course much interfered with by extraneous sounds, such as the noise made by his assistants in walking around the building or by other dogs barking. Some people in Moscow have contributed 80,000 roubles for a new building for his investigations and with this he plans to build a small experimental laboratory; if this proves satisfactory, and the work grows rapidly, he will undoubtedly have a larger Institute later.

While I found that many foreign investigators are inclined to think that Professor Pawlow is making a great error in giving up the work on digestion for these reflexes, nevertheless one is greatly impressed with the intense eagerness and earnestness of purpose that he exhibits in all of his work and with his broad-minded consideration of the problems involved. It is easy to see why he was the recipient of the Nobel prize.

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Practically all of the research work done in St. Petersburg on digestion and fistulas is carried out by E. S. London in another laboratory. Inasmuch as there have been professional differences between Professor Pawlow and London, I was interested to learn from the majority of physiologists that London's most recent investigations are not accorded the approval given to his earlier work, which was done in Professor Pawlow's laboratory.

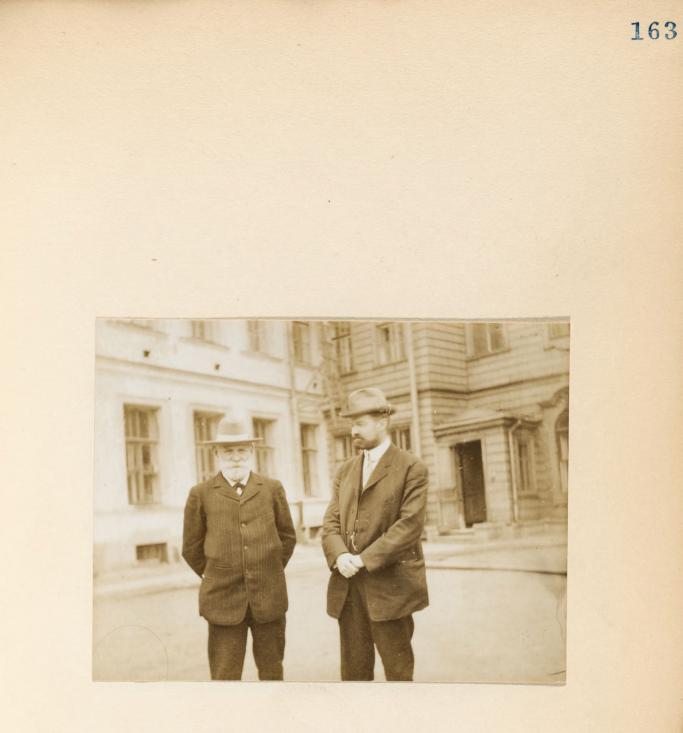


Fig. 77. <u>A photograph of Professor Pawlow and myself</u>. This was taken in the courtyard of the Institute for Experimental Medicine.

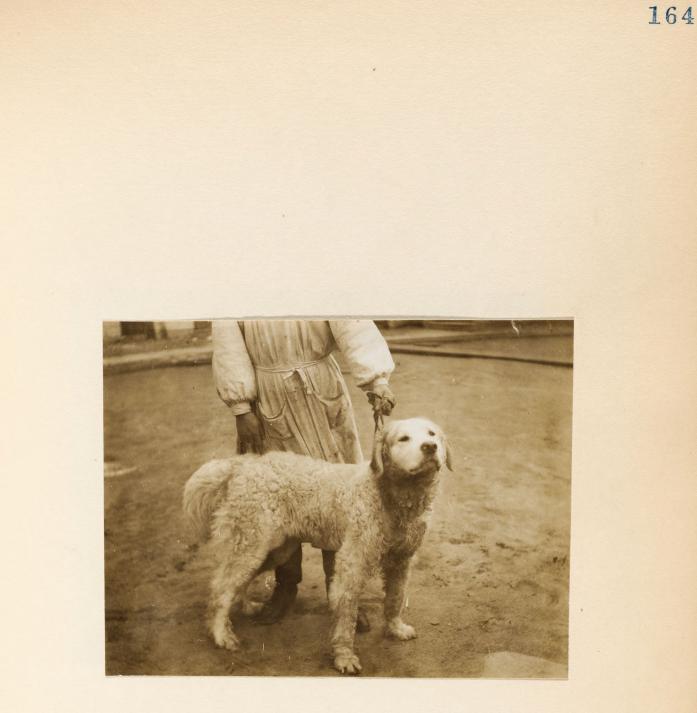


Fig. 78. One of the large dogs used by Professor Pawlow for collecting gastric juice by means of a tracheal fistula.



Fig. 79. Another view of the dog shown in Fig. 78.

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Laboratory of the Imperial Medical Academy.

Dr. Kartaschefsky.

My visit to this laboratory proved fully as interesting as the one I made three years ago, and I found that Dr.Kartaschefsky is still interested in the effect produced on the haemoglobin and lung gases by deficient oxygen in the air. At the time I was there, a rabbit was inside the respiration chamber who for several days had been breathing an atmosphere containing only 6 per cent of oxygen. Dr. Kartaschefsky proposed to make a blood gas analysis after the experiment was over and find out the effect on the haemoglobin of this deficiency in oxygen. (See Fig. 83).

The apparatus for the blood gas analyses seemed to me altogether too large and cumbersome for this work, and not at all in keeping with the modern idea of what a blood gas analysis apparatus should be. For the oxygen determinations, the explosion with hydrogen was employed. I noticed a Zuntz-Geppert apparatus put away in a glass case which, Dr. Kartaschefsky told me, they were unable to use, as the gas meter gave them a great deal of trouble and seemed to be entirely wrong.

In discussing the Pashutin respiration calorimeter which had been installed in this laboratory, but which is not now in use and probably will not be for some time, Dr. Kartaschefsky told me that Likhatcheff and Avroroff made alcohol check tests of this calorimeter and obtained very good results. They had, however, never made any short period tests. This apparatus is shown in Figs. 86 to 91. Dr. Kartaschefsky is very anxious to make experiments on men using an atmosphere deficient in oxygen and making the determinations in short period, but I told him that it was hardly probable that they could get satisfactory determinations for short periods with this apparatus. For the oxygen determinations, he intends to try our method of using coda lime as an absorber and admitting oxygen from a cylinder. Through Dr. Kartaschefsky's courtesy I was able to take a number of photographs of apparatus and lecture charts in the laboratory. These are shown in Figs. 81 to 93. Dr. Kartaschefsky impressed me as being a very serious and strenuous worker. He has two very intelligent dieners, who are evidently very efficient and upon whom he relies for much of the experimental work.

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julas experiments.

served as entjoute from two to seven years.



Fig. 80. <u>Two of the dogs used by Professor Pawlow in the gastric</u> juice experiments.

The Russian dieners holding the dogs may be seen in part. These dogs have served as subjects from two to seven years.

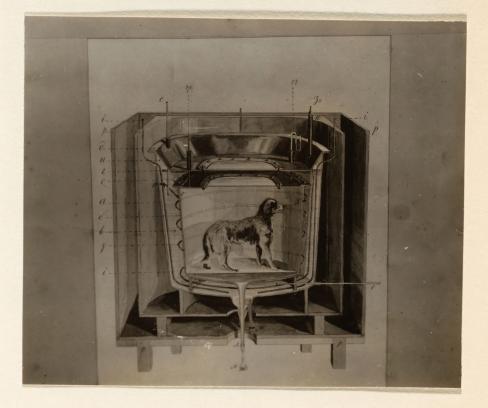


Fig. 81. Photograph of lecture chart showing details of Pashutin respiration calorimeter for small animals.



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Fig. 82. Lecture chart illustrating the schematic details of the Pashutin respiration chamber.

The rabbit used for the subject inside the chamber, the train of purifiers containing sulphuric acid and caustic potash, and the small gas meter for measuring the volume of air are shown here.

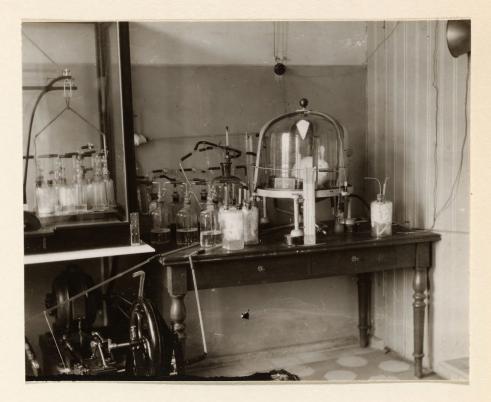


Fig. 83. Details of the Likhatscheff respiration apparatus for small animals as used in the laboratory of Dr. Kartaschefsky.

This apparatus is an exact duplicate of that in Professor Likhatscheff's laboratory. The method of weighing several carbon dioxide absorbers at once is here shown. The rabbit inside the bell jar was living in an atmosphere of about 6 per cent of oxygen.



Fig. 84. <u>System of water-levelling bottles used for the measurement of</u> <u>oxygen admitted to the closed-circuit apparatus of Likhatscheff</u> <u>in the laboratory of Kartaschefsky</u>.

At the left are shown two large copper tubes which are used as reservoirs and which give a definite pressure.

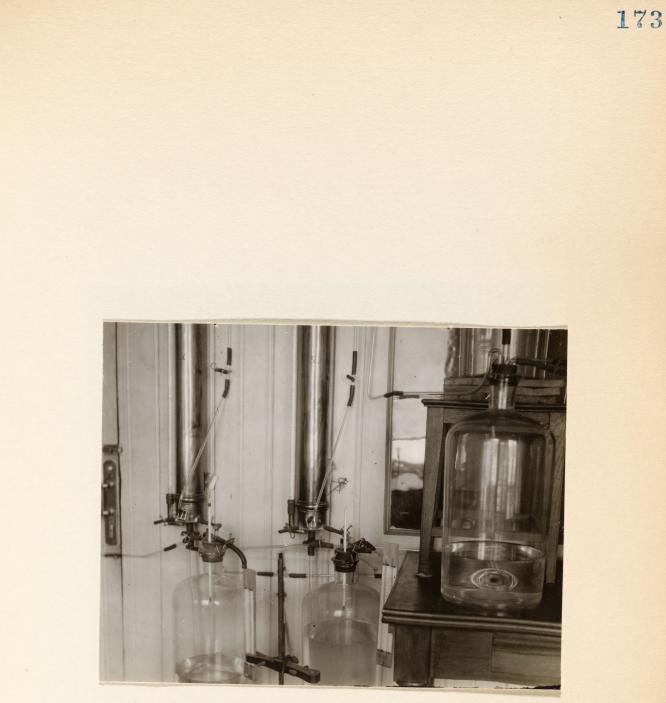


Fig. 85. <u>Details of the regulating system for admitting oxygen into the</u> <u>Likhatscheff respiration apparatus in Dr. Kartaschefsky's</u> <u>laboratory.</u>

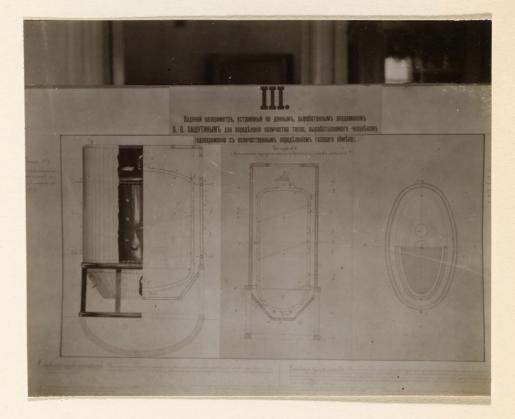


Fig. 86. Lecture chart illustrating a cross section of the Pashutin respiration calorimeter for human beings.



