The condition had improved somewhat at first but for several months had been almost stationary. She then had the same stock staphylococcus vaccine, combined with 20,000,000 of her own acne bacillus vaccine. This was followed by the appearance of fresh pustules and the aggravation of existing ones. Ten days afterwards another inoculation was given of staphylococcus, with this time only 10,000,000 acne bacillus, and inoculations were given regularly of the same doses of the same staphylococcic vaccine as she had previously been having, combined with doses of acne bacillus varying from 5,000,000 to 10,000,000 and in three months almost all traces of acne had disappeared. Later she discontinued treatment and a slight relapse occurred, but this has again improved with the mixed staphylococcic and acne bacillus vaccine.

Another case was that of a girl, about 26 years of age, who had had very bad pustular acne on the face for several years. The face was covered with deep indolent pustules; a film of pus showed no organisms; and of cultures from four pustules two were sterile and two showed a scanty growth of staphylococcus. From July till the end of September last year she had doses of mixed stock staphylococcus and acne bacillus vaccines in doses of 100,000,000 to 250,000,000 of the former and from 5,000,000 to 20,000,000 of the latter, with hardly any improvement. It is worthy of note that while a dose of 250,000,000 staphylococci + 10,000,000 acne bacilli produced hardly any negative phase, the next dose of 250,000,000 staphylococci + 20,000,000 bacilli was followed by a marked exacerbation of the pustulation, indicating the importance of the bacillus in the causation of these lesions. From the end of September till the beginning of January she had the same doses of staphylococcus with doses of from 5,000,000 to 10,000,000 of an acne bacillus obtained in pure culture from her own pustules, and from the very first her condition improved till on Jan. 7th of this year all suppuration had disappeared from the face with the exception of one very small superficial pustule.

Another case was that of a girl, aged 20 years, who had had very bad facial acne for five years. Films of pus showed many acne bacilli and in some pustules staphylococci were also to be seen. From Sept. 3rd, 1908, to Dec. 3rd she was treated with stock vaccines of staphylococcus (200,000,000) and acne bacillus (5,000,000 to 8,000,000) without showing any definite improvement. From Dec. 3rd to Jan. 22nd, 1909, she has been having the same doses of the same staphylococcus with 8,000,000 of an acne bacillus derived from her own lesions. The improvement was immediate and marked, and now there is practically no pustulation, merely some indurated nodules and many scars.

These cases illustrate the fact that not all the cases will show improvement when treated with a stock vaccine, and this is exactly in accordance with what one finds with other organisms, such as streptococcus or bacillus coli. They also furnish very strong evidence that the bacillus is largely responsible for the suppuration. The first case had been treated with staphylococcus for months, and it was only after acne bacillus vaccine was administered that a rapid improvement in the pustulation was observed. The first and second of these cases show that when an excessive dose is given them a definite negative phase is induced, although the dose of staphylococcus is unaltered. The second and third cases show that although the stock vaccine of staphylococcus combined with the stock vaccines of acne bacillus was of little avail, yet the same doses of the same stock vaccine of staphylococcus with an autogenous acne bacillus vaccine rapidly got rid of the suppuration.

While these cases illustrate the fact that in some cases an autogenous vaccine of acne bacillus is necessary, yet experience has shown that in the vast majority of cases great improvement has been induced by the inoculation of a stock vaccine combined with staphylococcus if an examination of films has revealed that that organism is present. The dose used has varied from 4,000,000 to 10,000,000 and the interval between inoculations from one to two weeks. The guide to treatment has been the appearance of fresh lesions either during the period of low resistance following the positive phase when too long an interval has been allowed to elapse or in the next two or three days after an inoculation indicating that too large a dose has been administered. By watching these signs and working the dose up till it just fails to show any "negative phase"

clinically one obtains the maximum benefit from the vaccine. In this way a large number of cases of acne in all its stages have been greatly improved and in a fair proportion the lesions have totally disappeared. On cessation of treatment in several instances, especially in some cases where attendance ceased before the condition had entirely disappeared, there was a recrudescence of the disease, which, however, rapidly gave way to subsequent treatment.

