While the evidence in these and many similar cases is incomplete—and it seems probable that the melanoma is a coincidence—yet it raises a suspicion that the development of melanoma may not always be limited to superficial cutaneous or subcutaneous structures. Very complete studies of such cases are required before they can be accepted as instances of melanoma of traumatic origin. They suggest a search for structures of the type of naevi capable of giving rise to melanoma, from the deep nerve fibres in subcutaneous tissues, lymph nodes, mucous membranes, and viscera.

SUMMARY.

1. The work of Soldan and of Masson has proved beyond a reasonable doubt that the naevus cell is derived from and belongs to the peripheral sensory nerve end-organs. Whether this cell is neuro-ectodermal or mesoblastic is uncertain, but an epidermal origin seems to be excluded.

2. The naevus cell in the nerve naevus produces chromatophores, and the two types of cells are more or less interchangeable. Yet the adult chromatophore seems to enjoy a more or less independent existence and function apart from naevus cells. Whether there are other sources of chromatophores is uncertain, but improbable.

3. In the epidermis there are slumbering unpigmented and wandering pigmented chromatophores and probably also other specialized cells similar to naevus cells belonging to the intradermal nerve-end apparatus. These latter cells may be the tactile corpuscles of Merkel-Ranvier. The conditions in the epidermis may therefore duplicate those found in the derma.

4. In the development of melanoma exactly the same processes seem to occur, and the same relations between naevus cells and chromatophores seem to be exhibited in the epidermis as in the nerve naevus of the derma and subcutaneous tissue.

5. The theory of the epithelial origin of the naevus cell and chromatophore has always been seriously questioned by most pathologists, and in the light of the new evidence has become less acceptable. All the appearances in the epidermis suggesting the active participation of epithelium in melanoma may be referred to the growth of specialized cells belonging to the nerve-end apparatus. Yet the histological evidence in this field is complex and inconclusive.

6. Melanoma has important relations to neurofibromatosis. This fact supports the view that the cells in melanoma are of neural origin, and it is difficult to reconcile with the epithelial theory.

REFERENCES.

- ¹ Dawson: *Edinburgh Med. Journ.*, 1925, xxxii, 501.
- ² Masson: *Ann. d'anat. path.*, 1926, iii, 417.
- ³ Soldan: *Arch. f. klin. Chir.*, 1899, lix, 261.
- ⁴ Ribbert: *Geschichte der Lehre*, 1897, xxi, 471.
- ⁵ Stockard: *Amer. Journ. Anat.*, 1915, xviii, 227.
- ⁶ Luna: *Arch. ital. di anat. e di embriol.*, 1920, xviii, 145.
- ⁷ Smith, D. T.: *Bull. Johns Hopkins Hosp.*, 1925, xxxvi, 185.

THE CLINICAL ASPECT OF DISTURBANCES OF THE PARATHYROID GLAND.*

BY

J. C. MEAKINS, LL.D.ED., M.D., F.R.C.P.ED.,
DIRECTOR, DEPARTMENT OF MEDICINE, MCGILL UNIVERSITY.

It may be stated briefly that the function of the parathyroid glands is the maintenance of the calcium content of the blood plasma at a definite level and the control of the calcium balance of the body. It would also appear that these glands have an important function in regulating the calcium metabolism of the fixed tissues, particularly the osseous system.

For some twenty-five years the absence or deficiency of the parathyroid function has been identified with a lowering of the blood plasma calcium and the associated occurrence of increased electrical excitability of the neuro-muscular system, producing the well-known clinical picture

of spasmodic tetany. But it has been only in comparatively recent years that clinical biochemical and pathological studies have enlarged our horizon and associated other abnormal conditions with disturbances of the parathyroid function. I think it may be taken that theoretically this function might be disturbed in one of three ways, as follows. There might be either: (1) a decrease in the normal function, (2) an increase in the normal function, or (3) a perversion of this function. As far as is known at the present time no such condition as would occur under the third category has been recognized as such. There are therefore left for consideration such conditions as might be identified under the first two sections. It might serve a useful purpose to consider at this time what conditions might be caused by a derangement of parathyroid function, and then determine if such an association is tenable on known facts.

On what basis or criterion may it be tentatively assumed that a disturbance of parathyroid function might exist? The function of the parathyroid has already been defined. There could therefore be no better tentative criterion than such as would indicate a disturbance of this normal function of calcium regulation. In the table are given the various disease conditions which are associated with a disturbance of the calcium metabolism. There has been included a record of the phosphorus content of the blood, as the calcium and phosphorus metabolism is so intimately associated that frequently it is impossible to interpret the significance of the first without a knowledge of the second. Of these six conditions there is definite knowledge that 1 and 6 ("parathyroid tetany" and osteitis fibrosa) are intimately connected with abnormal function of the parathyroid glands.

