

but the use of thymus counteracts this effect. Kerley and Beebe,<sup>20</sup> in a case of retarded development, obtained enlargement of the sexual organs, with growth of hair on the pubis and axillæ. In rabbits and guinea-pigs, as shown by Soederlund and Backmann<sup>21</sup> the thymus attains its greatest weight, while spermatogenesis is being prepared, and it is only when the sexual organs are developed that atrophy of the gland begins. The bearing of this asserts itself when we recall that, as illustrated by Kossel's labors, one of the chief sources of material for the study of nucleins has been the *heads* of spermatozoa of various animals. Spermatogenesis continuing, under normal conditions, throughout life, we are brought to realize that, as is the case with the bones, the brain and nervous system, the genital system and, in fact, the body at large, the thymic lymphocytes are specific in the sense that they are *abnormally rich in nucleus-building materials*. Their rôle is to add to the body during its evolution to puberty, or later if need be, the excess of nucleins required for this purpose.

Summarized these facts tend to substantiate the following definition of the function of the thymus, similar in its general lines to one first submitted by myself in 1903, in the first edition of the present work (page 182), before most of the confirmatory data adduced herein had been recorded:—

*The function of the thymus is to supply, through the agency of its lymphocytes, the excess of phosphorus in organic combination which the body, particularly the osseous, nervous, and genital systems, requires during its development and growth, i.e., during infancy, childhood, and adolescence or later if need be.*

We must not lose sight of the fact that besides being supported by the bulk of available evidence from various branches of biological science, this interpretation of the function of the thymus accounts for the many different rôles that have been ascribed to this organ, and which have led Howell<sup>22</sup> to state that "practically nothing is known concerning these functions."

STIGMATA OF DEFICIENT ACTIVITY OF THE THYMUS.—The foregoing data indicate plainly, from both the experimental and

<sup>20</sup> Kerley and Beebe: Amer. Jour. Med. Sciences, Aug., 1912.

<sup>21</sup> Soederlund and Backmann: Archiv für mikroskopische Anatomie, 73, 1909.

<sup>22</sup> Howell: Textbook of Physiology, 5th ed., p. 855, 1913.

clinical aspects of the question, the specific symptoms or stigmata which indicate hypothyria. They are as follows:—

1. Deficient development of the osseous system and deformities suggesting rickets or osteomalacia, due to deficient assimilation of calcium owing to the deficiency of thymic nucleins which take part in the building up of calcium phosphate. Deficient stature.

2. Deficient mental development entailing various grades of idiocy due to the insufficient production of thymic nucleins to supply the neurons of the central nervous system, during its development.

3. A low relative lymphocyte count owing to the inadequate formation of thymocytes.

In cretinism, as we have seen, most of the stigmata could be traced to the thyroid. This applies as well, I have found, to the stigmata of deficiency of the thymus, another form of idiocy that is now to be considered.

#### MONGOLIAN IDIOCY.

Mongolian idiocy, as its name denotes, is characterized by a striking resemblance of the little patient, even at birth, to a Mongolian, particularly the Chinese. The slanting eyes and the epicanthal folds are particularly noticeable. The distinguishing features of these cases coincide suggestively with physiological, pathological, and clinical phenomena traced to the thymus under the foregoing heading. The stigmata of deficient bone growth, so distinct in thymectomized animals, are very marked. Defective bone development is shown by the low average stature, the adult patient seldom exceeding 4 feet in height, due mainly to the fact that the long bones, particularly of the legs, are abnormally short.

Hence also the flat chest; the squatty nasal bridge; the small, undeveloped ears; the stubby, square hand, with its short, tapering fingers, the little finger being usually incurved. The skull likewise shows participation in the morbid process, the anteroposterior diameter being almost equal to the transverse, a fact which causes the head to appear round. It is, in fact, abnormally small. Although the forehead usually bulges anteriorly, the plane of the face and that of the occiput tend to

parallelism. The circumferential measurements are invariably below normal, sometimes as much as two and one-half inches, the average being, in 26 cases studied by J. Muir,<sup>23</sup> one and one-third inches. This is an important practical feature, for the deficient skull development and the resulting reduction of brain capacity when the fontanelles are closed (which fortunately occurs late), tends to reduce the efficiency of therapeutic measures calculated to improve the mental status of the child.