Fig. 87. <u>View of a photograph in the Military Academy showing the</u> <u>Pashutin respiration calorimeter for men in process of</u>

erection.

This gives a general view of the inner metal shell with the outer wooden covering.



Fig. 88. <u>View looking into the top of the Pashutin respiration</u> calorimeter for men.

The stepladder by which the subject descends is shown. Also the rubber gaskets on the two metallic walls which separate the outer water jacket. The outside is of wood sheathing, painted white, which forms the outer air insulation.



Fig. 89. Another view of the top of the Pashutin respiration calorimeter. This is from nearly the same position as Fig. 88, but with the first metal cover in place, all ready for the water to be turned on. The two glass portholes are shown, as well as the bolts over which the cover is fastened. The bolts ready for the second metal cover may also be seen, as well as the sheathing on the outside. Above this portion, the apparatus is completely filled with water after the subject is inside.



Fig. 90. <u>Outside metal cover for the Pashatin respiration calorimeter</u>. The two glass portholes are seen at the right and the left. In the centre is a metallic dome in which air can collect and be withdrawn as desired.



Fig. 91. Exterior of the Pashutin respiration calorimeter. The stairs at the right lead to the small gallery above, where entrance is obtained to the calorimeter, and from this gallery the pictures of the opening at the top of the calorimeter were taken.

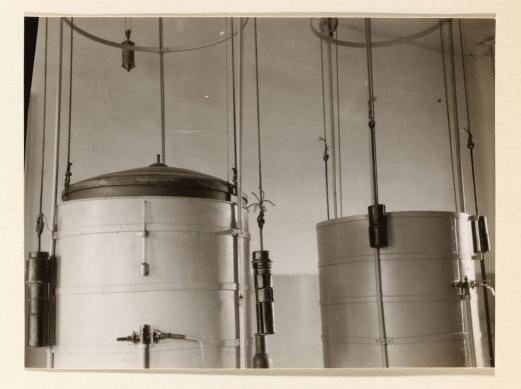


Fig. 92. Upper portion of two large spirometers used for studying the influence of varying percentages of oxygen on

respiration.

These spirometers hold 3000 to 4000 liters each.



Fig. 93. Lower portion of the two large spirometers used in the preparation of various gaseous mixtures in the laboratory of the Imperial Medical Institute.

Laboratory of the Pharmalogical Department of the

Women's Medical College.

Professor A. A. Likhatscheff.

<u>Respiration apparatus for small animals</u>.-Much to my surprise, I found installed in Professor Likhatcheff's laboratory a new respiration apparatus for small animals on the Regnault-Reiset principle, the details of which had been worked out in a very ingenious manner. Several photographs which were taken of it are given in Figs. 94 to 100.

The pump, which is clearly shown in Fig. 100, consists of two rubber bulbs with Bunsen valves in them, upon which pressure is brought alternately by a rocker arm, actuated by an electric motor. This pushes the air through a system of purifiers consisting of vessels containing sulphuric acid and a solution of caustic potash, and thence to the chamber. After leaving the chamber, it passes through another system of purifiers, these purifiers being placed upon the pan of a delicate balance. (See Fig. 97). As the oxygen is consumed, the pressure inside the chamber decreases and new oxygen is automatically admitted from a tall standpipe which is partly filled with water. As oxygen is admitted, the water rises in the standpipe and can be read on a graduated scale at the left. (See Figs. 98 and 99).

Professor Likhatscheff is evidently developing this apparatus with great care and is even so particular as to have oxygen above the water in the supply tank leading to his reservoir, so as to avoid any possibility of nitrogen in the water and therefore have oxygen replaced by nitrogen. As a matter of fact from the method of calculating the results I can see no reason why this should introduce a serious error. In an experiment like the one with a rabbit which was in progress when I was there, the percentage of carbon dioxide inside the bell jar is seldom above 0.1 per cent. As a matter of fact, for absorbing the carbon dioxide, Professor Likhatscheff uses seven Drechsel gas-washing bottles, two containing stick caustic potash, two with a solution of caustic potash, and finally, two or three with sulphuric acid. According to my calculations, there were 21 chances for leaks in these connections. This, I think, is a serious objection to the apparatus.

The bell jar is clamped down with a rubber gasket and sometimes a little vaseline and water is used to seal it, but he always finds it tight. The apparatus will be used mainly for experiments in pharmacology as that is Professor Likhatscheff's line. He is very desirous of studying the effect of chlorform on metabolism, etc.

At present he has only one assistant, but will probably have others later as he intends to construct a small Pashutin respiration calorimeter for animals. This is already partly constructed in the next room to the respiration apparatus, although not yet in working order. In the partition between these two rooms, there is an opening and a window, and all the preliminary preparations have been made for connecting the respiration part of the chamber with the Pashutin calorimeter. In the room where the calorimeter is placed is also a small walled room to assist in the temperature control.

Control tests of the respiration apparatus.-The control tests of this apparatus are evidently very strictly carried out. Professor Likhatscheff uses a small alcohol lamp, and a 50 c.c. flask with a very small wick and a glass tube. On one side of the lamp is a capillary tube so that air may enter as the alcohol is burned. This hardly seems necessary, as the air can work down through the wick. On the other hand, the size of the glass tube is such that there may be a possible retardation of the capillary action on the wick, and the small capillary opening in the tube at the side would then be necessary. From a large number of experiments Professor Likhatscheff has obtained many results. Thus, from the water level he is able to determine the oxygen administered to within 4 cubic centimeters, and thinks that the maximum error is 6 cubic centimeters on the whole. In ten alcohol check experiments, varying from 7 to 24 hours, he burned alcohol which theoretically would require 317.81 grams of oxygen and found actually 317.15 grams. The average error in percentage on the oxygen was -0.21 per cent; on the carbon dioxide -0.21 per cent.

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Professor Likhatscheff told me that Dr. Kartaschefsky of the Imperial Medical Academy had constructed his apparatus without seeing the technique of Likhatscheff's and had obtained equally good alcohol check tests, which spoke very well indeed for its accuracy. My chief criticism of Professor Likhatscheff's apparatus was that the oxygen was admitted by volume over water, with temperature changes in the long horizontal column of water, while a much simpler method would have been to weigh the bomb of oxygen.

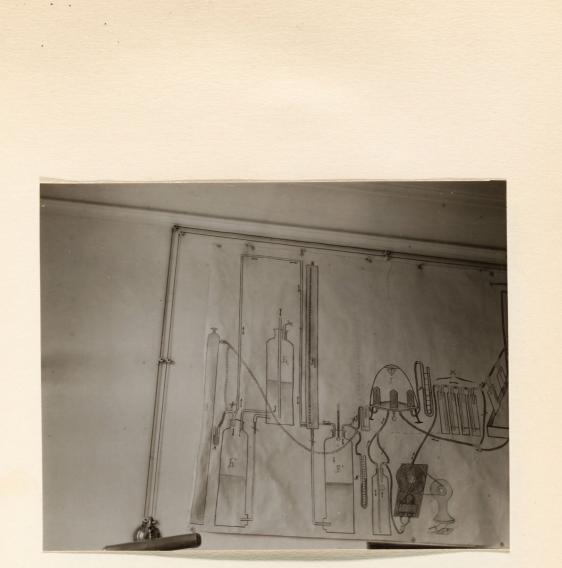


Fig. 94. Lecture diagram showing the schematic outline of the Likhatcheff respiration apparatus.

The chamber itself is represented by the small bell jar "T". At the right is shown indistinctly the schematic outline of the balance on which the absorbing vessels are placed. Below, at the right, are the pump and electric motor. At the left is the large cylinder of compressed oxygen with arrangement for connecting it with the reservoirs for constant pressure.

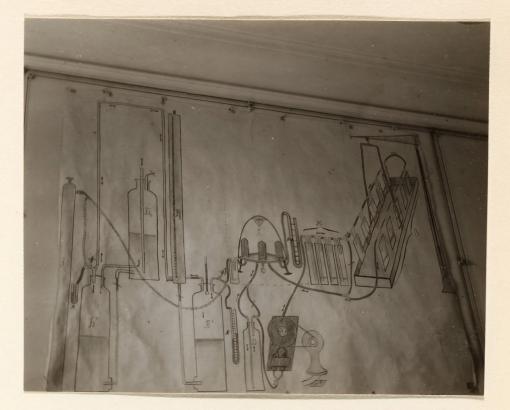


Fig. 95. Another view of the schematic outline of the Likhatcheff respiration chamber.

As the chart is hung on the wall, and the room is very high, the perspective is more or less distorted.

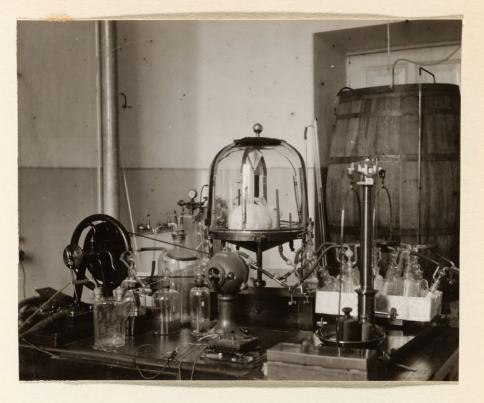


Fig. 96. <u>Complete view of the Likhatscheff respiration apparatus</u>. The connections between the pump, the sulphuric acid drying bottle, and the chamber are here shown, as well as the air connections between the chamber and the purifying train which is placed on the arm of the balance and weighed periodically. The large barrel seen in the rear of the room is for water pressure.

