Diet.

We have purposely avoided a prolonged examination of the theoretical considerations that underlie the mechanism of acidosis, but desire to raise one question as to its mode of production in patients with the status *seborrhoeicus*.

In his very admirable summary of the normal mechanism whereby a slightly alkaline reaction of the blood is continuously maintained, Sellards upholds three factors as of primary importance:

1. Intake of fixed bases in the food.
2. Elimination (a) of carbon dioxide by the lungs, (b) of acid by the kidney.
3. Neutralization of acid in the body by ammonia.

Now the fixed bases in the food are derived mainly from fresh vegetables and fruit, and a deficiency of these is well known to lead to a decrease of the alkaline salts, particularly the carbonates, and the mono-acid dibasic phosphates of sodium, calcium, and magnesium—the so-called buffer salts—in the blood and urine.

The army ration, excellent in all other respects, is unavoidably deficient in just those fresh materials that are most important in maintaining the requisite equilibrium between acid and basic radicals.

We have eliminated scurvy—a serious factor in the campaigns of previous centuries—by the judicious selection of dietary and by our advances in the preservation of protein substances.

At this juncture it would be altogether premature to lay it down as an axiom that the modern army ration is responsible for the *seborrhoeic* diathesis, but we will go so far as to suggest that it is probably contributory, directly or indirectly, in its production and aggravation. The biological influence of carbohydrates in the production of the catarrhal state, on which Czerny and Cameron lay great stress, is, in our opinion, an accessory factor. We may here cite the case of one of our colleagues—himself a dermatologist—with a remarkably *seborrhoeic* diathesis. He can produce at will (and has twice actually done so experimentally) an acute typical *seborrhoea* of the head and face by rapid ingestion of an excessive quantity of sugar.

It may be assumed that if the digestion and other functions of the body proceed normally, carbohydrate, if taken in moderate quantity, is completely oxidized to CO₂ and water, but if for any reason oxidation is interfered with, intermediate acid substances (of stronger acidity than CO₂) remain incompletely oxidized, and, in the absence of a sufficiency of neutralizing buffer salts, tend towards a reduced alkalinity of the blood and tissue fluids. Similarly, according to Sellards and other writers, protein, particularly meat, is one of the chief sources of acid substances during its metabolism. This being granted, an excess of meat (which is supplied very generously to our armies) will itself tend to the production of acidosis, and will thus reinforce the action of the carbohydrate factor in this direction.

A condition of relative acidosis is produced on these assumptions by two factors:

1. A deficiency of the "buffer salts" that counteract the production of acid.
2. An increased production of acid substances, probably owing to faulty metabolism of excessive carbohydrate and protein substances in the diet.

CONCLUSIONS.

As a result of our investigations we may conclude:

1. That there is a constitutional state, which may exist from infancy or may appear *de novo* in adults, and which may be termed the status *catarrhalis* or *exudativa* (Czerny). Where this condition exists the skin and mucous membranes show an abnormal susceptibility, not only to various bacterial infections, but also to mechanical and chemical irritation.
2. Persons in whom the status *catarrhalis* is present, either permanently or temporarily, are liable to develop the multitudinous eruptions which have been variously termed *seborrhoeic* eczema or dermatitis, true eczema, pustules, boils, and the wrongly termed "impetigo"—really an impetiginized *seborrhoeic* eczema. These manifestations, in whole or part, are intimately dependent or asso-

ciated with the existence of an underlying dyscrasia, to which we have ventured to give the name of

The Status Seborrhoeicus.

3. There is considerable clinical and therapeutic evidence to suggest that all patients with the status *seborrhoeicus* are suffering from a relative acidosis. We are of opinion that this condition may have resulted from a diminution of the intake in their food of the fixed bases—the mono- and di-sodium phosphates, and the carbonates, which are normally present in fresh fruits and vegetables, and which are largely responsible for the maintenance of an exact alkaline-acid equilibrium in the blood and tissue fluids.

4. As a practical outcome of these considerations there is abundant clinical evidence of the value of alkalis in the treatment of *seborrhoeic* eczema.