Additional evidence as to defective bone nutrition is shown by the frequency of rickets, of which clear evidences are commonly discernible at birth. This applies also to other congenital defects such as club-foot, dislocation of the hips, etc. Palatal deformities are present in approximately two-thirds of the cases. The teeth, surrounded by hypertrophied gums, are irregular and undergo caries early, particularly in the low grades of the disease; they appear later, the second dentition being also delayed.

While these phenomena point clearly to the thymus as deficient, a similar condition of other ductless glands is suggested by stigmata which are deemed characteristic of deficient secretory activity of these organs. The thyroid seems to be one of these. Thus, while the skin may be dark and soft in some patients, in others it is dry and rough, as it is in cretins, even though allowance be made in these cases for the frequency of eczema—another proof of deficient catabolism. As in cretinism also, the tongue is thick and heavy, and protrudes more or less, but it is the seat of phenomena which some regard specific to Mongolian idiocy, though this has not been confirmed by my experience: transverse fissures and roughness; owing to greatly hypertrophied papillæ. The lips are usually thin, but they may also be thick and everted, though the body may not show evidences of myxedema. The tonsils and the nasopharyngeal glandular tissues are often found enlarged. Middle-ear disease is therefore common.

Subnormal temperature, with marked sensitiveness to cold and sluggish circulation, is another symptom commonly noted in cretinism, which also prevails in Mongolian idiocy, but the adrenals might likewise underlie these phenomena, owing to

<sup>23</sup> Muir: Archives of Pediatrics, March, 1903.

the marked influence on cardiovascular dynamism and on tissue oxidation. Indeed, the development of the entire musculature is considerably delayed, muscular power likewise. The ligaments are so loosely strung, in fact, as to permit the freest movements and contortions; the fingers, for example, may be bent backward upon the dorsum of the hand with the utmost ease. And yet all muscular movements are clumsy, being poorly co-ordinated, a feature which, in affecting the lingual musculature, contributes considerably to the retardation of speech. The ocular muscles are likewise involved, as shown by the frequency of strabismus and nystagmus in these patients. This applies also to the abdominal muscles, hernia, especially the umbilical form, being common. The abdomen itself is usually large and distended owing to relaxation of its musculature. Most striking is the frequency of cardiac atony, owing doubtless to the deficient supply of adrenal secretion.

We have seen that the nucleins supplied by the thymus and the secretions of the thyroid and adrenals took an active part in tissue metabolism and immunity. Since inadequate activity of these organs lowers the development and functional activity of the osseous, muscular and nervous systems, it should, therefore, also lower, in the light of my views, the defensive efficiency of the organism. That such is the case is shown in various ways. The Mongolian idiot is peculiarly subject to bacterial infections of the tissues most exposed to them,—the respiratory and intestinal tracts, the eyes, skin, etc. He is an easy prey, therefore, to tuberculosis, bronchopneumonia, pneumonia, influenza, and bacterial diseases of the intestinal canal, succumbing promptly under their effects. The twenty-fifth year is reached in but 9.4 per cent. according to Wiggandt.

Deficient metabolism initiated during uterine life accounts also for the idiocy. Along with the rest of the body, the intelligence lags behind, owing to deficient development of the organ of mind. The Mongolian infant is unusually well behaved, so good in fact as to elicit comment and favorable comparison with the average lusty baby. Small at birth, it develops about one-half as rapidly as the normal child, but its emotions are still slower in developing, in keeping with its powers of observation, which in some cases are virtually *nil* during the first year. It

will lie in bed placidly hours at a time, apparently quite contented. As some evidence of mental activity appears, it follows a common trend. The child is not morose or torpid, as is the case with cretins; it is amiable and even affectionate, and often shows a remarkable predilection for music, dancing, and mimicry, though sometimes mischievously so. The imitativeness is sometimes so marked as to suggest atavism to a Simian type, a perpetual grin and frontal creases in some cases lending additional color to such a possibility. Important in this connection, particularly with a view to prophylactic treatment, is that the Mongolian cast of features is often noticeable very soon after, if not at, birth.