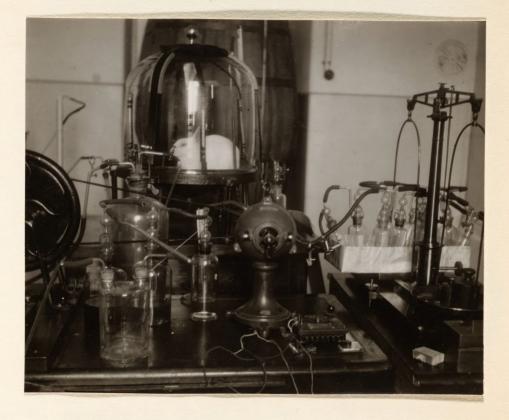


Fig. 97. A nearer view of the Likhatcheff respiration apparatus.

The motor, rheostat and purifying train on the balance arm are clearly shown.

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Fig. 98. Apparatus for admitting oxygen to the Likhatcheff respiration chamber.

The oxygen cylinder is shown at the right, the reservoir chamber at the left, and in the centre the glass bottle for regulating the pressure of the oxygen admitted.

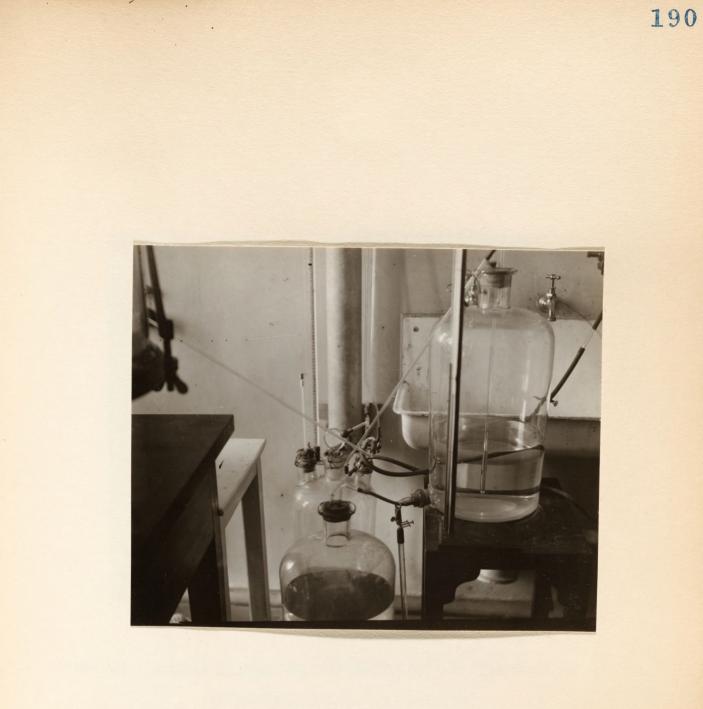


Fig. 99. Details of portion of the apparatus for furnishing oxygen to the system.

The volume of oxygen admitted is read by the graduated water scale beside the tall standpipe in the rear against the wall. The large glass bottles are raised on the Mariotte flask principle for securing constant pressure.

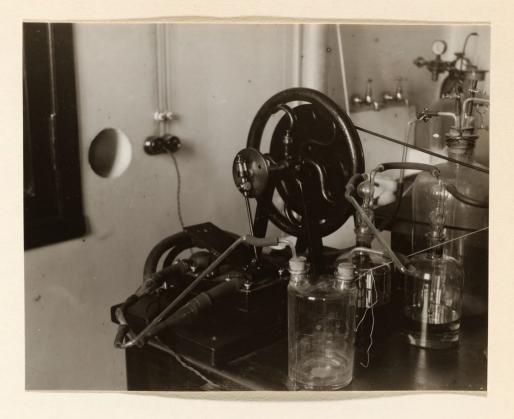


Fig. 100. Details of pump and preliminary washing bottles of the Likhatcheff respiration apparatus.

The pump consists of two rubber bulbs on which pressure is placed by means of a retary system actuated by an electric motor. The air first passes through an empty Woulff bottle in which there is an equalized pressure, next through sulphuric acid and potash, and then enters the chamber.

HELSINGFORS, FINLAND.

Physiological Laboratory of the University of Helsingfors.

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Professor Tigerstedt.

Professor Tigerstedt is chiefly occupied in literary projects now, being editor of the Scandinavisches Archiv f. Physiologie. He is also issuing a large handbook on physiology. He has one of the most remarkable private libraries of physiology and physiological chemistry in existence. Experimental work with the large Tigerstedt respiration chamber was not in progress when I was there, but I found much in the laboratory of interest.

Photographic registration apparatus .- In my visit three years ago, I talked with Professor Tigerstedt in regard to the possibility of photographically or electrically registering the pulse rate, indicating to him that I considered it of vital importance to note the number of pulse beats per minute during a metabolism experiment. Much to my surprise he has busied himself quite extensively on this point and has succeeded in utilizing the photographic registration apparatus of Frank. He had a rubber ball which could be strapped around the wrist or against the arm by means of a piece of webbing, and by air transmission, the pulse beat was transferred to a tambour. On this tambour was a small set of mirrors of silvered glass, and the movements were photographically recorded by means of a beam of light reflected from above. In this way he was able to study the actual character of the pulse. As it is practically impossible to use this method in our experiments since it is somewhat costly, and not adapted for long periods of experimenting, he had further devised the plan of using one of Sandstrom's celluloid tambours and recording the pulse on smoked paper. I was personally the subject of several experiments in which this photographic registration

apparatus was used, and came to the conclusion that the amount of traction required to press the rubber bulb with sufficient firmness against the arm to give the proper impulse was too great to use with ordinary individuals, and particularly objectionable for patients. Unfortunately, therefore, we cannot use this method in connection with our respiration calorimeter experiments.

Experiments on body temperature. An extensive investigation was in progress in regard to the effect upon the rectal temperature of warming the body by external heat. This was carried out with an apparatus like the one we use, the leads being fairly well protected by cotton batting. The men were put into the chamber, and electric light and air baths given. During these baths it was found that the body temperature fell, and the subject perspired profusely.

Another interesting line of investigation was a topographical study of the sense of heat in the body. Professor Tigerstedt had a mercury thermometer with a flat bulb, around which was wound an electrical coil. This flat bulb was placed on the body and heated by the electric current to the desired temperature. In this way a topographical study was made of the sensitiveness of the body at different temperatures and some very interesting results were secured which will be published shortly.

An investigation of general interest was the phonographic record of voices. To supplement the phonographic records, a study is made of the method of producing the sounds which are recorded by the phonograph. A plaster cast of the mouth is made which is silver-plated or tin-plated later, and after being smoked, the cast is placed in the mouth. When a special word or syllable is pronounced, the tongue touches the carbon soot deposit. The record is then magnified and photographed.

The laboratory was provided with a good operating room and I was especially interested in the series of cages for animals, which are shown in Fig. 103. Professor Tigerstedt told me that it was almost impossible to get dogs in Finland, and even for rabbits they had to pay 60 cents. A criticism made by Professor Tigerstedt, which has also been raised by others, was to the effect that Professor Zuntz has used one apparatus for thirty years without modifying it. On the other hand, he said that this apparatus has been of wonderful service to physiologists and an exceptional amount of work has been done with it, and very beneficial and profitable results obtained by its means.

A visit to Professor Tigerstedt is always full of interesting reminiscences as well as of interesting discussion in regard to current problems in physiololgy. His thorough command of the literature of the subject is marvellous and he is always instantly ready to supply a reference to any particular paper or to any particular discussion of a topic in physiology. It is a source of great regret to me that he is so remote from most physiologists. On the other hand, he is an ardent patriot and believes that he is doing most for his country by remaining in Helsingfors. The same may also be said of Professor Pawlow at St. Petersburg. The loyalty of both these men to their respective countries is most inspiring.

I was fortunate enough to obtain two very good photographs of Professor Tigerstedt, doubtless as good photographs as he has ever had taken. (See Figs. 101 and 102). He has rendered a great service to the Nutrition Laboratory by translating into German and into Swedish many of the results of our work, and was one of the first, if not the first, of the foreign investigators to incorporate in an extensive discussion the results presented in Publication No.77. It is obvious that Professor Tigerstedt's writings are eagerly read by all Continental observers.

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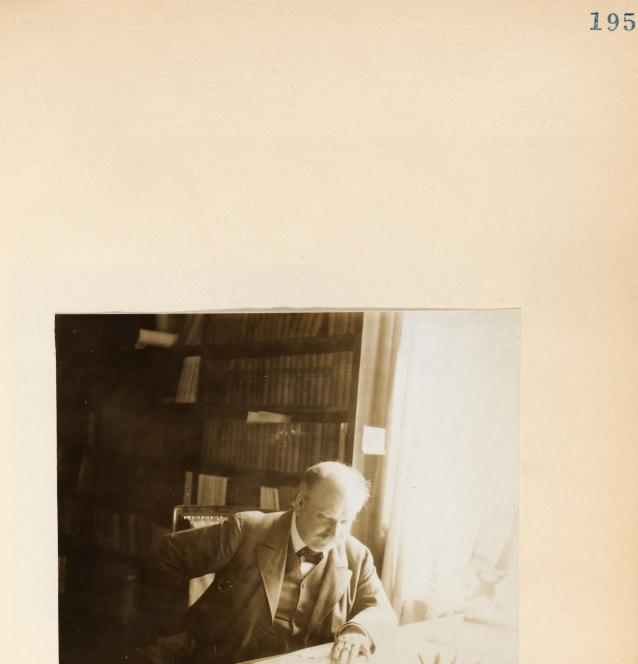


Fig. 101. Professor Tigerstedt at his library table, -an excellent likeness.

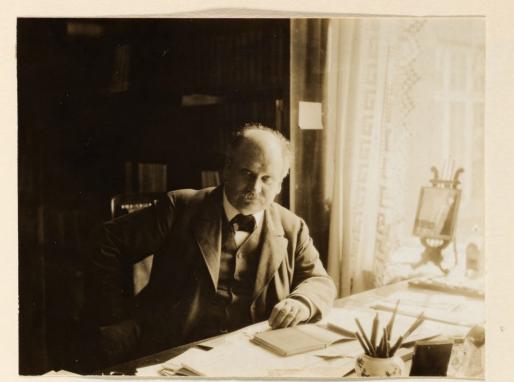


Fig. 102. Another portrait of Professor Tigerstedt.