REFERENCES.

- ¹ MacCormac: *Skin Diseases and their Treatment under War Conditions*, *Proc. Roy. Soc. Med.*, 1917, vol. x, pp. 121-149. MacCormac and Small: The Scabies Problem on Active Service, *BRITISH MEDICAL JOURNAL*, September 22nd, 1917, p. 384. Semon and Barber: *Pyodermitis of Parasitic Origin*, *Brit. Journ. of Dermat. and Syph.*, July, 1917. ² *Précis de Dermatologie*. ³ *Jahrb. der Kinderheilk.*, 1905, p. 199; 1909, p. 529. ⁴ *BRITISH MEDICAL JOURNAL*, June 9th, 1917. ⁵ *Principles of Acidosis*, chap. iv, 1917.

A Collective Investigation

OF

TEN THOUSAND RECRUITS WITH DOUBTFUL HEART CONDITIONS.

Conducted at the National Hospital for Diseases of the Heart by C. CHAPMAN GIBBES, R. O. MOON, S. RUSSELL WELLS, P. HAMIL, F. W. PRICE, and J. STRICKLAND GOODALL.

REPORT II,*

BY

S. RUSSELL WELLS, M.D., B.Sc.

BEFORE investigating the etiology of any particular cardiac disorder, it was considered desirable to determine the incidence, on the whole 10,000 cases, of the various diseases which have been supposed to lead to damage of the cardiac valves or myocardium. In every case inquiry was made for a history of the following ailments:

Rheumatic fever	Tonsillitis	Influenza
Chorea	Scarlet fever	Syphilis
Rheumatism	Diphtheria	Gonorrhoea
Growing pains	Pneumonia	

and also as to whether the recruit had been subjected to muscular strain or not.

Rheumatic Fever.

Since rheumatic fever, or acute rheumatism, is commonly agreed to be one of the most frequent causes of organic lesions of the heart, it was felt desirable to determine the percentage of the cases examined giving a history of this disease. It is important to define accurately what is meant by the term rheumatic fever. The word "rheumatism" is popularly used to describe a variety of affections. Rheumatoid arthritis is frequently spoken of by the laity as rheumatism. The aching pains in the joints which accompany various acute diseases such as influenza are often called rheumatic pains, as are the joint pains occurring in tonsillitis, though here some consider that there is more justification for the use of the word "rheumatic." In addition to this there are the various slighter forms of rheumatism which may differ only in degree from rheumatic fever. Some writers, following Poynton, regard chorea as a manifestation of rheumatism, and go so far as to speak of chorea as "cerebral rheumatism." We have, therefore, thought it well to confine the term "rheumatic fever" to cases in which there is a distinct history of fever, pain and swelling of the joints, and confinement to bed for several weeks. This, of course, does not exclude the possibility of some cases of gonorrhoeal rheumatism being classified as rheumatic fever, but the absence of a history of any urethral discharge and a consideration of the patient's statement usually prevented any doubt arising.

* Part I was published in the *BRITISH MEDICAL JOURNAL*, May 18th, 1918, p. 556.

On account of the painful nature of the complaint and the inability to use the affected joints, together with the long confinement to bed which the disease usually entails, the patient's recollection of an attack of acute rheumatism is generally fairly vivid, so that, as a rule, little doubt arises as to the nature of the illness from which he has suffered.

Of the 10,000, 1,921 cases—that is to say, 19.2 per cent.—gave this clear and unequivocal history of rheumatic fever.

Since the 10,000 cases were all sent up for examination because a doubt had arisen in the minds of the examining medical boards as to their cardiac condition, and since acute rheumatism is a recognized cause of cardiac derangement, these figures cannot be used to estimate the incidence of rheumatic fever on the general population. The 10,000 cases are a selected sample, and the selection was such as practically to ensure that a history of acute rheumatism would be commoner in the sample than in the corresponding classes of the population of London.

Chorea.