ETIOLOGY AND PATHOGENESIS.—The etiology of Mongolian idiocy is clear in only one direction, viz., that no special hereditary vice or disease is communicated to the child, though here and there syphilis, gout, violent emotion, and other disorders usually incriminated may be found in the near or remote parentage. Analyzing this point closely, however, we are soon brought to realize that such disorders are not direct factors in the genesis of Mongolian idiocy, though ancestral neuroses or parental emotions may add some influence to that which seems seriously to impose itself—parental unbalance or procreative asthenia. Thus, the majority of these cases occur as offsprings of couples that have been prolific, the little Mongolian being the last brother or sister of many normal children. Leeper,<sup>24</sup> for example, in a study of 176 Mongolian idiots found that one-half of them were the last-born of large families, and that neuroses were common in their ancestral histories. Again, they will occur as the product of aged couples or where there is a marked disparity in ages. To use a homely comparison, the factory is worn out *in toto* or in part, and the product is below par. This is illustrated by the characteristic facies of the Mongolian child, which is that of all other patients of the same special class. They look alike to such a degree, in all countries, that they might be taken for closely related members of a single family.

Suggestive from the standpoint of etiology in its bearing upon the pathogenesis and treatment of Mongolism is the

<sup>24</sup> Leeper: Review of Neurology and Psychol., Jan., 1912.

fact that the Mongolian facies may not be due to mere hazard. A deeper search into its causes than has been accorded this phenomenon so far has led me to a pathological factor of a biochemical order quite in keeping with observed facts. Indeed, if our knowledge of the dietetics of the Mongolian branch of the human family is taken into account, many of the morbid phenomena so common among the poor of that race seem plainly ascribable to what hygienists have termed an "unbalanced diet." As is well known, lack of fresh fruits and vegetables, with a preponderance of salt meats, causes scurvy, and beriberi results from a monotonous diet, of which unpolished or unmilled rice is the main component. But we are aware also that rickets and marasmus are produced through lack of animal and an excess of starchy foods. Now, the Mongolian race, and particularly that part of it composing the "coolie" element in Asia, shows indubitably the subtle influence of centuries of unbalanced diet. The polished rice which constitutes their main diet fails to furnish them, owing to the absence of the pericarp sacrificed in the milling process, an adequate proportion of elements necessary to the physiologically perfect organism.

Prominent among these is phosphorus. The labors of Fraser and Stanton,<sup>25</sup> Aron,<sup>26</sup> Dehaan,<sup>27</sup> and others have shown that the outer layer of the rice, the pericarp, removed during the process of milling, is precisely that which contains soluble organic compounds rich in phosphorus. Conversely Bréaudat and Denier<sup>28</sup> found that the administration of this pericarp in the form of rice bran proved prophylactic against the development of beriberi; it has also been used as a cure for the disease by Heiser<sup>29</sup> and others. Briefly the deficiency of phosphorus in the form of phosphorus pentoxide in milled rice has been identified as the passive cause of beriberi. In individuals who, through a long line of forbears, have become habituated to its use, with perhaps a little fish, as main diet, as is the case with the bulk of rice-fed Asiatics, phenomena of another order become manifest, viz., those of deficient development of tissues in which phos-

<sup>25</sup> Fraser and Stanton: Lancet, Feb. 13, 1909.

<sup>26</sup> Aron: Philippine Jour. of Science, vol. v, p. 81, 1910.

<sup>27</sup> Dehaan: *Ibid.*, vol. v, p. 65, 1910.

<sup>28</sup> Bréaudat and Denier: Annales de l'Institut Pasteur, No. 2, Feb., 1911.

<sup>29</sup> Heiser: Jour. of the Am. Med. Assoc., vol. 11, p. 1237, 1911.

phorus is the preponderating agent, the *osseous and cerebro-spinal systems and also primarily of the thymus gland, which, through its nucleins, insures the development of these systems.*

Analyzing the pathogenesis of Mongolian idiocy from this standpoint, the kinship between the characteristic features of this disease and the attributes peculiar to rice-fed Mongolians is striking. The small size of the Japanese, Siamese, Tonkinese, Annamites, etc.; the slanting eyes, the narrow palpebral fissure and the epicanthus, especially marked in the Chinese, and the high cheek-bones are all peculiar to the Mongolian idiot. In the "yellow race," so called, the skin is pasty, yellowish, doughy, but smooth; the hair is straight; the nose is squatty, exposing the openings of the nostrils—all morphological characteristics of the Mongolian idiot. Another peculiarity of the latter is his predilection to infection and the deficient resistance shown to infectious diseases; we know how readily rice-fed Asiatic coolies acquire such diseases and succumb to them.