It is interesting in view of Sabouraud's contention that this bacillus is the cause of seborrhoea and of alopecia areata to note the effect of treatment on a patient—a woman aged 25 years—who suffered from comedones on the face and a rapid loss of hair which had been persisting for some months in spite of ordinary treatment. In October last she was first inoculated with the acne bacillus and from the first week after this the loss of hair practically ceased. Since that time she has had inoculations every 7 or 14 days, and there has been no return of the loss of hair. One cannot argue from one case, but it is possible that if, as Sabouraud maintains, seborrhoea of the scalp is due to this bacillus and the loss of hair is due to seborrhoea, then inoculations with the bacillus may prove of benefit in checking this loss.

THE PHYSIOLOGICAL AND THERAPEUTICAL PROPERTIES OF THE SERUM OF MILK (LACTO-SERUM).¹

BY DR. RAOUL BLONDEL,

CHEF DE LABORATOIRE AT THE MATERNITY HOSPITAL, PARIS.

(Specially Translated for THE LANCET.)

WHEN the casein of milk is separated by coagulation the residue is a serous liquid commonly called whey. If the coagulation has been produced by means of an acid the whey contains a certain amount of albuminoid substances, but if rennet (*le ferment lab*), assisted in its action by a salt of calcium, has been used, only traces of such substances remain. The present investigation was commenced in the year 1902 and the first results were made known in a preliminary note read at the Medical Congress held in Madrid in 1903. In conducting it I took no account of the dietetic uses of whey—a subject on which many works have been published, and I administered the lacto-serum by the hypodermic method which had not been previously employed so far as I am aware.

My first observations were made in Dr. Maygrier's obstetric wards at the Charité, where I held an appointment, and in them lacto-serum sterilised in an autoclave was used. Sterilisation by heat, however, has the disadvantages that the product changes in colour if it contains a trace of alkali and becomes turbid if it contains a trace of acid, absolute neutrality being almost impossible of attainment in a solution of amphoteric reaction. For these reasons recourse was ultimately had to sterilisation without heat by filtration through a d'Arsonval bougie. The d'Arsonval bougie is a porcelain tube like the Chamberland bougie, but larger and thicker, in which the organic liquids to be filtered are forced through under pressure of carbonic acid gas. The pressure is considerable and causes a filtration of thick albuminoid liquids which will not traverse ordinary filters. The lacto-serum, whenever it is well prepared and a little patience is used, can be filtered through ordinary bougie filters. The lacto-serum used by me is derived from cow's milk; it is a clear fluid, almost tasteless, and practically isotonic; it contains the mineral salts of the milk, occasional traces of albumin varying with the method of preparation, and more especially the natural ferments of the milk which are destroyed by sterilisation with heat but remain in solution after filtration without heat as above described. This fluid possesses some very interesting properties. As regards its saline constituents it behaves like a solution in which chloride of sodium, milk sugar, and phosphates of the alkalies and alkaline earths predominate. As regards its ferments, it has a resemblance to extracts of animal organs and to animal serums; like them, it contains certain oxydases, the importance of which is only beginning to be known and which impart to all

¹ Memoir communicated to the Paris Academy of Medicine on April 9th, 1909.

serums several properties in common. This last and very remarkable fact was suspected by Pasteur and has been confirmed by the successful employment in different diseases of a serum such as that of Dr. Roux, which has produced such good effects in diphtheria that it deserves to be called a specific.

