A NOTE ON THE "AMMONIA COEFFICIENT" IN MENSTRUATION.

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FROM some observations made upon the composition of the urine of a normal subject, it would appear that there is a certain relation between the value of the "ammonia coefficient" and menstruation.

In the post and inter-menstrual periods the coefficient varies little from the inter-menstrual average, but during the seven days previous to the period—i.e., the pre-menstrual period—there is a marked rise. This rise appears to be due to a rise in (total) output of urinary ammonia rather than to a decrease in (total) output of urinary nitrogen (Charts I. and II.).

In this subject the usual pre-menstrual rise in body temperature was shown.

(Chart II.)

CHART I.

CHART II.

COLLOIDAL CALCIUM IN MALNUTRITION, CHRONIC SEPSIS, AND EMOTIONAL DISTURBANCE.

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IN previous papers^{1 2} I communicated the general results observed following the oral administration of calcium lactate in the treatment of excited and agitated mental states, and in 1920 I inquired of the Crookes Laboratories as to the possibility of the manufacture by them of a colloidal calcium preparation, in the hope that such a form would avoid both the production of the painful localities stated to follow the injection of the water-soluble salts due to protein precipitation,³ and the probable difficulty of insufficient absorption from the alimentary canal of the water-soluble calcium salts, which might explain the variation in results obtained in different cases. E. C. Dodds has recently suggested that defective absorption of lime salts, due to pancreatic disorder, may be a factor in the causation of rickets.⁴

On observing from the report of E. E. Prest⁵ that a colloidal preparation of calcium was then available and had been used by him with beneficial results in the treatment of tuberculosis, I commenced treating cases of mental disorder, some complicated by tuberculosis, with the colloidal preparation of calcium

oleate. Later, at my suggestion, Mr. J. F. Ward, B.Sc., chief chemist of the Crookes Laboratories, kindly prepared a colloidal form of calcium and lecithin; my object was to administer subcutaneously—thus avoiding the destructive digestive processes in the alimentary canal—a colloidal preparation which contained not only calcium, but a phosphorised lipid, in the hope that such a combination would be useful to meet the needs of nervous and other tissues exhausted by the stresses of bodily disease and mental disorder. Mr. Ward has kindly informed me that there is reason to believe the calcium lecithin is a definite chemical compound and not a mechanical mixture. It would also appear that lecithin is more easily prepared in a colloidal form in this manner than as lecithin alone.

Both preparations have been used, but it is too early to determine with any degree of certainty that the lecithin combination is to be preferred to the oleate. The toxicity of the lecithin preparation has been tested on rabbits. Seven and eleven cubic centimetres, injected intravenously, produced no noticeable effect. The salts of calcium have been advised for many diseased conditions, and a critical attitude is therefore necessary. Some observers have obtained clinical results which others have failed to confirm, yet recent experimental work continues to emphasise the importance of the function of calcium in the chemistry of nutrition and growth.⁶ Zilva, summarising the work of McCollum, Simmonds, Shipley, and Park⁷ writes: "It is only necessary to assume that the greater the deficiency of calcium the more

urgent the demand for fat-soluble vitamin, a not improbable hypothesis." For conditions of nutritional loss due to over-activity of the kinetic drive one regards the treatment by calcium as a metabolic one—it assists anabolism and possibly hinders excessive katabolism—and not in any way as in the nature of a drug medication.

Scope of the Treatment.

The treatment is not advocated as a panacea for all mental disorders; the following cases, some of which must be regarded as irrecoverable owing to long-standing disease, are submitted, not as triumphant cures, but in order to indicate the improvement which has followed a line of treatment, the further development of which may yield more fruitful results in these and other diseased states—if applied early enough. In each a definite alteration in the mental state has been observed associated with some bodily improvement. As to the permanency of improvement, time alone can testify. In some cases the treatment may be required merely to assist in building up a reserve which has fallen from various causes below normal—or perhaps never was normal, as in old rachitic cases; in others, the treatment may be a permanent necessity, thus leading to a consideration of the simplest dietetic measures capable of giving similar ameliorative results.

In connexion with this latter group the absorbability question arises. In some cases, although they have been treated with the water-soluble salt, improvement apparently does not ensue until the calcium preparation has been injected into the tissues. If calcium is absorbed as a soap, disturbance of the pancreatic secretion may account for diminished absorption from the alimentary canal, provided the food contains lime in a form suitable to convert into a soap.

Cases Showing Response to Treatment.

The following cases are submitted as examples of the response to the treatment. Other cases are also under treatment.

CASE 1.—Female, aged 33, Standard VI. on leaving school. Father and two paternal uncles and an aunt died of pulmonary tuberculosis. Patient has always been nervous, excitable, easily frightened, and quick-tempered; for last three years complained of a subjective sensation in the head, worse premenstrual, became depressed after death of father, head sensation intensified, had to leave work a year before admission, and three months before admission went off food, lost weight (had been 8 st.), wandered from home muttered to herself, always talking about her brains.