That the mentality is not necessarily dwarfed in the rice-fed Asiatic, as it is in the class of patients in question, is doubtless due to the adjustment of his nervous system to his deficient diet throughout the thousands of years he has employed it. But there is greater disparity between the lower and the higher classes of Asiatics in this particular than there is among the white races, owing doubtless to the greater variety of foods the upper classes utilize in Asia, which causes them to avoid unconsciously the harmful influences of a deficient intake of phosphorus. This probably accounts also for the fact that these upper classes seem, in most instances, not to resemble their ill-fed compatriots, the slanting eyes, squatty nose, etc., being less frequent among them.

**PATHOLOGY.**—In typical cases the brain and, in fact, the entire nervous system show no organic lesion other than imperfect cellular and general development, varying in degree with that of the mind. The osseous system is also the seat of nutritional lesions varying in degree with the severity of the case. Shuttleworth<sup>20</sup> has aptly referred to these characteristic examples of the disease as "unfinished children." The condition

<sup>20</sup> Shuttleworth: Quoted by McKee and Wells: "Practical Pediatrics," p. 622, 1914.

of the thymus has not been studied at autopsy in a sufficient number of clearly defined typical cases to warrant definite conclusions, but percussion and radiography suggest absence or atrophy in some and hypertrophy in other cases. The latter form probably represents an effort at compensation, what remains of the thymus undergoing compensative hyperplasia—precisely as does the thyroid in hypothyroid goiter. This is further suggested by the fact that puberty may be precocious in these cases.

**TREATMENT.**—Mongolian idiocy is generally considered about the most rebellious form of idiocy, judging from the literature of the subject. Comby,<sup>21</sup> for example, who urges rightly that it is more frequent than is believed, writes that the results of treatment have not been found encouraging. Some good, it is stated, may be effected by hygienic means, especially good and substantial nourishment and country air, while in mild cases satisfactory results may be obtained by appropriate education. Other authors have tried in turn: thymus, thyroid, the iodides, mercury, etc.—the whole gamut, in fact, of agents suggested by any possible etiological factor that the history of a given case might indicate,—but without avail.

Our efforts should tend, if better results are to be attained, in two directions: prophylactic and remedial.

As to prophylaxis, we should be constantly on the watch for Mongolism when the causative conditions—aged parents, marked discrepancy in the age of parents, prolific parents with the new infant as last offspring, strong mental emotion or affliction in the mother, syphilis and alcoholism—are features of the parental history. A very quiet and "good" baby, giving the parents so little trouble that they take pride in mentioning it, may be found on examination to show the facial characteristics of Mongolism. This diagnosis may then be further suggested by the presence of unusually loose joints, as shown by an abnormally wide range of motion, unusual helplessness and muscular asthenia, indicated by inability to hold up its head. Treatment of the infant through the nursing mother is then indicated. As will be shown in the second volume, organic products are transmitted to the child through the maternal milk. This may be

<sup>21</sup> Comby: Archives des Maladies des Enfants, April, 1906.

taken advantage of to modify the trend of the infant by supplying to its body those it needs for its development. Thymus gland 5 grains, thyroid gland 1 grain, and pituitary gland 1 grain, to replace adrenal gland advantageously, three times a day *during* meals, with a varied diet, and, as much as possible, out-of-door life may be given. Where maternal nursing or wet nursing cannot, for good reasons, be carried out, *direct nursing, using goats' milk* in some such way as that carried out in Italy, Egypt, South America, and other countries. If an intermediate electric milking apparatus is used, *cows' milk, which is well tolerated by infants when fresh from the udder*, can be used, the milk being pumped into the nursing bottle in quantities required, adjusted to the age of the infant. Organic preparations finely powdered, if dry, may be consequently dissolved in milk thus given.<sup>32</sup>

The older the patient when first seen, the smaller the chances of success. Yet in all *some* improvement is obtained, particularly as to growth and any cutaneous disorder that may be present. The doses mentioned for a nursing mother are suitable for a child of 5 years, but the dose of thymus may be increased gradually until, if need be, 15 grains (1 Gm.) are given three times daily. If the stigmata of either one of the three ductless glands involved in the morbid process appear more prominently than those of the other two, the dose of the organic preparation representing that gland should be increased.