Fig. 103. <u>Animal cages in which animals are kept after operations</u>. The bottoms of these cages are of wire grating which can be withdrawn by means of the two handles shown in the photograph, and thus readily cleaned.

STOCKHOLM. SWEDEN.

Physiological Laboratory of the Karolinska Institutet.

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Professor J. E. Johansson.

Since my visit of three years ago, an addition has been built to the Physiological Department, and among other changes, the large Sondén-Tigerstedt respiration chamber has been demolished. In a special room in the basement, however, a small respiration chamber has already been constructed and plans have been made for a larger one. The large chamber will in all probability have calorimetric features. In the center of the floor of the large room in the basement is a cemented pit which is 400 centimeters long, 518 centimeters wide, and 67 centimeters deep. In the bottom of the pit is a recess $7\frac{1}{2}$ centimeters deep, 240 centimeters wide, and 320 centimeters long, with slightly sloping sides. This pit was planned for when our Publication No. 42 was issued, as Professor Johansson hoped to use it in the construction of a calorimeter. He is particularly desirous of determining the heat in periods as short as 2 hours, but is not so much interested in making determinations of the carbon dioxide and oxygen.

<u>Respiration chamber</u>.- The new respiration chamber, which is already constructed in one corner of this basement room, is 267 centimeters high, 200 centimeters wide, and 297 centimeters long, with the corners cut off at an angle, so as to diminish space. It is painted white both inside and outside and one end is almost wholly of plate glass. Like the Middletown calorimeter this chamber has a series of walls, one inside the other, the inner wall being of soldered zinc, outside of this an air space, then building paper, then a second air space, again building paper, and finally an outside wall of matched lumber. The threshold of the door is about one foot above the floor. The ingoing air can be drawn from three places on different sides of the building, so that if it is stormy, the air may be taken from the most sheltered side. Before entering the chamber, the air must usually pass through at least 6 or 7 meters of a pipe 14 centimeters in diameter. This pipe goes through the wall of the building and at the outer end is protected with a wire netting and a grating to shed water. One of the openings, that on the river side of the laboratory, is only about a meter in length, and is the shortest and most direct route by which air may enter the chamber, but apparently this is not at present in use. Inside the chamber there are two radiators, ond at the top for cold water and another below for steam, so that in experiments with hard muscular work, heat may be brought away from the chamber, and in very cold weather the chamber may be warmed. The series of photographs designated as Figs. 104 to 111 give different views of the respiration chamber and accessory apparatus as they now appear, and also of the pit for the new apparatus.

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Experiments on the ingestion of carbohydrate. - By far the most important feature of my visit to Stockholm was the prolonged discussion with Professor Johansson of his published experiments on the ingestion of carbohydrates.

Professor Johansson's theory is that the amount of material in the body is not as a rule essentially changed from time to time; on the other hand, he is a firm believer in the intermediate steps of metabolism, and believes that there are certain depots in the body in which food may be deposited and that these depots are drawn upon by the living processes of the body. When no food is taken, these depots are diminished in size, but when food is taken, instead of its being immediately burned, it is first stored in these different depots. When the body is glycogen-poor and carbohydrate is ingested, the carbohydrate is first deposited as glycogen to make up the deficiency. If the body is saturated with glycogen, then the carbohydrate ingested is converted into fat and deposited as fat. In this process, carbon dioxide is given off unaccompanied by any oxygen, but during this time, the fat combustion also



Fig. 104. General view of Johansson chamber.

This shows the meter with the pipes leading to the chamber. The stepladder inside the apparatus was used in the earlier experiments of Johansson, Sonden, and Tigerstedt for climbing up and down in muscular work. A part of the rail around the pit prepared for the large chamber is shown and a view of the mechanician Jarl standing near the door.





Fig. 105. <u>Outside of the Johansson respiration chamber</u>. The system of collection pipettes for the gas, and the gas meter through which the samples are taken may be seen in this view. The storage pipettes were being installed at the time the photographs were taken. 201

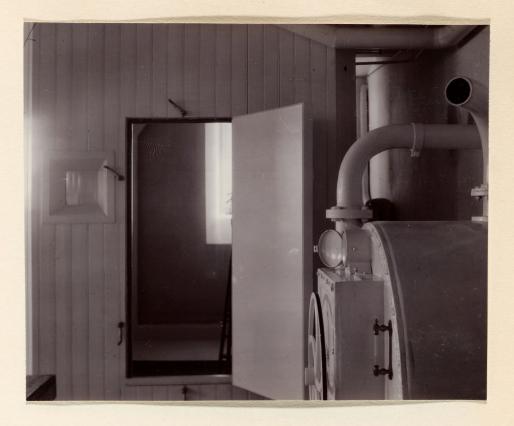


Fig. 106. Front view of Johansson chamber.

The gas meter is shown at the right and the door opening into the chamber can be seen directly in front. The levers for closing the door are also shown, as well as the small opening at the left which serves as a window.



Fig. 107. View of the interior of Johansson chamber.

The round opening at the bottom near the center is for the outgoing air. The window in the rear is covered with a large sheet of glass. On the outside, at the left, is a small opening which serves as a window, and at the right of this window may be seen the lever used for closing the door of the chamber.



Fig. 108. Interior of the Johansson chamber.

This photograph shows two radiators which are used for regulating the temperature in the chamber. The small opening serving as a window is at the left, together with the lever used for closing the door.

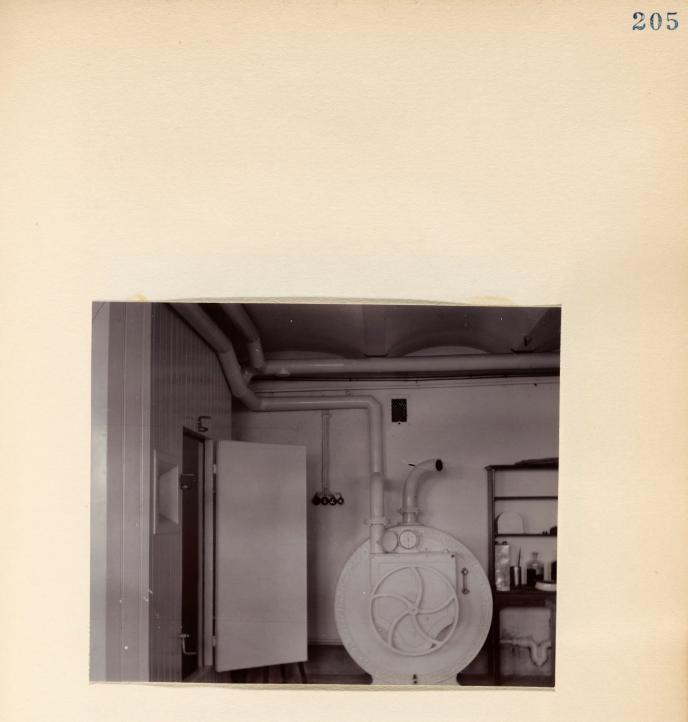


Fig. 109. Large gas meter used in the Johansson apparatus. The door at the left leads into the respiration chamber.



Fig. 110. Photograph of the pit prepared for the construction of a large Johansson chamber.

This is in the center of the large room in which the present small Johansson chamber is constructed. It is at present not in use, but is protected by a railing.

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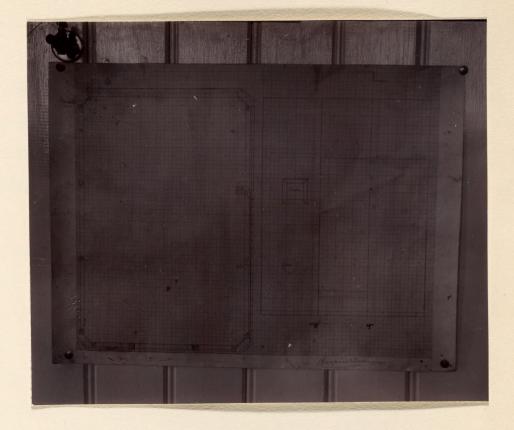


Fig. 111. Chart made by the mechanician Jarl for the construction of the tin work of the interior of the new Johansson

chamber.

The small square opening serving as a window is noticeable at the right of the center of the picture. The alternate layers of wood and metal and the supporting beams are also shown, particularly in the left part of the sketch. continues. The result, therefore, would be equivalent to saying that all sugar before reaching the end products of combustion i.e., carbon dioxide and water, passes first into an intermediate stage, namely, fat.

As I pointed out to Professor Johansson, however, it is singular that this relation is so closely held to that the respiratory quotient rarely goes above ' 1 for short periods. Respiratory quotients above 1 have been found for short periods but they are not common and in such cases, the plans of the experiments, the apparatus, and the investigator and his technique are not always above criticism. Additional experiments are much needed on this point and it seems to me that Professor Johansson himself must make them.

After the ingestion of carbohydrate, Professor Johansson gets an exceedingly large increase in carbon dioxide production. There may be three explanations for this: First, that this increase in carbon dioxide production resulted from a combustion of carbohydrate previously ingested and deposited as glycogen; second, that the increase in the carbon dioxide was due to increased muscular activity; and third, that the increase was caused by the transformation of sugar into fat according to Professor Johansson's theory. In the first and second of these cases, it is plain that there would be no abnormal respiratory quotient, while in the third, it would be very abnormal. Inasmuch as Professor Johansson asserts that the muscular . activity was the same in all experiments, the only possible muscular activity by which the increased carbon dioxide could be explained would be an enormous amount of work caused by the digestion of sugar. This is highly improbable. The rapidity itself is of very great importance and it is not impossible that the increased carbon dioxide production may be due to peristaltic action. I suggested to Professor Johansson that he try giving some sugar and a little sodium sulphate, for example, and note whether or not the absorption is hastened.

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Professor Johansson has made an extensive contribution to Energiestoffwechsels in Abderhalden's Handbuch. He gave me a separate of this paper which was entitled "Methodik des Energiestoffwechsels" and on it I made a large number of marginal notes and references which we subsequently went over together very carefully. These references have been amplified by certain additions which have been made.