Chorea, like acute rheumatism, is so definite an ailment, and persists, as a rule, for so long a time, that histories of this affection may usually be relied upon. Of the 10,000 cases examined, 265—that is, 2.6 per cent.—gave a history of chorea. With a view to determining if the material with which we have to deal lent any support to Poynton's theory of chorea being really a form of rheumatism, the coefficient of correlation between the two was worked out on Pearson's formula: 101 of the 10,000 cases gave histories of both chorea and rheumatic fever, 164 of chorea without rheumatic fever, 1,820 of rheumatic fever without chorea, and 7,915 gave no history of either of these affections. The coefficient of correlation was 0.31 ± 0.02 , χ^2 being 63.

The correlation coefficient is a figure which shows the degree of relationship between two sets of facts or measurements. If every case of chorea gave a history of rheumatic fever, and every case of rheumatic fever was followed or preceded by chorea, the correlation coefficient of chorea and rheumatic fever would be +1; that is, there would be absolute correlation between them. If there was no association between them, and a patient who suffered from chorea was no more or less likely to give a history of rheumatic fever than the rest of the population, the correlation coefficient would be 0. If chorea and rheumatic fever were mutually exclusive the correlation coefficient would be -1. Where the correlation coefficient is between 1 and 0.75, we speak of high correlation; between 0.75 and 0.50, considerable correlation; between 0.50 and 0.25, moderate correlation; below 0.25, low correlation. It is obvious that in working out such correlation as this there will be a margin of error. This can be calculated, and after any correlation coefficient we shall state what it is. Thus, the correlation coefficient between the history of rheumatism and chorea is 0.31, the error being ± 0.02 ; that is, the correlation coefficient is not greater than 0.33 nor less than 0.29. But the probability of our calculated correlation coefficient being wrong depends upon the number of cases taken, and how they are grouped. We have, therefore, to calculate the likelihood of it being correct; for it may be that our grouping of figures is purely due to chance. We can calculate this probability. To do so we work out the value of what is called χ^2 . The higher χ^2 is, the less likelihood is there of our correlation coefficient of not more than 0.33 or less than 0.29 being due to chance. If χ^2 were 1 the likelihood of our figure being a chance association is 8 in 10; if χ^2 were 5 the likelihood would be 17 in 100; if it were 10, 19 in 1,000; when χ^2 is 15 the probability of our correlation figure being due to chance sinks to less than 18 in 10,000. The actual number for χ^2 here was 63, so that the likelihood of our correlation coefficient of 0.31 ± 0.02 being a mere chance number is infinitesimal. This coefficient comes within the limit of what Pearson has defined as moderate correlation, and is about the same as the correlation between the severity of an attack of small-pox and the number of years since vaccination. It affords a certain amount of support to Poynton's theory.

Rheumatism.

As has been pointed out, when speaking of rheumatic fever, a history of rheumatism or rheumatic pains must

be received with considerable doubt, the popular use of the word being too vague to enable one to arrive at any definite opinion as to the pathological entity referred to. If the histories of "rheumatism" referred to some form of the same disease as rheumatic fever, or were all really accounts of a slighter attack of the same affection, we should expect to find a definite correlation between them. We therefore calculated out the correlation coefficient for rheumatic fever and "rheumatism" in our cases; 266 gave a history of rheumatic fever and "rheumatism," 1,347 a history of "rheumatism" without rheumatic fever, 1,655 a history of rheumatic fever without "rheumatism," and 6,732 no history of either rheumatic fever or "rheumatism." The coefficient of correlation was 0.08 ± 0.02 , χ^2 being 9.2. This correlation coefficient is so small as to be practically negligible. We have therefore no right to assume that where a recruit gave a history of "rheumatism" he had suffered from anything of the same nature as true acute rheumatism.

Growing Pains.

The arguments used with reference to rheumatic fever and "rheumatism" equally apply to a history of growing pains; 563 cases gave a history of both rheumatic fever and growing pains, 2,086 a history of growing pains without rheumatic fever, 1,358 a history of rheumatic fever without growing pains, and 5,993 no history of either rheumatic fever or growing pains. The correlation coefficient works out at 0.06 ± 0.02 , χ^2 being 9.7. We are therefore not justified on these figures in assuming the identity of growing pains and acute rheumatism.