Condition on admission: Weight 5 st. 11 lb., facial pallor, poor peripheral circulation, skeletal development, nutrition and muscularity; heart limits and sounds normal, pulse 112, regular, wave weak. Wassermann reaction negative. Lungs normal. Anxious, agitated, depressed, impulsive, restless, resistive, disorientated. After long latent period replies, "I don't know," to simple questions; cannot name days of week or any simple article when shown her. Later became destructive, wet, and dirty, but took food well. Temperature subnormal.

Treatment: Cod-liver oil and calcium lactate produced no improvement, and later injections of colloidal calcium oleate were given 0.5 c.cm. daily, then 0.5 c.cm. twice daily for a week, then 1 c.cm. twice daily—later, when improvement was noted, reduced to 1 c.cm. daily. Cod-liver oil continued. During the second week the subnormal temperature began to oscillate above the line and she became less resistive and excitable, and during the third week became cleaner in habits and more quiescent. Soon pus was noted to be oozing from around some buried stumps.

The variation in weight and other matters were as follows: Height, 4 ft. 10 in. Weight on admission from home, June 6th, 1922, 5 st. 11 lb.; on the 28th, 5 st. 11 lb. Became more restless and agitated. Put on cod-liver oil, July 4th; on the 12th, put on calcium lactate. Restlessness not improved; she began to be wet and dirty on the 14th. Weight on the 16th, 5 st. 8½ lb. Colloidal calcium ½ c.cm. daily on the 16th, 1 c.cm. twice daily on the 30th. Weight then 5 st. 10½ lb. Ceased to be wet and dirty on August 9th. Weight on the 14th, 6 st. 5½ lb. Wrote a sensible letter to her mother on the 24th. 1 c.cm. daily on the 24th. Helps in ward, Sept. 9th. Weight then 7 st. 6½ lb. Old stumps extracted (patient insisting on no gas) on the 15th. Weight on the 24th, 7 st. 2½ lb.; on Oct. 1st, 7 st. 5 lb.

CASE 2.—Female, first attack. History: One brother, three sisters, alive and well. At school, patient only reached third standard, always being ill. At age of 7 had pneumonia and pleurisy for several months. At age of 12 phthisis became definite, involving right upper lobe and to a less extent the left. Temperature close on 100° F., rapid pulse; treated with tuberculin injections, the acute phenomena subsided and condition became chronic; since then patient has constantly had cough and sputum. Domiciliary treatment with cod-liver oil and emulsion brought up large quantities of sputum; patient ate little and lost weight. Menstruation regular up to November, 1921; often when unwell her sputum was streaked with blood. In December menstruation slight and thereafter ceased. Sudden onset of mental disturbance occurred beginning of November, 1921. She became "silly," heard and answered "voices"; slept poorly, continually talking all night, cried without apparent cause, saw doctors and nurses on curtains, threatened to commit suicide, memory poor, impulsive if thwarted, kicked and struck relatives, used obscene language, conversation irrational though when awake never ceased talking. Appetite later became capricious, at times refused food, at other times ravenous.

Condition on admission: Admitted April 13th, 1922, aged 22. Physical condition: Emaciated, bruises and abrasions, temperature 97°, pulse 78, respiration 26. Narrow high palate. Thyroid enlarged, complexion sallow. Cardiac limits normal. Peripheral circulation very poor, all toes of both feet very cyanosed. Lungs (difficult to examine) some hollowing above clavicles, no dullness, air entry fair, but breath sounds not heard so well at back of right apex as at the left. No adventitious sounds. Cough present. Much purulent sputum, in which after diligent search three tubercle bacilli were found. Abdomen slightly distended, tympanitic, no dullness, no mass. Feeble gait. Urine, nothing abnormal.

Mental condition: Changeable facial expression, at times worried and depressed, at other times apathetic. Attention very poor. No reply to questions. Occasionally spontaneously uses obscene language. Very self-absorbed, spends much of her time answering voices, generally in whispers. Cries for no apparent reason. Disorientated, negativistic, impulsive, violent when washed—kicked the nurse several times and slapped her face. Judgment and insight lost.

Course of case: Followed much same as described. A note on May 15th states that she "lies in bed most of day taking no interest in her surroundings, is at times noisy, resistive, and difficult to nurse, rarely replies to questions, continues to hear 'voices.' Subnormal temperature. Purulent sputum about 2½ oz. daily."

Treatment: Cod-liver oil and malt since two days after admission. May 19th, calcium lecithin subcutaneously; 1 c.cm. every third day until 28th, subsequently increased to 1½ c.cm. daily, later changed to one dose weekly. On August 9th 1 c.cm. twice daily. Up and dressed every day since treatment commenced.