As a result of our discussion, a number of experiments have been definitely planned for with particular reference to a study of the influence upon the body of the ingestion of large amounts of carbohydrate both before and after muscular exercise so that the body may be studied when in a glycogen-rich or glycogen-poor condition. It is very difficult to reconcile Professor Johansson's results with those obtained by us in preliminary experiments on the effect of the ingestion of large amounts of sugar and also with the results obtained by Professor Zuntz on dogs in which large amounts of sugar were also given. By reference to the discussion with Professor Zuntz given in this report, it will there be seen that when he gave a very large amount of sugar to a dog, he found no such increase in the carbon dioxide production as was found by Professor Johansson. Obviously, this great discrepancy should at once be cleared up as Professor Johansson is too careful a worker for his results to be rejected as unreliable. Furthermore, the technique of the Sonden-Tigerstedt respiration apparatus has been subjected to so many tests that it would seem almost umpossible to criticize it adversely. Whether any possible change in the technique took place subsequent to Professor Tigerstedt's going to Helsingfors and the apparatus since then has not been sufficiently controlled by alcohol check tests, I cannot say, and yet we must look somewhere for this discrepancy.

Professor Johansson is firmly convinced that this excessive excretion of carbon dioxide unaccompanied by muscular activity must be due to the splitting off of carbon dioxide from sugar in the forming of fat. This is, however, directly opposed to what we would expect under these conditions unless we are to accept Professor Johansson's theory in regard to the depots in the body and the transferring from the carbohydrate depot to the fat depot. We are planning to make experiments in the Nutrition Laboratory shortly which will be primarily designed to control and check Professor Johansson's experiments, and thus hope to definitely settle this point, as a fundamental principle is involved in the whole investigations.

Laboratory of the City Board of Health.

Dr. Sonden.

Discussion of results of air analyses .- For some months we have been making a series of air analyses in the Nutrition Laboratory and in this connection we have used a very delicate Pettersson gas analysis apparatus. modified by Dr. Sonden and built for us by Grave of Stockholm. I had with me a large number of results from this investigation to show to Dr. Sonden and our discussion proved most profitable. The fact that there were considerable alterations in the oxygen content of the atmospheric air was very difficult for him to explain. He thought that this variation might be caused by a very rapid air current and that the air which we breathe on one day might have been in the middle of Africa the day previous and subjected to very different conditions. In proof of this, he instanced the fact that volcano dust is carried rapidly out to sea for thousands of miles. We would have, therefore, no grounds for assuming a constancy in the oxygen content. On the other hand, in air coming from a land of rich vegetation, one would expect not only a low percentage of oxygen but also a high percentage of carbon dioxide. Our researches, however, show a wonderful constancy in the carbon dioxide content from day to day.

Dr. Sonden told me that Professor Pettersson had worked a great deal upon the question of air analyses and had used phosphorus, pyrogallic acid, sodium-hydrosulphite, burning in copper, and all possible methods, but his results had never been published. One interesting point brought out by Pettersson was the possibility of there being a respiration of the ocean, carbon dioxide being at times absorbed, and at other times given off. Vegetation gives up oxygen and Sonden believes that factories give up a very large amount of carbon dioxide, although they of course also use oxygen. However, as this oxygen is used to burn not only carbonaceous matter but also hydrocarbons, there will be a change in the composition due mostly to the hydrogen burned, independent of the carbon dioxide produced. In this case, however, there should be a change in the percentage on the basis of the absolute value. For example, if the carbon dioxide changes from 0.028 to 0.038, there would be an absolute increase of carbon dioxide amounting to 33-1/3 per cent. On the other hand, if the oxygen only changes from 20.90 to 20.94, the absolute change would not be noticeable. However, if we consider the actual change in the oxygen if the whole atmosphere changes from 20.90 to 20.94, there is clearly a much greater change in the total amount of oxygen than there is in the carbon dioxide.

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In discussing the method of making an air analysis and the general principle involved, Dr. Sonden referred especially to the saturation of the potassium hydroxide solution by nitrogen and oxygen. He pointed out that at the beginning of an air anlysis, nitrogen is left over the pyrogallic acid and that the potassium hydroxide in the carbon dioxide pipette is saturated with a gas mixture of about four-fifths nitrogen and one-fifth oxygen. After the carbon dioxide is absorbed, the gas with which the solution is brought in contact is fairly rich in oxygen, despite the carbon-dioxide-free air, namely, one-fifth oxygen. If, however, there is an exchange between the nitrogen and the oxygen in the caustic potash and the nitrogen and oxygen in the air, this would vitiate the determinations of the carbon dioxide. We should therefore use an apparatus in which the caustic potash is saturated with a nitrogen and oxygen mixture, that is, carbon-dioxide-free air, as we cannot otherwise secure accuracy in our results for carbon dioxide and nitrogen. Dr. Sonden and I reasoned that in all probability, with 20 per cent of oxygen, there would be no error, as the solution was saturated with nitrogen at the beginning and the end of each determination.

With the apparatus used in the Nutrition Laboratory, which determines not only the carbon dioxide but also the oxygen, the measurements are made of air which is actually under a diminished pressure and this fact necessitates the use of corrections. For instance, the volume of air in the bulb of the pipette at 0 indicates a sample of 60 c.c., and a change from 0 to 1 would represent an increase in the volume to 60.6 c.c. As a matter of fact, however, this graduation should allow for the expansion of the gas. Thus, if from alpha (the mark at the top of the bulb) to 0 (the mark at the bottom) represents a volume of 60 c.c., from alpha to 1% should represent a volume of 60.6 c.c., and as the air is under a diminished pressure, the scale should not be in equal divisions. I took this matter up with Grave and he assured me that if Dr. Sonden stipulated that this should be done, the instructions were followed when the instrument was made.

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These air analyses are of value to us not so much for the purpose of studying the composition of the outdoor air as for studying the change in composition of the air passing through the respiration chamber. I suggested to Sondén that if we had a duplicate analysis apparatus in which the air entering the chamber was analyzed over exactly the same pyrogallic acid as was used for the analysis of the air leaving the chamber, we would then be able to obtain a more accurate differential per cent than we were able to do at this time. Sondén had had no experience with oxygen determinations except with an apparatus in which the oxygen was determined by admitting to the air a definite volume of pure hydrogen (electrically prepared), passing this through a quartz tube containing platinum which was heated to incandescence, and then determining the diminution in volume. This apparatus I described in my report of 1907, but Dr. Sondén said that the apparatus did not prove to be practicable. He said, also, that Dr. Pettersson was not satisfied with the apparatus. As a result of our conversation, Rudolph Grave of Stockholm is now constructing for us a gas analysis apparatus according to a set of plans drawn up by myself and Dr. Sonden. This apparatus will have two pipettes, immersed in the same water bath. The caustic potash and pyrogallic acid in these pipettes will be of the same composition. By this means, we hope to, obtain a differential analysis of the air entering and leaving the respiration chamber and thus to eliminate many of the errors incidental to a single gas analysis absorption vessel. Dr. Sonden is giving a great deal of time to planning this apparatus and in working out the details. When Grave has finished its construction, Dr. Sonden will have one of his assistants test the apparatus.

Personal impressions of Dr. Sondén and his work.-It is always a source of regret to me that Dr. Sondén cannot occupy some large university position where he can devote his time primarily to research. I have seldom met a man who combines mechanical ingenuity, technique, and precision of skill with such a general breadth and grasp of the problems involved. Undoubtedly he is doing a great deal of important work for the Board of Health in Stockholm, but as it is, he is nearly lost to abstract scientific research.



Fig. 112. Apparatus case containing a large number of different forms of Pettersson and Sondén gas analysis apparatus, and hygrometers.

COPENHAGEN, DENMARK.

Laboratory of the Experiment Station.

Professor V, Henriques and Professor A. Krogh.

Professor Henriques was extremely cordial and showed me his laboratory as he did in my visit of three years ago. In this laboratory the feeding of a hydrolytic products of protein has been studied and they have found that if the protein was broken down by enzymes, it is possible for the body to synthesize protein from it and keep up the nitrogen balance, for the tryptophane was not broken down by the enzymes. If the protein is treated with acid and heated, however, the tryptophane is broken down. Professor Henriques is now working on goats using ammonium salts, such as the acetate, and finds that he can keep them in nitrogen balance even with armonium salts. I asked him about the thermal junction calorimeter used by Bohr and Hasselbach in their respiratory work on eggs. Professor Henriques said that in this apparatus they used two chambers, one with the egg and the other without, air being passed through both. Between the chamber, there was a thermal junction system. The whole apparatus is now broken down, and is not used.

Dr. A. Krogh.

Pending the construction and equipment of a new laboratory, Dr. Krogh is working in the laboratory of Professor Henriques. He is very enthusiastic over the Jaquet principle for respiration experiments, but believes, as do I, that we must have very exact air analyses, if possible to 0.001 per cent. In Greenland he used an apparatus which gave analyses of 0.01 per cent and he feels sure that most of his data were as accurate as this, but said that one or two experiments were absolutely wrong.

Dr. Krogh's experiments in Greenland .- In the Greenland experiments, he gave the subjects a diet containing a large amount of protein and thought that in this way he might be able to get some light on the formation of fat or glycogen from protein. He used seal meat and removed all the visible fat but found that there was an enormous amount of fat in the meat itself, -a fact which he had not realized. The apparatus was not air-tight, but there was always a dminished pressure, and he always got outdoor air with no leak outward. He believes that the carbon-dioxide in such an apparatus could easily rise to 1 per cent and the oxygen content would be not far from 20 to 21 percent. He calculates the total ingoing air from the nitrogen in the outcoming air, and analyses of the ingoing air. All the nitrogen coming out of the apparatus must have had a definite amount of oxygen with it when it went in. He also emphasizes the importance of an analysis of the residual air. He told me that his gas meter was accurate to 0.25 per cent with a constant level water attachment, and thinks this of the greatest importance, and that the gas must always be measured wet. He has no use for the paraffin oil arrangement of Stachelin. Kroch praised the Haldane gas analysis apparatus very highly.