No.	Disease.	Blood Calcium.	Blood Phosphorus.	Calcium Balance.	Bony Changes.
1	"Parathyroid tetany"	Low	Normal or increased.	Positive	None.
2	Nephrosis	Low	Normal	Positive	None.
3	Steatorrhoea with megalocolon (sprue, coeliac disease)	Low	Normal	?	None.
4	Rickets—infantile	Low usually.	Low sometimes.	Relatively negative.	Present.
5	Osteomalacia	Decreased, normal, or increased.	Variable	Negative	Present.
6	Generalized osteitis fibrosa	High	Low	Negative	Present.

"Parathyroid tetany" is a condition which occurs subsequent to removal of the parathyroid glands or to their injury or degeneration from some other abnormal cause. It is characterized by increased mechanical or electrical excitability of the neuro-muscular system with muscular hypertonicity leading to painful spasmodic contractions of the muscles of the limbs, trunk, and certain internal muscles such as those of the larynx, diaphragm, bladder, and bowel. There is also a pronounced decrease of the calcium content of the blood, which is usually in proportion to the degree of muscular irritability. There is little or no change in the pH of the plasma. This syndrome may be either permanent or temporary. In the former case it may lead to a painful death unless corrected by the constant use of parathyroid extract. On the other hand, it may be but temporary, disappearing completely, or being latent with but mild and temporary manifestations. Tetany is a syndrome, however, which may occur with any condition where there is a low blood calcium, or even a normal blood calcium with a prolonged negative balance, provided the pH of the blood and its phosphorus content be not conspicuously lowered. Such conditions are to be found in steatorrhoea with megalocolon, infantile rickets, and osteomalacia, in all of which there is a low calcium content of the blood and either absolute or a relative negative calcium balance. But the mere occurrence of tetany does not necessarily imply that the pathological condition is primarily due to a deficiency of parathyroid function. In fact there is no evidence, either experimental or clinical, to warrant such an assumption, except such as may be concluded from the fact that both in rickets and in steatorrhoea with megalocolon, or what is sometimes

* A paper read in the Section of Bacteriology, Pathology, Physiology, and Biochemistry at the Annual Meeting of the British Medical Association, Winnipeg, 1930.

called "non-tropical sprue," the administration of parathyroid extract, with or without an abnormal increase of calcium in the diet, relieves the symptoms of tetany by raising the level of the blood calcium. There are, however, other means whereby this may be accomplished in rickets, although in non-tropical sprue the most efficient method of treatment is undoubtedly the use of parathyroid extract, not only in controlling the paroxysms of tetany, but also in ameliorating the intensity of the gastro-intestinal signs and symptoms. In fact, cases have been reported in which it would appear that a permanent cure had been effected by this means. In osteomalacia the effect of parathyroid therapy has not as yet been determined, but its close relationship to infantile rickets would appear to indicate that this form of therapy might be fruitful of beneficial results.

In the last five years a considerable interest has been aroused in the relationship of parathyroid tumours to diseases of the bone. In 1891 Recklinghausen described a generalized osteitis fibrosa, a disease which now bears his name. This pathological condition was more intensely studied by Askanazy in 1904. The first to draw attention to the association of parathyroid tumours and bone disease was Erdheim in 1907, in which connexion he described a parathyroid tumour associated with osteomalacia. Hoffheinz in 1925, in a series of 45 cases with parathyroid tumours either hyperplasia or adenoma, found 27 with diseases of the bone, 17 of which were classified as generalized osteitis fibrosa, 8 so-called osteomalacia, and 2 rickets. In the same year Mandl reported a similar case, and in 1927 Gold reported another. Mandl found a great increase in the calcium excretion, while Gold described an increase in the blood calcium. This subject has recently been reviewed by Hunter in his second Goulstonian Lecture. He here records that 14 carefully studied cases have been published up to date giving the clinical characteristics of hyperparathyroidism. These characteristics are briefly as follows. Whether the disease be due to a tumour, a hyperplasia of the parathyroids, or whether these glands be found normal histologically, the condition occurs twice as commonly in women as in men, and generally between the ages of 30 and 55. The patients complain of pains in the bones, and spontaneous fractures are common. Hypotonicity of the muscles is sometimes present, and radiograms show a greatly diminished density of the bone shadows, at times with evidence of cystic formation. There is an increased serum calcium, varying from 13 to 23 mg. per 100 c.cm., a reduction in the plasma phosphorus to between 1 and 2.7 mg., and in all cases there is an increase of the calcium output which may vary from a moderate degree to eight times the normal figure. It would appear, therefore, as if this condition were the opposite to that found in parathyroid tetany, except that there is the additional anatomical finding of pronounced bone destruction.