Tonsillitis.

Tonsillitis has been considered by many writers as a rheumatic affection. It was therefore thought well to calculate the correlation between acute rheumatism and tonsillitis in the 10,000 cases: 525 cases gave a history of both rheumatic fever and tonsillitis, 1,685 a history of tonsillitis without rheumatic fever, 1,396 a history of rheumatic fever without tonsillitis, and 6,394 no history of either disease. The coefficient of correlation was 0.13 ± 0.02 , χ^2 being 38. The correlation here is appreciably higher than in the case of "rheumatism" or growing pains, but is too low to be seriously considered.

Scarlet Fever.

Of the 10,000 cases examined, 2,185—that is, 21.8 per cent.—gave a history of scarlet fever. Since scarlet fever is stated to be not infrequently followed by acute rheumatism or some affection resembling that disease, it is of some interest to determine the association between a history of scarlet fever and rheumatic fever in these cases. Of those who had had scarlet fever, 479—that is, 22 per cent.—gave a history of rheumatic fever as well. In 70 of these cases there was a definite history of the rheumatic affection having immediately followed the scarlet fever, but, when the association between scarlet and rheumatic fevers in the 10,000 cases is investigated by Pearson's formula, it is found that the correlation coefficient is so small as to be negligible—namely, 0.08 ± 0.02 .

Summary as to Rheumatism, Chorea, and Growing Pains.

Reviewing the above results, it may be stated that the investigation of the material at our disposal by means of the correlation coefficient lends some slight support to the view that chorea and acute rheumatism are the same disease, but none to the supposition that a history of "rheumatism" or growing pains is any evidence of a true rheumatic affection, nor does it afford any evidence of the rheumatic nature of tonsillitis or reveal any association between true rheumatism and scarlet fever.

It must not, however, be assumed that because we are unable to find any association between these affections and acute rheumatism, they may not be the efficient cause in producing valvular lesions of the heart. That can only be determined by a detailed examination of the etiological factors in the different cardiac disorders. Nor must it be assumed that we consider a statistical inquiry, such as this is, can definitely dispose, in all cases, of the rheumatic nature of tonsillitis, growing pains, and the like. What is described as tonsillitis, for example, may well be only the reaction of the tonsils to a variety of noxious agents. In some cases the agent may be the same organism as that which causes acute rheumatism, but if this only produced

a small minority of the cases described as tonsillitis, they would be "swamped" by the rest, and the association with true rheumatism might not appear. We do assert, however, that our inquiry makes it advisable to be cautious in suggesting a rheumatic origin for any valvular lesion, where a history of "rheumatism," growing pains, or tonsillitis is alone obtained.

Diphtheria.

Of the 10,000 cases, 728 gave a history of diphtheria. While the association between diphtheria and scarlet fever is not directly related to the present inquiry, it may be worth while putting on record the correlation we found between these two diseases, for, though ours is a selected material, the association between diphtheria and scarlet fever on the one hand, and heart disease on the other, is probably not sufficiently intimate to affect materially the results.

A history of both scarlet fever and diphtheria was given by 267 cases, of diphtheria without scarlet fever by 461, a history of scarlet fever without diphtheria by 1,918, and 7,354 gave no history of either disease. This gives a correlation coefficient of 0.27 ± 0.002 , χ^2 being 101. This correlation coefficient, though only moderate to small, is distinctly higher than one would, *a priori*, have expected, for it does show some definite correlation between the two histories. It is possibly due to the septic tonsillar infection so frequent in scarlet fever being described as diphtheria. Still, whatever the explanation, it is enough to be worth recording.

Pneumonia.

Of the 10,000 cases, 537 gave a history of pneumonia.

Influenza.

No fewer than 5,629, that is to say, over 56 per cent. of the recruits examined, gave a history of one or more attacks of influenza. Though there is no doubt that this disease is extremely common in England, it may be doubted whether this high figure really represents its prevalence, for it is notorious that at the present time patients delight in dignifying colds and other slight ailments by the more sonorous title of influenza.