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New apparatus for gas analysis. - As he believes that the Jaquet principle is of fundamental importance in studying metabolism problems, and recognizes that it depends in general upon very accurate gas analyses, Krogh has busied himself during the last year with developing a new gas analysis apparatus. The pipette holds 50 cubic centimeters and is so divided that 1/20 of each division equals 0.001 per cent of oxygen. By using a lens, he feels perfectly sure that he can read to 0.001 easily, as he has had a great deal of practice. After measuring the gas he dries it over phosphorus pentoxide and says that the gas should always be thoroughly dried in a special chamber for this purpose. The pyrogallic pipette is unique in construction. It consists of a U-tube having a series of inverted cones. These tubes are seen in Figs. 113 and 114. He thinks by means of this cone construction, all possibility of air bubbles is avoided, but in using rods and glass tubes, there may be an occlusion of gas bubbles which may occasionally catch in the tube. In speaking of the partial pressure of nitrogen in the liquid he said he uses potassium-hydroxide, saturated with air, as a solvent for carbon dioxide. The question occurred to me, does not the Sonden apparatus eliminate any errors in carbon dioxide, since Krogh always measures carbon dioxide plus oxygen, and later deducts carbon dioxide?

The Krogh apparatus is remarkably accurate, without doubt, and is fully up to the standard of his usual type of work. I question whether others could learn to use it, but he believes that the technique could be easily acquired by other experimenters. The whole apparatus is kept at a constant temperature in a water bath, the temperature being regulated by means of the Toluol regulator of Ostwald. If he uses the liquid saturated at different temperatures, it affects the results and a constant temperature is necessary. To keep this bath at a constant temperature, he burns gas night and day. He uses a tube with absolutely dry air in it as a compensation tube, though he says with but a little water-vapor, it would act as a perfect gas. All of the gas has to be dried by passing it over phosphorus pentoxide a second time into a reservoir with mercury in it. He says that for drapide the setting of the mercury, or potassium pentoxide, or pyrogallic acid on the is very accurate, though the calibre of the tube is small. He lays great weight upon the fact that the mercury must be absolutely clean in order to obtain a good reading on the meniscus, and consequently it must be absolutely dry and not come in contact with rubber tubing. For the mercury reservoir, he uses a glass standpipe with a bulb at the bottom and great pressure is required to force the gas into the mercury reservoir

and to suck the mercury back and forth. By connection with a vacuum water pump, he sucks the mercury up and lets it fall back by gravity. (See Figs. 115 and 116). This arrangement is very practical. It is possible that water may be left adhering to the walls of the glass tube below the meniscus at times, i.e., water carried below the meniscus by the mercury and left there. This would lead to an error. If there is such a possibility for error, then our oxygen determinations may be inaccurate, as when we raise mercury, it may leave a drop of water on the walls of the smaller bulb and the quantity may not be constant in amount. This point is very important. Such details as these emphasize the importance of the utmost accuracy and painstaking care in using delicate gas analysis apparatus. For example, the level of the mercury stands in the measuring pipette at zero. We are actually measuring nitrogen plus oxygen, plus carbon dioxide, plus some water vapor, plus a small amount of water. After the absorption of the carbon dioxide and returning the gas to the pipette for measuring, we assume that the nitrogen, oxygen, water vapor, and water are unchanged in volume and that the decrease in volume as indicated by the change in the level of the mercury is due to loss of carbon dioxide. Krogh thinks that a very important point is the adherence of moisture to the walls of the glass vessel while reading these volumes. This applies more particularly to the oxygen pipette on the Sonden apparatus. While with the carbon dioxide, there was but relatively slight change in the level of the mercury, in the oxygen pipette there is a small bulb and quite a long length of tube which is filled with gas at the start and at the end filled with mercury. Theoretically, there should not be any water adhering to these walls, and all the water should be above thermercury. Two series of tests should be made, in the first series raising the mercury very, very slowly until it reaches the proper mark, and in the second, raising it rapidly. In these tests, observations

should be made as to whether a change in level is noted due to the water rising on the side of the tube and collecting on top of the mercury.

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A careful examination of Krogh's new apparatus leaves one divided between admiration of its delicate construction and the ingenuity displayed. It is to be regretted that probably very few people can use it and secure such results as Krogh has secured. Even estimating the subdivisions of the graduations on the scale may be a matter of great conjecture. To estimate 1/20 of a subdivision is not easy, and very few poeple would agree in estimating with the unaided eye the difference between two marks in terms of twentieths. I called Professor Krogh's attention particularly to the importance and necessity of making a series of ordinary outdoor air analyses with his apparatus and comparing the results, also to the storing of a definite amount of outdoor air in a metal vessel and analyzing from day to day. Air having a constant composition should give the same results with the apparatus on different days. The apparatus is new and the control tests have not yet been sufficiently extended to throw light on these points, but I understand that Dr. Krogh will carry his investigations further.

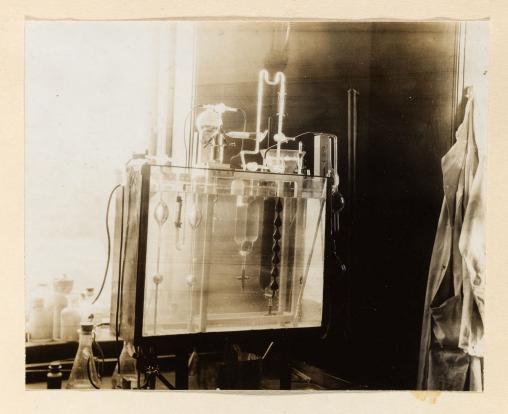


Fig. 113. <u>General view of the Krogh apparatus for the analysis</u> of atmospheric air.

The whole apparatus is immersed in a water bath which is kept at a constant temperature by means of a thermo-regulator. The two measuring pipettes are shown at the left. The potassium-hydroxide is in the reservoir in the middle, and the peculiar shaped series of bulbs at the extreme right is the potassium pyrogallate pipette. The mercury is raised and lowered by means of compressed air, or by suction through the water current. Above is shown the curved manometer in which there is a small drop of petroleum oil. At the left of this is the chamber for explosion, filled with mercury.

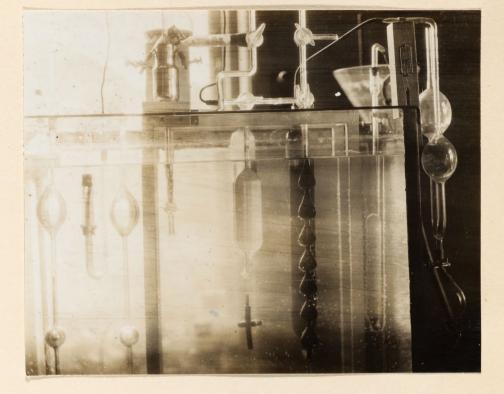


Fig. 114. <u>A somewhat closer view of the gas analysis apparatus</u>. The two measuring pipettes at the left, the potassium-hydroxide pipette in the middle, and the peculiarly shaped potassium-pyrogallic pipette is seen at the right. At the extreme right is shown the Toluol regulator for temperature control.

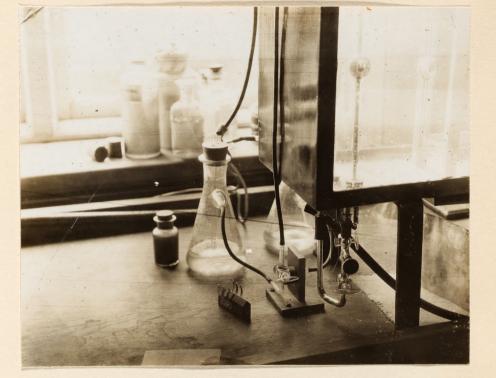


Fig. 115. <u>Suction flask and arrangement for raising mercury in</u> a pipette by suction.

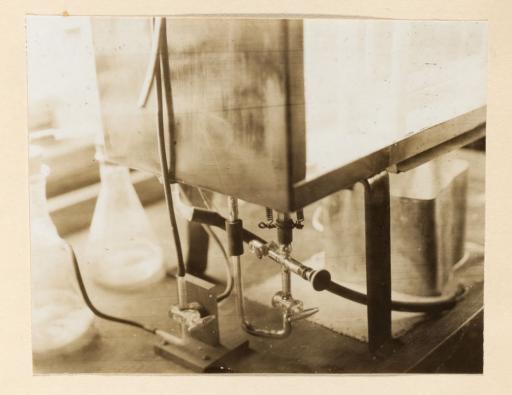


Fig. 116. <u>A closer view of the stopcock arrangement for raising and</u> <u>lowering the mercury.</u>

The fine-thread graduation tube for exactly adjusting a level of mercury in the measuring tube is .shown.

EDINBURGH, SCOTLAND.

Physiological Laboratory of the University of Edinburgh.

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Professor E. A. Schaefer and Dr. W. Cramer.

Professor Schaefer's activities are confined almost exclusively to literary work and to experiments on the feeding of hypophyseal extract to animals. The reconstruction of a part of his laboratory, and the preparation of a new edition of an old book, occupies much of his time. I discussed with him at considerable length the experiments made by Dr. Homans and myself on the removal of the hypophysis from animals. He is very strongly of the belief that we should try experiments on feeding the hypophyseal extract.

While at North Berwick, Professor Schaefer's home, I was much interested in acquiring the technique and hearing the development and subsequent history of the Schaefer method of resuscitating asphyxiated and drowned persons. Professor Schaefer used some valves on the Chauveau principle for measuring the amount of air that he could actually pump into and out of the lungs of a person, and by this means he was able to develop that technique which allows for the maximum ventilation of the lungs, believing that this is an important point in resuscitating drowned persons. The method, which is extremely simple, calls for no complex technique and has been used by the Metropolitan Police of London for the past year with very great success. It seems to be in every way, both practically and theoretically, far in advance of the older Sylvester method.

Dr. W. Cramer.

Dr. Cramer has been doing considerable work on the excretion of creatine in diabetes, and has found very noticeable excretions of this compound with different diabetics. I pointed out to him that it was important before drawing too many deductions to establish clearly the fact that the presence of acetone, B-oxybutyric acid, and other allied products, does not affect the Jaffe reaction. He will probably make further experiments along this line.

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GLASGOW, SCOTLAND.

Physiological Department of the University of Glasgow.

Professor Paton and Dr. Cathcart.

This was my first visit to the University of Glasgow. The laboratory is a magnificent building, beautifully situated, and admirably adapted for student work. In treating the animals used in their experiments, the investigators have found that the porridge diet works very well indeed; the feces are good and not fat, but are hard and do not stick to the bottom of the pan. The routine of the laboratory is so established that feces are removed as soon as passed, there being an attendant in the building practically all of the time; in fact, the attendant makes it a part of his regular duties to inspect the boxes and remove feces as soon as passed.