Further course: Nutritional gain in this case has been interesting considering the long history and condition on admission. Relatives state they coaxed her with all varieties and amounts of food when at home, but she never was so well nourished as now.

The variations in weight, &c., were as follows: On admission, April 13th, height 5 feet, weight 5 st. 10½ lb. May 19th, calcium lecithin injections commenced; on the 27th, 6 st. 8½ lb. June 3rd, 7 st. 1 lb.; 18th, 7 st. 6½ lb.; 26th and 27th, menstruation (first since Christmas). Weight on 27th, 7 st. 11 lb.; July 11th, 8 st. 3 lb. On the 23rd and 24th, menstruation; 25th, weight 8 st. 6 lb.; August 8th, 8 st. 8 lb. On the 9th, 1 c.cm. calcium oleate twice daily. On the 15th and 16th, menstruation. On the 18th, three septic teeth extracted under gas. On the 22nd, weight 8 st. 9½ lb.; 31st, 8 st. 8 lb.; Sept. 5th, 8 st. 8½ lb.; 7th–9th, menstruation; 19th, weight 8 st. 8½ lb.; 24th, 8 st. 10 lb. Oct. 1st, 8 st. 9 lb.

Sputum diminished in amount almost immediately after commencement of injections, is often absent and when present rarely exceeds ½ oz.; never any blood-streaked sputum. The skin, formerly dry, became greasy. Peripheral circulation improved, cyanosis of toes passed from blue to purple, then more reddish. During the early part of these stages some cedema over the instep was noted, which later subsided.

Comment.—A case of chronic pulmonary tuberculosis in which the element of sepsis appeared to be predominant. The diminution in the amount and alteration in character of sputum, the improved hedonic tone and gain in weight appear to date from the commencement of injections of the colloidal calcium preparations. It is not suggested that the cod-liver oil had no part in these alterations, but the calcium apparently played an important rôle. That such a case of long-continued ill-health, from child-

hood, should show such nutritional gain is somewhat remarkable.

CASE 3.—Female, aged 40. A case of violent and destructive confusion, habits wet and dirty. Apyrexial as far as could be ascertained. Required tube feeding. Lost weight. Following injections the patient developed two cuticular whitlows of the fingers, these healed soon. She became quiescent, lucid, manageable, and took food well. Later a boil developed on the buttock and the temperature rose. The gums were noted to be oozing pus. The weights, &c., were as follows: On admission, August 31st, 1922, 9 st. 13 lb. On Sept. 11th, 8 st. 9½ lb.; 1 c.cm. twice daily. On the 17th, injections ceased. On the 22nd, 9 st. 4 lb.; 30th, 9 st. 4 lb.

CASE 4.—Female, aged 37. Epileptic. Admitted in a state of epileptic confusion, poorly nourished, and generally debilitated. On emerging from the epileptic confusion she developed a boil in flexure of right elbow, which appeared as though it would make slow healing progress. Three injections of colloidal calcium caused rapid healing. Gums noted to be oozing pus.

CASE 5.—Female, aged 44. Well-defined case of agitation, confusion, hallucinosis and negativism. Weight on admission, Oct. 29th, 1921, 6 st. 9 lb.; November, 7 st. 8 lb.; December, 6 st. 3 lb.; on the 27th put on cod-liver oil. January, 1922, weight 5 st. 13 lb.; February, 5 st. 12 lb.; March, 5 st. 6½ lb.; on the 22nd, 0.5 c.cm. colloidal oleate every five days. April, weight 7 st. 13 lb.; May, 8 st. 3 lb.; June, 8 st. 7 lb.; July, 8 st. 12 lb.; injections ceased. Sept. 26th, weight 8 st. 7 lb.

The gain in weight following the injection of the calcium oleate was paralleled by a diminution in the intensity of the emotional symptoms; patient fed herself and appetite was good. Shortly after the commencement of the injections she developed a large boil on the cheek and another on a buttock. These rapidly healed and were not connected with the sites of injection.

CASE 6.—Male, aged 32. Gonorrhoea in France, 1919, kept condition secret, treated himself and at home for gleet. Nocturnal emissions, urethral irritation, persistence of gleet, shame and financial fear-processes caused worry. Took up spiritualism, soon convinced he was a "medium," began to hear "voices," considered he was capable of being controlled, his dead father "charged him with electricity," told him not to eat, to get dismissal from his firm, to go to a lunatic asylum, &c. He lost weight, appetite, sleep, became pale, ill-nourished, fearful, timid, and hallucinated. On admission gleet treated locally with partial results, at times disappearing and then recurring.

Injections of colloidal calcium subcutaneously resulted in complete disappearance of gleet, nocturnal emissions, and urethral irritation. Patient soon became more cheerful, slept well every night, skin became greasy. Has been out on parole and is recommended for discharge.