The ferments contained in milk have been the subject of many investigations. Some of them, such as pepsin, trypsin, lipase, the glycolytic ferment, the oxydases, and the anaëro-oxydases, are common to the milk of all the mammalia, while others, such as the amylolytic ferment and the ferment which attacks salol, are present in human milk but not in that of the cow. The importance of these ferments from the dietetic point of view has given rise to long discussions among those who advocate respectively either raw milk (*lait cru*) or sterilised milk for the feeding of new-born infants. The practical results observed in the use of sterilised milk deprived of its ferments seem to show that the latter are of only secondary importance when the milk is introduced into the digestive tract. The case, is however, quite different when the milk is converted into lacto-serum which is injected under the skin, the specific action of the ferments being now very pronounced. If the lacto-serum has been sterilised by heat there may be some increase in the amount of urine, but otherwise the effects are not very different from those of "artificial serum," whilst the injection of lacto-serum sterilised without heat is followed by some novel consequences. At first there is a slight rise of temperature coming on soon after the injection and lasting only a few hours. In the next place there is an increase in the polynuclear leucocytes, while there is often a remarkable increase in the excretion of uric acid, especially in febrile cases; finally, as a distinctive and peculiar phenomenon—for those just enumerated belong in common to almost all serums—there is a notable lowering (or what might more correctly be called a "regularisation") of the blood pressure in the arteries and capillaries. This phenomenon is novel and could not have been foreseen, because analysis of the lacto-serum does not reveal the presence of any substance capable of producing such an effect. Neither the very small amount of milk sugar contained in the 10 cubic centimetres which I gave as a dose, nor the trifling increase in the amount of urine which might be attributed to it, could be considered as the cause. There is, however, no doubt as to the fact, for a considerable number of observations both on the human subject and on the lower animals have enabled me to prove that when the blood pressure is increased, either from pathological conditions or artificially, injections of lacto-serum will cause the pressure to fall to normal more or less quickly and to remain at that level for a time. In cases of hypotension the blood pressure is not further reduced but has rather a slight tendency to rise. A case observed in the wards of Professor Robin, the patient being a female suffering from tuberculosis whose blood pressure measured by Verdin's apparatus fell to practically seven millimetres of mercury, is absolutely conclusive in this respect.

In some experiments made in the laboratory of Professor Richet in July, 1902, the arterial pressure in a dog was artificially raised by means of extract of suprarenal capsules, this being followed by an injection of cocaine for the purpose of prolonging the artificial rise of pressure which would otherwise be of short duration. I then found that the injection of lacto-serum brought down the pressure to the normal either quickly or at least in a much shorter time than would have been required for a spontaneous return to the normal without the administration of lacto-serum. Similar results were obtained in the human subject. In a patient whose radial artery showed a blood pressure reckoned in millimetres of mercury equivalent to 24, an injection of lacto-serum caused it to fall to 21, and sometimes to 20, in from three to four hours, the pressure rising again to 22 at the end of 24 hours. By means of a series of daily injections the pressure was brought down to the normal amount in six, eight, or ten days according to the nature of the cases, and a still more curious fact was that it remained normal for a month or more, whilst in one instance it remained normal for five months. Some cases resisted the treatment, but they were very few in number. It must also be remembered that the true cause of arterial hypertension is not as yet completely known, neither is it certain that the cause is always the same.

The therapeutical applications to which my inquiries led me have been as follows:—

1. *Puerperal infections*.—I made observations on four cases of this kind in the wards of which Dr. Maygrier has charge and on two cases in private practice. The results were variable, being sometimes successful and well marked, but at other times either uncertain or of short duration.

2. *Post-operative peritonitis*.—Three cases occurring in private practice were observed. The treatment was unsuccessful; there was an evident prolongation of the patients' resistance to the disease, but a fatal issue was not averted. In this condition the arterial tension is always low.

3. *Typhoid fever*.—Cases of this disease were observed in the wards under the charge of Professor Robin. In one there was a remarkable result, but of doubtful interpretation; in three cases there was no result.

4. *Pneumonia*.—Observations were made on 12 patients in the wards under the charge of Professor Robin and Dr. Maygrier. The results were in every way remarkable and constant. Defervescence always followed the second or even the first injection, sometimes on the fourth day of the treatment, the defervescence being as usual accompanied by an abundant excretion of uric acid. It must, however, be admitted that in pneumonia many kinds of serum give the same results as above described, and that the "metallic ferments" which came into prominence after my researches had been commenced produce even more remarkable effects. This merely proves the similarity of action of lacto-serum and of these ferments, a similarity on which Professor Robin has laid great stress in his important work on this subject.

5. *Arterial hypertension in arterio-sclerosis*.—It is in this condition that lacto-serum appears to me to find its most interesting application. My observations, 63 in number, were made upon patients in the wards under the charge of Professor Robin, M. Huchard, M. Oulmont, and M. Vaquez, as well as in private practice; ten have been described in communications received by me from brother practitioners. In one patient who was under the care of M. Vaquez and who received only a single injection the treatment was a complete failure. In almost all the others the fall of the blood pressure was constant and occurred under the conditions already detailed. Simultaneously with this fall of pressure there was a mitigation of the subjective symptoms such as headache, insomnia, general oppression, and shortness of breath on exertion. Every time that the treatment was applied according to the rules suggested by experience and continued for a sufficient period the results were surprising. There were at least 26 cases which I was able to keep under observation as private patients for a longer time than the hospital patients, because all the latter left the hospital as soon as they felt themselves better; these 26 cases showed a general improvement so well maintained as to amount to recovery, provided that from time to time the injections are repeated for several days as soon as signs of hypertension recur. Under these circumstances the patient is often free from symptoms for several months. All these patients resumed their ordinary course of life which had been interrupted by the illness, and some in opposition to my advice even discontinued the special *régime* which had been prescribed for them.