Professor Paton in conjunction with Dr. Cathcart has been attempting some work on fever in animals and has tried to make a calorimeter. I could not find out just what it was as all I could see was a plain pine box with two rubber tubes. From what he told me I imagine that the apparatus has not been very successful and that it is hardly more than preliminary.

Dr. Cathcart.

Dr. Cathcart is much interested in the study of creatine in diabetes; when the carbohydrate in the diet is low, he says he always find creatine, He also finds that bodies other than acetone do not appreciably affect the Jaffe reaction. (This is interesting in connection with the point I raised at Edinburgh). Subsequently other investigators have found that there is a noticeable effect, so the question is by no means settled. Cathcart thinks that carbohydrate is extremely important in metabolism. He is somewhat inclined to the glycogenic transformation idea, and was very keen about the possibility of forming glycogen from fat. He thinks that even if there is a low nitrogen output, there may be a very large cycle of nitrogen metabolism, in which but a part of the nitrogen, perhaps only a small part, is excreted at the end. On a carbohydrate-free diet he says they invariably get creatine. In phloridzin diabetes in dogs they get creatine, which is not due to the action of the phloridzin, for if the phloridzin is given plus excessive carbohydrate, there is no creatine. They use a Duboscg colorimeter, and a very strong Welsbach light, but must have a blue glass to cut out certain rays. I found in the laboratory, also, a Haldane respiration apparatus for small animals.

Dr. Cathcart impressed me as being one of the keenest men that I saw in England. He has travelled considerably and has spent some time in St. Petersburg, working with Professor Pawlow on problems in metabolism and also on psychical stimulation. I find that he is very well thought of throughout the whole of England.

LONDON, ENGLAND.

Physiological Laboratory of Guy's Hospital Medical School.

Professor Pembrey and Dr. Ryffel.

Professor Pembrey has been extremely interested in the effect of training, diet, clothing, etc., on the work of soldiers. He and Dr. Haldane have been on a Commission and have studied the army diet and the general conditions of nutrition. In discussing the experiments made by Carpenter and myself on muscular work, he said that he believed in training there is a certain coordination which is rather quickly acquired. If we should take a man with no experience whatever in riding a bicycle and let him ride without any resistance, we would unquestionably get one series of muscles working against another series of muscles, and a diminishing carbon dioxide excretion and heat output each succeeding day. Even if he does not work at the maximum rate, the muscles of the leg pull against one another, and the muscles of one leg against the muscles of the other, until they become trained and work coordinately. Professor Pembrey suggested having the bicycler also use his arms for working the ergometer and see if the same efficiency and the same amount of work would be obtained as with the legs. Of course he would be as unaccustomed to the work in using the arms, as in using the Professor Pembrey emphasized the fact that of course the colegs. ordination required for riding a bicycle may be very small and quickly Our subjects learned to ride in a few days. On the other hand, learned. the expert bicycle rider may be so used to instinctively balancing himself on

a moving wheel that in riding a stationary bicycle he would do the same and thus bring into play extra muscles that were not necessary and hence lower his percentage of efficiency, while those unaccustomed to the use of the bicycle did not use these muscles, for balancing and they rapidly increased in efficiency by training. I personally believe that Pembrey thinks of efficiency too much in the light of increased work done, irrespective of the percentage of internal total combustion to the heat of external work. Professor Pembrey is very anxious that we should try the effect of training on soldiers in carrying different weights of loads, in marching different distances, and in having the load definitely distributed about the body. These experiments ought to be repeated with athletic subjects.

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Alveolar air .- Professor Pembrey states that he usually "breaks", that is, he is compelled to expire air after holding a maximum inspiration when the carbon dioxide rises to about 7 or 8 per cent in the alveolar air. After ventilating with oxygen he can go to 10 or 11 per cent of carbon dioxide before "breaking". Also, if he has excessive ventilation he gets approva; this does not last so long with excessive oxygen ventilation but is more apparent after muscular work. He believes that the lack of oxygen as well as the increase of carbon dioxide is a stimulus to respiration. If he ventilates and pumps out all of the carbon dioxide and the oxygen is lowered before sufficient carbon dioxide has accumulated to stimulate respiration, the lack of oxygen causes the respiration to increase, which pumps out the carbon dioxide and again we have appoea. This is an explanation of the Cheyne-Stokes type of respiration. Pembrey emphasises the fact that the alveolar air is remarkably constant with the same person, and cites three examples, 5.61, 5.64, and 5.63, etc. He maintains that Haldane has actually tested the efficiency of the burette by means of his own alveolar air. This is not confirmed by Haldane's publications as I find that the agreement between his different experiments is by no means as constant as this.

Dr. Ryffel.

Dr. Ryffel has made a number of experiments on the formation of lactic acid in the body. He finds that in 100 cubic centimeters of normal urine there are 6 milligrams of lactic acid. Glycuronic acid interferes with the reaction, but if this is removed by lead subacetate, it also lowers the actual lactic acid, and a correction must be made. If he performs muscular work by running about the laboratory, he can increase the lactic acid up to 0.05 grams of lactic acid in 100 cubic centimeters of urine. He finds that there is very little relationship between the lactic acid and the sugar in the urine of diabetics, and believes that it plays but a very small rôle. As yet he has found no disease with a great amount of lactic acid. Dr. Ryffel impressed me as being a very serious and studious individual, I think that his work can be absolutely relied upon.

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Professor Leonard Hill.

Professor Hill has been doing a great deal of work recently on the breathing by athletes of air containing a high percentage of oxygen, and his results are very striking indeed. At the time of my visit to his laboratory he was much interested in studying the regenerative power of an ozonizer which is to be used to disinfect and purify the air in a room. For this purpose he has constructed a small chamber, about 2 meters square, in which he has placed an electric fan and the ozonizer, the latter being run by a high tension, alternating current. With seven young men in this chamber he has allowed the carbon dioxide to increase very noticeably, and the relative humidity to rise to about 95 per cent. He then found that the men became very much distressed; they felt much better, however, when the electric fan was turned on and stirred up the air, especially as the air passing over the face caused a small amount of vaporization. Although the air was previously saturated at 25°, at the temperature of the face. say 32° or 33°, it was not saturated, and the cooling effect was very noticeable. He could not at the time I was there, however, detect any result from the ozonization. I had the pleasure of assisting him in one or two experiments and making some of the observations.

I was much interested in the experiments he is making on the saturation of the blood under high pressure and particularly of the saturation of the gases of the urine, the assumption being that the analyses of the urine for gases would correspond to analyses of the blood gases, i.e., the dissolved gases, particularly nitrogen. In the study of this subject, he had put one of his assistants in a high pressure chamber and had drawn urine from time to time. A very delicate method of gas analysis has been used for the analysis of the urine. We can look forward with much interest to his publications on these points. Physiological Laboratory of the King's College Medical School.

Professor Halliburton.

Professor Halliburton was not engaged in active research at the time I was in London. The laboratory accommodations are very limited and wholly inadequate for either good teaching or good research work; they are hoping for a better equipment ere long. His literary work keeps Professor Halliburton very considerably occupied. He was much interested in the question of high versus low protien, and said that Professor Starling had attempted to live on a low protein diet but had finally changed to a high protein diet.

Professor A. D. Waller.

This laboratory, which was primarily a research laboratory, or for advanced work, was one of the most interesting which I visited during my trip. It was very well equipped with all conceivable forms of apparatus, and Professor Waller's work is very much diversified. His experiences with the capillary electrometer are well known. I saw here the photographic registering apparatus devised by Bull of the Marey Institute, and also three Blix-Sandstrom kymographs.

Professor Waller was very much interested in the chemical problem of the development of hydrocyanic acid in laurel leaves and in the toxicological problem of determining minute quantities of hydrocyanic acid. The whole subject matter of the investigation was very important toxicologically. The absorption of hydrocyanic acid by the different organs of the body was also investigated and obviously has its interesting application to medicolegal discussions. By distilling blood with a little tartaric acid, the hydrocyanic acid was driven off and condensed in the distillate, and subsequently determined by the color reaction with picric acid.

Manufactory of Siebe, Gorman & Company, Ltd.,

187 Westminister Bridge Road.

Through the kindness of Professor Haldane of Oxford, I was given a letter of introduction to Mr. Davis and Mr. Fleuss of this plant, and I received every courtesy that could possibly be shown me. Mr. Fleuss is a most interesting man, being a professional diver of long experience. He told me of his experience many years ago in using pure oxygen in diving. He was under water one hour and during this time admitted pure oxygen into the diving apparatus and let the carbon dioxide out through the valve. Since there was a mixture of carbon dioxide, nitrogen and oxygen continually going out, and only pure oxygen going in, at the end of the period there must have been a very high percentage of oxygen in the atmosphere breathed. He told me that he felt very well, although it was predicted by all of his coworkers that he would be very blue and very dangerously ill. Professor Benjamin Ward Richardson published a report of this experiment, of which a copy was sent to the laboratory by Mr. Davis.

Diving apparatus. - Evidently this plant has given a great deal of attention to methods of respiration through tubes with valves, etc. They say that when the valves are moistened they work much better than when dry. The valves used in their apparatus are constructed with a peculiar slant that is very important. The tubing leading from the valve to the mouthpiece is of special construction, being corrugated and reinforced inside with wire. It is absolutely impossible to kink it. For the absorption of carbon dioxide in the closed circuit apparatus, either for diving or for resuscitation in mines, they use a specially pure sodium hydroxide, and stipulate that it must be 99 per cent pure. The carbon dioxide is absorbed on the outside of the reagent and the water from the breath is also absorbed. The carbonate which forms drops off in sticks until the mass looks very much like a stick of candy that has been partially sucked away. Four pounds of caustic soda are used in the apparatus. Potassium hydroxide has been tried but does not give satisfactory results, as it is too liquid. The rubber bag hangs in front of the man and is of very ingenious construction, having two compartments. The air goes down through one compartment, comes in contact with the caustic soda, and returns through the other compartment. As the bag is clamped together at the top, it is impossible for the air not to pass through both compartments. The scales of sodium carbonate which form may be knocked off by crumpling up the bag. The front is made tight by spreading powdered graphite between the rubber fittings before they are clamped together. Down between the compartments are ribs of rubber so that if the man should lie down on the bag, he does not stop the respiration as the air would pass down the ribs. The oxygen is delivered from a compressed air bottle at the rate of 2 liters per minute, and if the bar gets too full, there is a release valve, which allows the excess air to escape, without disturbing the respiration. This also provides against the accumulation of too much nitrogen.