Syphilis.

Since the 10,000 cases examined were selected because they presented a doubt as to their cardiac condition, and the presence or absence of a history of venereal disease was not taken into consideration in making this selection, they may be regarded, from the point of view of incidence of syphilis, as a random sample of the male population of London between the ages of 18 and 41, provided that syphilis was not a material cause in producing those cardiac symptoms which determined their selection. We shall hope to show later that the importance of syphilis as a cause of cardiac derangement was minimal in the cases with which we are concerned, and, since practically all the cases examined were engaged in their ordinary avocations, and very few could be regarded as invalids, there is no reason for supposing that the incidence of syphilis would be less in the cases considered than among the general population from which they were drawn.

Unfortunately, on account of the time involved, it was not possible to make a determination of the Wassermann reaction part of the routine of the examination. Consequently, we are dependent chiefly on the recruits' statements in determining a syphilitic history; but, from the very circumstances of the examinations, these histories are far more likely to be truthful than those usually obtained. The atmosphere in which they were conducted was official; each man was privately catechized, and knew that it was highly improbable that he would ever see the examiner again, or that there would be any opportunity of his secret being betrayed to his friends or relations, while there was the ill-defined fear of punishment if an untruthful statement were made in what was, in essence, an inquiry by the State. Further, as the great bulk of the men were conscripts, it was found that a not inconsiderable proportion were only too ready to state any fact which they thought would militate against their acceptance for full military service. We are therefore of opinion that the wilful concealment of a syphilitic history has, in these cases, been reduced to a minimum. Of course a man may have contracted specific disease without being aware of the

fact, but such cases must, in all probability, constitute but a small proportion of the whole. Where there was a doubt as to whether the history given was that of true specific disease or not, the cases were usually recorded as syphilitic so as to avoid under-estimating the incidence of the disease and with a view to neutralizing to some extent any instances of wilful concealment. Probably, therefore, the incidence of syphilis on these 10,000 cases does fairly represent the incidence of the disease on the corresponding classes in the population of London.

It was found that 200, or exactly 2 per cent., of the 10,000 cases gave a syphilitic history. On account of the difficulty in obtaining any reliable and unbiased estimate of this nature, these figures are valuable for other purposes than that of determining the relation of specific disease to cardiac conditions, for which they were primarily worked out.

Gonorrhoea.

The remarks which have been made under the heading of syphilis apply in a great measure to gonorrhoea as well, and the incidence of this disease on the 10,000 recruits may probably be fairly taken as representing the incidence on the male population of London between the ages of 18 and 41. An analysis of the records showed that 596, or 5.96 per cent. of the 10,000 recruits, gave a history of gonorrhoea. The fact that among these men three times as many had suffered from this ailment as those who had been affected by syphilis is about in accordance with common experience as to the relative frequency of the two diseases. These numbers are interesting as putting on record the frequency with which the two affections occur in a large body of men in civil life, and may form a useful standard of comparison with comparable figures for men after various periods of service with the colours.

Strain.

The classification already given into occupations gives some idea of the amount of muscular work the different classes of men concerned habitually undertake. While it has in many cases been distinctly difficult to decide whether any particular vocation should be placed at the top of the light work category or at the bottom of the medium, or whether a trade properly belongs to the medium or heavy group, still, on the whole, we believe that the arrangement adopted is sufficiently accurate for the purpose we have in view, and that, on account of the large numbers involved, such errors as we may have made will tend to neutralize one another.

In estimating the amount of muscular work any individual performs, we ought not to confine ourselves to his occupation alone but should consider also how he employs his leisure. A clerk in a Government office, who has short office hours and devotes an ample leisure to various heavy athletic amusements such as football and boxing, would, from the point of view of muscular work, be better classified with the carpenter or gardener, or even with the blacksmith, than with the desk clerk in a shop, who has long hours and who very likely indulges in no form of athleticism. In discussing the effect of muscular work upon the circulatory system the total number of foot-pounds done per diem is not the only factor of importance. The blacksmith who has been gradually trained to his work from youth may well undertake with ease an amount of physical exertion which would break the city clerk, whose total active daily exercise is not infrequently confined to a short walk from his dwelling to the train, from the train to his office, and back again in the evening. We should distinguish clearly between the effect of a large total amount of work on a heart which has been gradually accustomed to bear the load on the one hand, and the effect of sudden strain on the other.