Several of the patients whom I treated had in their urine albumin, the amount of which was almost always slightly increased during the first days of the treatment. If there is no renal lesion and the albuminuria depends on hypertension only it disappears quickly and permanently in patients who persevere with the treatment even though they discontinue the *régime* prescribed for them, but if there are renal lesions the albuminuria after the initial increase returns to its original amount. This supplies a convenient method of distinguishing between the albuminuria of hypertension and true organic albuminuria, serving in fact nearly the same purpose as the use of nitrites.

My ordinary method of administration is to give a daily injection of 10 cubic centimetres and to repeat it in 24 hours if the effect has not been sufficient until the blood pressure has fallen to normal. After this the injections are continued for four or five days longer, and then a weekly injection is given for a month, with more frequent repetitions if the pressure rises. When the pressure remains normal a monthly injection is given for three months. The injections are not repeated unless the symptoms of hypertension recur. The

injection is made into the muscles of the thigh or of the gluteal region, or else under the skin of the flanks. Usually it is not painful; when pain is felt it shows that the serum has not been made isotonic in the process of preparation. Sometimes a little erythema is seen at the site of the puncture. No abscess has occurred in a total of more than 1000 injections.

The preparation of the lacto-serum is very simple. Milk as fresh as possible is warmed to 30° C. and rapidly coagulated by some drops of hydrochloric acid. The curd is removed by filtration through fine muslin and the liquid, after exact neutralisation with carbonate of sodium, is filtered through paper (*papier Chardin*); the final stage is filtration through a d'Arsonval bougie under pressure of carbonic acid gas. This filtration may be very tedious, for colloid substances liable to block the pores of the filter are sometimes present. This process introduces into the lacto-serum a little chloride of sodium which raises the natural low tonicity (*hypotonie naturelle*) of the liquid; it also introduces traces of peptone, appears to reduce somewhat the richness of the serum in oxydases, and leaves a small quantity of albuminoid substances which hinder filtration. Coagulation of the milk by means of some drops of rennet (*présure*), sterilised by filtration and with its action strengthened by a trace of chloride of calcium, produces a better curd, leaves no albuminous substances in the whey, does not form peptone, interferes less with the oxydases, and secures a more rapid filtration, but it requires the liquid to be made isotonic by the addition of a little chloride of sodium in order that the injection may not be painful. The lacto-serum is preserved in flasks (*ampoules*) hermetically sealed after being filled with carbonic acid gas. Under these conditions it may retain its activity for one month, two months, or even longer.

Boulevard Hausmann, Paris.

THE TREATMENT OF GRAVES'S DISEASE WITH THE MILK OF THYROIDLESS GOATS.

By WALTER EDMUNDS, M.A., M.C. CANTAB.,
F.R.C.S. ENG.,

SURGEON TO THE PRINCE OF WALES'S HOSPITAL, TOTTENHAM.

FIFTEEN months ago a communication on this subject was made to THE LANCET,¹ and three cases were recorded. Of the first of these nothing more has been heard; the second case was again treated with the milk during the whole of last summer down to the end of September, and the patient's medical attendant reports:—

I last saw her on Nov. 10th, 1908, when she expressed herself as feeling well and able to do much more than she had been able to do previously; her pulse was 78 and her weight was 10 stones 1 pound (at one time her weight went down to 7 stones 9 pounds and her pulse could scarcely be counted, it was so rapid).

In the third case the patient continued to take the milk until Dec. 30th, 1907, when the supply failed. After this she was not quite so well, the pulse-rate increasing and there being some return of the oedema in the legs. Another goat came in milk in March, 1908, and the patient took the milk all last summer. Although the large goitre remained the same, yet the patient had very few subjective symptoms and but slight acceleration of pulse. The exophthalmos remained stationary. The supply of milk failed at the end of September, 1908, and the patient went to the seaside. Here she had a bad attack of gastro-intestinal disturbance with persistent vomiting and diarrhoea; since then she has been mainly in bed and subject to occasional severe attacks of palpitation and choking sensations at night. During the past two months the patient has been treated with dried blood from a thyroidless goat, five grains three times a day, but without improvement. Although milk is again available it cannot be taken on account of the gastric symptoms.