I found a number of interesting respiration masks. A copper piece is used to aid in forming the mask to the face, the copper being more or less soft. A rubber tube around the edge of the mask is commonly inflated to fit about the face, but Fleuss, himself, does not inflate this. He says that the men should have no mustache, and that under these conditions, the face mask is tight. As a matter of fact, with such a face mask he walked across the Thames under water without using any diving dress at all. The rubber fitted the face well, but the tightness depended on the mouth and nose mask. There was a larger flap of rubber which went all around the outside of this mask, which also rested against the face and helped in

making the mask tight. For deep diving work they use a mixture of 50 per cent of oxygen and 50 per cent of nitrogen. The diving dress is self-contained and therefore without holes, so that it can be used in places where a hose could not be dragged, such as, for example, into and but of a cabin on a wreck. Usually it is adjusted for 5 liters of oxygen per minute. The oxygen is admitted as a fine jet which acts as an inspirator, pushing the gas around the closed circuit. This apparatus has been used for 45 minutes in ordinary diving. There are no valves to actuate and no mouthpiece.

Reduction valve.- I found a very sensitive reduction valve, which was set to give, say, 2 liters per minute and which could be made very tight indeed. There was a small by-pass which enabled the man to get a quick supply of oxygen if desired. This valve was so tight that they can blow a soap-bubble on it of any size and cut if off immediately as desired. These valves, Siebe & Gorman say, were made by Brin in London from their specifications.

Accessory apparatus. - An interesting piece of apparatus they showed me was a one-stage compression pump which compressed air or gas at 2000 lbs. with one stage. There was no leakage as the gauge holds indefinitely. The dead space was very small and all the valves and couplings had metal to metal seats. Occasionally they use fibre gaskets for the couplings, but do not find them particularly satisfactory.

A large diving tank with glass walls was used by this firm for training divers and testing their apparatus.

<u>Use of sodium-peroxide</u>.- Sodium perioxide, or Oxylithe, is used very much in their submarine rescue apparatus. In this there is a helmet with a life buoy attached. This life buoy can be inflated by the man. The apparatus can be put on with a face plate opening, and water is let into the compartment until the pressure of the air is equal to that of the pressure of the water. The face plate is then closed and the air in the

helmet is under considerable pressure, but the water is up to the armpits. (See sketches and description in catalogues of Siebe, Gorman & Company(Cat.D.ete)...) When they get out of the submarine rescue apparatus, for example, and are floated up to the surface, they inflate the life buoy with 3 breaths, open the face plate, and are then all ready to be picked up by the boat. In certain of their apparatus such as, for example, the smoke and gas rescue apparatus, they use Oxylithe to regenerate the air in breathing. The moisture in the breath liberates the oxygen, while the carbon dioxide is absorbed. For this purpose they have a very light diving helmet. Mr. Fleuss did not believe that even 2 liters of oxygen per minute were necessary, and some of their best men cut it down to 1 liter per minute, thereby giving them a longer time to remain under water.

I was much interested in the mouthpiece used for some of their apparatus. Like the Zuntz mouthpiece it had flanges placed between the teeth, but Fleuss preferred invariably to cut them off. There was a mustache band which held the mouthpiece very firmly in position, so that the two flanges for biting with the teeth are entirely unnecessary.

My visit at this manufactory was very profitable and Messrs. Siebe, Gorman & Company have sent a number of interesting valves, tubes, and connectors to the Nutrition Laboratory as a gift. They also sent us a large amount of printed matter, giving some important information with regard to diving, and the construction of helmet, oxygen cylinder, respiration apparatus, and mouthpieces of different kinds. The printed material regarding these practical appliances is a very important contribution to our literature and the apparatus may be utilized for physiological experiments.

OXFORD, ENGLAND.

Physiological Laboratory of the University of Oxford.

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Professor J. S. Haldane.

Never having met Professor Haldane, nor seen his laboratory, I was particularly interested in making this visit to Oxford. I have seldom met a man with whom conversation was so profitable along the particular lines of gaseous exchange and gas analysis. The laboratory is by no means modern and research work is not carried out under the most ideal conditions. Recently, however, two or three rooms have been added to the laboratory and Professor Haldane is somewhat better off than formerly. The laboratory impressed me as being the workroom of an accurate scientist; Professor Haldane's work with the gas analysis apparatus shows especially the highest degree of accuracy.

<u>Gas analysis</u>.- In discussing the gas analysis apparatus, Professor Haldane pointed out the errors that are liable to occur in the calibration, the contraction of glass tubing, etc. In calibrating, he usually fuses the stopcock in the bottom of the apparatus and draws out the mercury there. He finds that if a rubber connection is used, the pressure may vary, as the rubber contracts or stretches, causing the level to change. In discussing the Sondén apparatus, Haldane reports that he found a diffusion of gas into the arm of the compensator or manometer tube in the Sondén apparatus. He furthermore reports that the gas is taken into the pipette partly dry, then passed into caustic potash and measured, leaving a varying amount of moisture in the capillary tube between the pyrogallic acid and the cock. This gas may be moistened by the water hanging to the walls of the tube. At first, the tube is very dry but as the gas passes from the burette, it is saturated with moisture. This moisture may condense on the walls and subsequently be given up. The inside diameter of the capillary tubes should not be too small, otherwise they are sluggish in delivering the gas. He says the small gas analysis apparatus that has recently been made by Rittenhouse is so accurate that it can be used for analyzing oxygen, getting from 17.02 per cent to 17.04 per cent. They use a certain amount of dead space with T-cocks, but I found out that if an L-cock is used, there is less dead space, and I have ordered the apparatus from Rittenhouse with L-cocks instead of T-cocks. Haldane thinks that the small apparatus is as practical as the larger one, for a great deal of work. He has a rack and pinion apparatus with hooks and holes to raise and lower the reservoir, the reservoir being raised by hand to approximately the desired point, the finer adjustments being made by means of the rack and pinion. Professor Pembrey pointed out to me that Barcroft or Brodie had found that if a small amount of bile salts is added to the water, it is very much better for the manometer. as the water will then flow smoothly on the interior of the glass.

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In the interior of his explosion chamber, he uses a platinum wire which can be glowed by an electric current. This is glowed quite brightly for carbon monoxide, marsh gas, and hydrogen.

Experiments with carbon monoxide.- Professor Haldane has performed a great many experiments on the influence of carbon monoxide and its combining with the haemoglobin of the blood, thus reducing the total oxygen-carrying capacity of the blood by a very large amount. In these experiments he has used as subjects both animals and men, including himself. He finds that it takes about 900 cubic centimeters of carbon monoxide to completely saturate the blood of man. He has a small Regnault-Reiset apparatus, into which he can introduce oxygen and carbon monoxide. To absorb the carbon dioxide and water, he uses soda lime or stick potassium hydroxide. He introduces into this apparatus say, 300 c.c. of carbon monoxide, and thus saturates the blood one-third with carbon monoxide. After having breathed this gas mixture, he breathes into another Regnault-Reiset apparatus and tests the carbon monoxide given up by shaking a bottle of the air with some blood, and then titrating the blood. In the blood titrations, he adds a carmine solution of a definite strength to bring back the color to normal.

Professor Haldane is very sure of the accuracy of this method, but Zuntz is very much afraid of it. In his experiments he saturates the body with carbon monoxide to about 35 per cent; then if ordinary air is breathed, it requires a long time to get rid of all the carbon monoxide, say, three or four hours. If pure oxygen is breathed, one-half of the carbon monoxide is given off in about half an hour. If the blood of an animal is wholly saturated with carbon monoxide, and the animal is then put into a pressure chamber, and pressure is applied, the dissolved oxygen in the blood will support life. He cited as an illustration a case where he was working with a mouse, with a large amount of carbon monoxide in its blood. He tried to drown it in water charged with oxygen, but the mouse lived. Professor Haldane thinks that carbon dioxide plays a very important rôle in pathology. It stimulates circulation and the high carbon dioxide also stimulates the centers.

Discussion of experiments with oxygen-rich atmospheres.- I was very glad to have the opportunity of discussing with Professor Haldane our experiments with oxygen-rich atmospheres, and found his ideas very valuable. I told him that I had heard from a number of research investigators that experiments had been made which showed that the use of oxygen-rich atmospheres produced a tendency to oxygen pneumonia and that I understood the work had been done by Lorrain Smith and Haldane. The investigators found that animals kept three or four days in pure oxygen contracted this oxygen pneumonia. The animals recover quite readily and probably this tendency will never be observed with man, at least

not with 40 per cent of oxygen. With mice, they found no tendency to pneumonia when 40 per cent of oxygen was used, so a man could probably breathe an atmosphere containing 40 to 60 per cent of oxygen with perfect safety any time without pneumonia. This of course agrees with observations of divers who use 40 to 60 per cent of oxygen constantly.

Professor Haldane has done considerable work on caisson disease and the question of decompression. In rapid decompression, bubbles are formed and these cause emboli in the blood vessels, which produce death. This is treated by pressure, the pressure being allowed to decrease slowly. Professor Haldane is a firm believer in the so-called stage decompression as opposed to the more rapid decompression of Professor Leonard Hill.

Professor Haldane is much interested in the army work and incidentally in the navy, so far as diving is concerned, and has been on many investigating commissions in connection with the navy. He was good enough to give me a large collection of reprints showing some of his past work. Tests have been made recently in connection with the army work to find some emergency rations that can be used on long marches. At Professor Haldane's request I spent part of the day with Colonel Melville and Major Beveridge at the Royal Army College, looking into their diet, their methods of measurement, and the methods of analysis. I made a number of suggestions in regard to substitutions in the emergency diet and some of the suggestions will undoubtedly be tested shortly.

CAMBRIDGE, ENGLAND.

Physiological Laboratory of the University of Cambridge.

Professor Joseph Barcroft.

Professor Barcroft is particularly interested in the analysis of blood gases and in the carbon monoxide experiments which he has begun with Professor Haldane. At the time of my visit, he had just returned from an expedition to Teneriffe with Professors Zuntz and Durig and was much interested in the results obtained. He evidently has the technique of blood gas analysis most elaborately worked out; in fact, I consider it of great importance that this technique should be acquired for use in the Nutrition Laboratory. At the moment of writing, Mr. Higgins of our staff is planning to go to Oxford where he will work for several weeks with Professor Barcroft. Professor Zuntz was most enthusiastic regarding Barcroft's experiments and his general technique, skill, and ideas. He is evidently a very strong man.