If a clerk who during the week confines himself to his walk to and from the station, on Sunday undertakes long bicycle rides in competition with more athletic people than himself, he may well expose his heart to a greater strain than the blacksmith does in his more strenuous occupation. We may regard the amount of strain on the heart produced by any particular piece of muscular work as bearing some sort of proportion to the ratio which this work bears to the work habitually done by the person in question. The blacksmith, who is accustomed to put out regularly many thousands of foot-pounds per hour, is not likely to have his heart strained by running, in 30 seconds, up an

incline rising 30 feet vertically; but the clerk, whose hourly muscular work is measured in hundreds rather than in thousands of foot-pounds, might very well manifest symptoms of distress if forced to take the same run.

We therefore propose to use the word "strain" as a convenient term for the risk to which a man is exposed who does muscular work considerably in excess of that to which he is habituated, and to use the word "strenuous" for habitual heavy labour. In this sense, all the heavy occupations in our list involve strenuous work and in most cases there is also the liability to strain. The railway goods porter, for example, is habitually accustomed to strenuous work, but at any time the moving of an unexpectedly heavy load or the slipping of some weighty piece of goods which he is handling may expose him to strain. While we have endeavoured to ensure that all men whose occupations are strenuous in the sense defined above are classified in the heavy labour groups, it is obvious that many of the cases exposed to strain are necessarily placed in the medium, light, and sedentary occupations groups. Since, in every case, the habits of the recruit with regard to exercise were inquired into, the records have enabled us to form some sort of an estimate regarding the exposure to strain, and a careful inspection of the individual records induces us to believe that out of the 10,000 recruits examined, 2,711, that is to say 27.1 per cent., were subject to strain as defined above, either in their work or in their amusements.

With a view to representing our results in as concrete a form as possible, we append tables of the percentages and correlation figures we have found for our 10,000 cases.

Percentages.

History of rheumatic fever...	19.2	History of diphtheria ...	7.2
" chorea ...	2.6	" pneumonia ...	5.3
" "rheumatism" ...	16.1	" influenza ...	56.0
" growing pains ...	26.5	" syphilis ...	2.0
" tonsillitis...	22.1	" gonorrhoea ...	5.95
" scarlet fever ...	21.8	" strain ...	27.1

Correlation Figures.

Correlation between History of	Coefficient.	χ^2 .	Degree of Correlation.
Rheumatic fever and chorea ...	0.31 ± 0.02	63.0	Moderate.
Rheumatic fever and "rheumatism" ...	0.08 ± 0.02	9.2	Negligible.
Rheumatic fever and growing pains ...	0.06 ± 0.02	9.7	"
Rheumatic fever and tonsillitis ...	0.13 ± 0.02	38.0	Low.
Rheumatic fever and scarlet fever ...	0.08 ± 0.02		Negligible.
Scarlet fever and diphtheria ...	0.27 ± 0.002	101.0	Moderate to low.

THE REACTIVITY OF THE BLOOD

IN RELATION TO CARDIAC BREATHLESSNESS, SURGICAL SHOCK, AND ALLIED CONDITIONS OF THE NERVOUS AND CIRCULATORY SYSTEMS.

By BENJAMIN MOORE, D.Sc., F.R.S.,

FORMERLY PROFESSOR OF BIO-CHEMISTRY, UNIVERSITY OF LIVERPOOL.
(From the Department of Applied Physiology of the Medical Research Committee.)