The following seven cases were under treatment at the Prince of Wales's Hospital, Tottenham, and I am indebted to the physicians under whose care they were for permission to publish them.

CASE 4.—The patient was 19 years of age and unmarried.

Her illness had commenced four years ago after some domestic trouble. The symptoms then were pain in the cardiac region and fulness of the throat and these symptoms continued. On admission to hospital there was found to be an obvious enlargement of the thyroid gland and the pulse-rate was 104. There was slight prominence of the eyes, slight tremors in the hands, and occasional attacks of a sense of suffocation in the chest, the patient's weight being 6 stones 12½ pounds. She was treated with milk from a thyroidless goat and strophanthus and she improved and was able to leave the hospital in 41 days, having gained 5½ pounds in weight. The pulse-rate remained about the same.

CASE 5.—The patient was a married woman, aged 36 years. The illness had commenced four months before attendance with marked prominence of the eyes, neuralgia in the forehead and the face, enlargement of the thyroid, difficulty in swallowing, palpitation, shortness of breath, and increased appetite. When first seen there were present pronounced exophthalmos, enlargement of the thyroid, and marked tremors. At first the patient was treated as an out-patient with rodagen and under this treatment the exophthalmos diminished. After a month she was admitted to the hospital and was treated with milk from a thyroidless goat, about a pint and a half a day. In six weeks she was much improved and was able to go to the seaside, where she gained 11 pounds in weight, but the exophthalmos remained the same. On her return she again took the milk and continued to improve till December, when the supply failed. Ten days later the patient was much worse; she was weaker and more tremulous, and was suffering also from shortness of breath and from attacks of cardiac pain; she had not had any of these attacks since the early days of her illness. She was readmitted to hospital and was treated with thyroidectin and she has much improved.

CASE 6.—The patient was a married woman, aged 36 years, and the mother of six children. The illness had commenced four years ago during pregnancy. On admission to hospital there were found to be severe palpitation, oedema of the legs, nervousness, with tremors in the hands, and enlargement of the thyroid, but there was no exophthalmos. The patient was treated with milk from a thyroidless goat and she improved, but she left too soon, to look after her children.

CASE 7.—The patient was 20 years of age and unmarried. She had a large soft goitre giving a sense of pulsation and a well-marked thrill. There was distinct exophthalmos, and the pulse was 120; slight tremors with occasional attacks of shortness of breath were present. The patient was treated with milk from a thyroidless goat and she quickly became much better, leaving the hospital in 39 days.

CASE 8.—The patient, aged 20 years, unmarried, had had appendicitis six months ago, for which she was operated upon. Three months later there were symptoms of gastric ulcer with vomiting of blood and the present symptoms followed. On admission to hospital the patient was markedly pale and the pulse was 144; the thyroid gland was felt on examination to be enlarged and there was shortness of breath, but no exophthalmos was present. The treatment consisted of milk from a thyroidless goat and under it the patient improved greatly.

CASE 9.—The patient was 17 years of age and unmarried. On admission there was distinct enlargement of the thyroid gland, with tremors of the hands and anæmia, but there was no exophthalmos. This was a mild case. The patient quickly improved under the milk treatment, only remaining in hospital 20 days. The pulse on admission was 104 and on leaving it was 80.

CASE 10.—The patient was a married woman, aged 29 years, and the mother of four children. On admission to hospital there were present marked exophthalmos, nervousness, with constant movement of some part of the body, headache and giddiness, enlargement of the thyroid, and a systolic murmur at the apex. Treatment with milk from a thyroidless goat brought about an improvement, but the patient left too soon, in order to look after her children. 15 months later she attended the out-patient department for a time with all the symptoms of the disease well marked.

CASE 11.—Treated in the country. The patient was a married woman, aged 32 years, who had suffered from the disease for four years. The symptoms were palpitation, a pulse-rate of 130, fulness of the throat, with pulsation of the thyroid gland, and slight exophthalmos. She was treated