Weight on admission, May 30th, 1922, 8 st.; June 28th, 8 st. 1 lb.; July 27th, 8 st. 5 lb.; injection of colloidal calcium. August 6th, weighed 8 st. 11 lb.; 20th, 9 st. 1 lb.; Sept. 3rd, 9 st. 3 lb.; 18th, 9 st. 3 lb. Diet the same throughout. No cod-liver oil.

CASE 7.—Male, aged 33. Imbecile with epilepsy. Treated in colony, but certified owing to unmanageable conduct consequent on persecutory ideation and post-epileptic confusion. Seizures had been 16 a month. Old rachitic development. Soon after admission and following influenza pulmonary tuberculosis diagnosed. Seizures ceased coincident with septic state. Rapidly lost weight, much sputum, numerous bacilli. On cod-liver oil and extra diet nevertheless became emaciated and peripheral circulation cyanosed. Skin dry. Radiogram shows fibrosis over whole left lung, obliterating cardiac outline, and upper lobe right lung.

Height, 5 ft. ½ in.; weight on admission, August, 1921, 7 st. 13 lb.; September, 7 st. 12 lb.; October, 8 st.; December, 6 st. 10 lb.; January, 1922, 6 st. 7 lb.; February, 6 st. 6 lb. Injections colloidal calcium oleate Feb. 7th at varying intervals. March, weight 7 st. 6 lb.; April, 8 st. 4 lb.; May, 8 st. 12 lb.; on the 30th, injections ceased. June, weight 8 st. 9½ lb.; July, 8 st. 13 lb.; August, 8 st. 13 lb. From the 9th to the 23rd, twice daily 1 c.cm. injections. Sept. 2nd, 9 st.; 17th, 8 st. 12 lb.

Sputum diminished in amount, some days absent, rarely exceeds 1 oz. per day; skin greasy, appetite good, sleeps well. During the treatment the epileptic fits were only occasional. Is cheerful and manageable.

Summarised Observations.

Chronic Sepsis.—It would appear that calcium plays a part in the re-excitation of the activities of the mobile defences of the body in conditions of chronic sepsis, and, after the removal of the cause of the chronic sepsis by the induced reaction, calcium

"dries up the exudates." In this direction one might describe the action of calcium as being an indicator of or pointer to the existence of a possibly unsuspected chronic sepsis which is inducing little or no active phagocytic reaction. Hamburger found that calcium increases the amoeboid movement of phagocytic leucocytes, while barium, strontium, and magnesium had no such effect.⁹ Many observers have noted the effect of calcium in reducing or inhibiting exudate formation, probably by increasing the consistency of the colloidal systems of the cell membranes which foreign protein reduces. Grove and Vines¹⁰ working with parathyroid extract observed a rise in the calcium index to be associated with an improvement in chronic septic conditions. They draw the conclusion that "the ionic calcium of the blood becomes deficient in cases where a chronic toxæmia is present. Such a deficiency may be regarded as one of the manifestations of the presence of a chronic toxic state, and is an indication that the septic focus should be carefully sought for and treated where possible." In the preceding cases this chronic sepsis was variously located, oral, pulmonary, urethral, &c. The relation of chronic sepsis to nervous exhaustion has been recently discussed.¹¹ The production of phagocytic reactions, as a mode of treatment in disturbed mental states, has been noted to follow injections of colloidal calcium, the results being comparable to the nucleic acid reactions.¹²

Circulatory.—Improved peripheral circulation is a characteristic response to treatment by calcium, and is shown in the colour of the face, lips, gums, &c. This improvement may similarly obtain in the alimentary tract leading to improved digestive processes—certainly the gain in appetite suggests this to be the case.

Skin.—Increased activity of the sebaceous glands—due to improved peripheral circulation—is a usual calcium response. The diminution of night sweats is a result associated with a lessening of chronic septic absorption. This response has been fully described by E. E. Prest.⁵

Emotional Tone.—Broderick¹³ quotes Prof. Meyer as having shown that the withdrawal of calcium from the body leads to an increased irritability of the sympathetic nervous system, glands controlled thereby secrete more freely and serous exudations into the tissues are more likely to occur, the administration of calcium does away with this hyper-irritability. Swale Vincent¹⁴ states that "in many respects there appears to be a true antagonistic action between adrenin and calcium chloride." It would appear from the preceding cases that the treatment has improved the hedonic tone and diminished the activity of the destructive emotional (fear) processes.

Nutrition.—Nutritional gain is a feature of these cases. The diminution of the drain on nutrition by chronic sepsis and the improved peripheral circulation assist an ascendancy of anabolic processes probably associated with a diminution of the katabolic proceeding from the hyperactivity of the sympathetic system—a reduction of the activity of the chronic kinetic drive.¹⁵

I have to thank my several colleagues for their observations on the cases and for carrying out the treatment.

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