The plasma of the blood possesses the remarkable property of being able to neutralize large amounts of either acid or alkali without itself being or becoming markedly acid or alkaline. This property ensures the immediate neutralization of acidic or alkaline metabolites thrown into the blood stream as the result of physiological or pathological processes. Without this protection the life of the human race and all the higher animals and plants as at present constituted would be impossible, for it has been shown by the researches of Moore, Roaf, and Whitley¹ that the strip of variation in acidity or alkalinity within which life is possible is a very narrow one, and that it suffices to render the medium within which living cells are situate acid or alkaline to the feeble limit of one-thousandth normal, or less, in order to destroy all life.

It will suffice to give a few illustrations of the importance of small variations in this property of balanced alkalinity and acidity (or hydrogen ion concentration, as it is termed in the language of physical chemistry) in order to prove the necessity of a clear understanding of the problem by physiologists and clinicians alike, and, since the recent communication of Professor Bayliss² clearly demonstrates that there is not agreement either as to facts or interpretations regarding the cause or mode of operation of this protective influence, some service may be rendered by a discussion of the question and a reply to his criticisms.

When Haldane and Priestley³ discovered that the respiratory centre was most delicately balanced in relationship to the concentration of carbon dioxide in the blood, it was sought to correlate the increased respiratory activity after muscular exercise with the production of lactic acid and other organic acids by the muscles, and much research was expended on the determination of lactic acid in blood and urine. At an early discussion of the subject at a meeting of the Physiological Society the present writer suggested that the increased acidity or hydrogen ion concentration of the plasma due to increased dissolved carbonic acid was quite sufficient to form an adequate stimulus to the respiratory centre without any invocation of lactic acid or other organic acid. After some years of vain searching for increase in lactic acid or other partially oxidized metabolites, it has now been proved by the labours of Barcroft, Peters,⁴ and others that this is the correct explanation of the regulation of respiratory activity.

An interesting corollary to this physiological discovery is the recent clinical one by Lewis, Cotton, Barcroft, Milroy, Dufton, and Parsons⁵ that breathlessness in soldiers suffering from irritable heart is accompanied by a condition of acidosis of the blood. It has been shown by these observers that the blood plasma of such patients possesses less protective power against carbonic acid, or other acid, than that of normal individuals, for the addition of acid causes a quite disproportionate rise in hydrogen ion concentration—that is to say, in that acidic property which stimulates the respiratory centre. Accordingly such patients become breathless on much less exertion than ordinary individuals because they are deficient in alkaline reserve with which to combine the carbonic acid set free by the muscles. As will be pointed out later, this acidic condition of the blood is communicated to all the nerve and muscle cells, voluntary and involuntary, bathed by the altered plasma, and a pathological condition is induced in these, so that their irritability is increased like that of the nerve cells of the respiratory centre. At a deeper stage the increased excitability passes into shock accompanied by physico-chemical changes in the proteins of plasma and cell protoplasm, which will presently be described.

Another interesting development of the problem is that different varieties of shock to the system, such as haemorrhage, surgical operation, infection of wounds, and gassing by irritant gases, are accompanied by acidosis or deficiency of alkali reserve, and when once this vicious condition has been established it gives rise to physico-chemical alterations in plasma and cell protoplasm which tend to retain the circulatory system in a relaxed condition, and this relaxed condition in turn keeps up the acidosis through the stagnation of the circulation. The presence of acidosis in conditions of shock, and its influence in lowering arterial blood pressure was shown by Yandell Henderson⁶ and others in America prior to the war, and quite recently has been amply confirmed by Cannon in observations on wounded in casualty clearing stations in France.

A similar drop in the alkali reserve of the plasma following prolonged anaesthesia and operation has been established by many American surgeons, such as Crile and Menten,⁷ Austin and Jonas,⁸ Morris,⁹ and Caldwell and Cleveland.¹⁰ The danger of surgical shock followed by coma and death in diabetes, where there exists high acidosis accompanied by defect of alkali reserve, is known to all surgeons. It has recently been proven by Sir Almroth Wright¹¹ that there is a marked increase in acidity of the serum in gas gangrene, termed by him "acidemia," and that the bacillus of this disease flourishes with ease in partially neutralized serum, but is inhibited by serum of normal alkalinity. A similar condition in severe cases of gassing in soldiers and of experimental