The superficial similarity of generalized osteitis fibrosa and osteomalacia has led to considerable confusion in the study of this subject. Hunter brings forward arguments which would seem conclusive to warrant the opinion that these are entirely different diseases. Furthermore, the general course and accessory clinical manifestations such as tetany, which occurs in osteomalacia, would make it much more likely that it is a disease more closely allied to infantile rickets than it is to the hyperparathyroid condition so intimately connected with generalized osteitis fibrosa.

Nephrosis is an interesting condition which would appear, in part at least, to be a disturbance of the permeability of the capillaries. This is manifested by an intense degree of albuminuria and generalized oedema. There are, in addition, two interesting disturbances of metabolism, one or other of which is usually present—namely, decreased basal oxygen consumption and/or a lowered blood calcium. The chief interest in this disease, which shows such pronounced renal factors, rests in the fact that a marked lowering of the blood calcium is present in a considerable number of cases, and that some of them respond most favourably to the use of parathyroid extract, not only in so far as the restitution of the blood calcium is concerned, but

also in promoting a rapid disappearance of the generalized anasarca. As has been said concerning numbers 3, 4, and 5 in the table, so it may be said in regard to this disease, that although there be a disturbance of the calcium metabolism which may be rectified by parathyroid extract, there is no concrete evidence that the disease is primarily due to a deficiency of the parathyroid function. It is interesting to note in this instance that, although the serum calcium is reduced, there is never in these cases any suggestion of neuro-muscular hyperexcitability or tetany. The explanation is probably to be found in the tendency in these cases of the reaction of the blood to be towards a decreased pH.

In conclusion, we may state that, clinically, two conditions are identifiable with disturbed parathyroid function, the first being parathyroid tetany due to a hypoparathyroidism characterized by a low serum calcium, a positive calcium balance, and great hypertonicity and excitability of the neuro-muscular system. On the contrary, there is generalized osteitis fibrosa, a condition of hyperparathyroidism in which there is a high serum calcium, a negative calcium balance, and a tendency to hypertonicity and hypo-excitability of the neuro-muscular system, a pronounced rarefaction of the bones, and a resorption of the corticalis and original spongiosa, this being in striking distinction to the cessation of calcification characteristic of osteomalacia and rickets.

ALBUMINURIA OF PREGNANCY AND ITS LATE RESULTS.*

BY

J. B. BANISTER, M.D., F.R.C.S.ED., F.R.C.P.,
CONSULTING OBSTETRIC PHYSICIAN, QUEEN CHARLOTTE'S HOSPITAL;
OBSTETRIC PHYSICIAN, CHARING CROSS HOSPITAL.

THE presence of albumin in the urine during pregnancy and labour may be fairly regarded as the commonest abnormality during these states. On reviewing some 6,000 cases in which there has been a complete routine examination, it is found that about 30 per cent. of all patients exhibit this abnormal urinary constituent. About seven-eighths of these only show albumin in the urine during the labour itself, and its presence may be regarded simply as the expression of severe muscular effort; therefore for clinical purposes this type of case may be disregarded. The remaining examples of the phenomenon mainly occur during pregnancy, and it has been my endeavour to ascertain as to what extent this abnormal condition influences the subsequent history of an individual.

It is necessary to say at the outset that when we try to formulate an answer to this question we soon become impressed by the futility of the effort. In the first place, we are struck by the absence of statistics bearing upon this point. It is only during the past few years that, at any rate in England, any attempt has been made to learn the subsequent history of patients who have suffered from this complication. As an example of the paucity of records, it is only necessary for me to say that, in answer to my requests for help, I have received from one hospital a statement that their records are in a condition of complete chaos, and from another that there are no records whatever bearing on this point. I think this sufficient to suggest that there is great need for more careful compilation of statistics in maternity institutions. The move for a unification of method in preparing clinical reports of maternity institutions should be productive of much good in this direction, especially if attention be focused on this class of case. It would, of course, be necessary to collate all details of the subsequent histories of albuminurics, both as regards the course of future pregnancy and the general health. Moreover, such investigations to be of material assistance should be extended over a period of at least five years from the date of the initial illness. We must also remember that the statistics

* Read in opening a discussion in the Section of Obstetrics and Gynaecology at the Annual Meeting of the British Medical Association, Winnipeg, 1930.