Removal of enlarged tonsils and adenoids is always indicated. It enhances progress even as regards the mental condition in some instances. Syrup of the hypophosphites to promote the nutrition of the cerebrospinal system and iron to assist in building up the hemoglobin are of signal advantage. A substantial and varied diet is likewise indicated.

The mental status may be materially improved, but at the cost of much patience and perseverance, though the Mongolian idiot is usually a good worker. The imitative instinct of the little patient should be taken as starting point of a systematic education, selecting a special line of work, music for instance, to which the child is normally attracted, as main aim. He should not be deprived of the company of normal children, the

<sup>32</sup> Sajous: New York Medical Journal, page 1126, May 29, 1915.

excitement and fun involved and the out-of-door exercise doing much to enhance the functional activity of his ductless glands.

## THE ADRENALS IN IDIOCY.

One of the most striking features of *anencephaly*, a monstrosity (shown in the annexed illustration) characterized by absence of the brain and spinal cord, is the fact that the ad-



ANENCEPHALY (McKee and Wells).  
Samaritan Hospital.

renal cortex is so poorly if at all developed that the absence of this portion of the adrenals may be predicated with practical certainty. It may also be diminutive or absent in certain forms of idiocy. Thus, as Apert<sup>33</sup> states, "atrophy of the adrenal cortex is the rule in anencephaly. Since this was first observed by Morgagni it has been verified in hundreds of cases of anencephaly, pseudoencephaly, cyclopia, and even in a few instances of congenital hydrocephaly and microcephaly." When the cen-

<sup>33</sup> Apert: La Presse médicale, Oct. 28, 1911.

tral nervous system is very poorly developed, the adrenals may be no larger than a lentil. Indeed these organs may be totally absent, as in an anencephalic monster studied by the same author. That the adrenal cortex is mainly at fault in this condition is suggested by the fact that Elliott and Armour<sup>34</sup> witnessed a case in which the cortex was alone atrophic, the medulla of the adrenals and the paraganglia being normal. That this structure is of paramount importance in the development of the organ of mind is obvious. What are the relations between the two?

At the beginning of this chapter, I outlined the process of nutrition of the nerve-cell, including, of course, those of the cortex, as I interpret it. Referring the reader to pages 518, 915, and 946 of the present work for the physiological process involved, I may mention here that, in referring to the secretion of the adrenals, no distinction is made between the cortex and the medulla, it being inferred that, as far as prevailing knowledge will permit, the products of both structures unite in carrying on the functions of the organ.

As regards the relationship between the adrenals and idiocy, the fact that the secretion of these organs is converted into adrenoxidase in the lungs sustains, from my viewpoint, oxidation in the nerve-cell by reacting with its myelin, which contains phosphorus-laden nucleoproteid (supplied with nucleins by the thymus, during development, as we shall see presently), explains the morbid influence of absence or insufficiency of these organs on brain nutrition. While absence of the adrenals or any part of their mechanism inhibits this physiological process sufficiently to arrest the growth of the neurons, thus constituting anencephaly, deficient activity of the adrenals correspondingly restrains their growth, thus leaving the brain in a state of partial development, which in turn entails a correspondingly marked degree of idiocy.

As emphasized by Mierzejewski, the basis of all anatomical lesions in the brains of idiots is an inhibition of the nervous tissues; its origin must be sought either in embryonic life or in pathological lesions produced in early infancy which are the starting point of future anomalies of development. There is

<sup>34</sup> Elliott and Armour: Jour. of Path. and Bact., April, 1911.

no true arrest of development in a morphological and histological respect affecting the brain as a whole, judging from the average post-mortem evidence, but there is a true arrest of development of certain regions of the brain-tissue which may be recognized by the presence of neuroblasts. Some regions, in fact, seem to compensate for these defective areas, for idiots frequently show abnormal aptitudes in certain directions—music, arithmetic, extraordinary memory, etc.—which renders such “freaks” acquisitions for showmen.

The examination of brains of idiots proves that an abundance of gray matter and of nerve-cells may be accompanied by idiocy, but in such cases the system of connections between the convolutions is arrested in its development, and this want of paths of communication and the lack of harmony of development in the different nervous elements render the organ imperfect. In the central nervous system everything depends not on the quantity but on the quality of the elements, and their combinations with each other. The richness of the layer of neuroblasts in the hemispheres of idiots, which indicates true arrest of development of certain parts of the cerebral tissue, undoubtedly produces insufficiency of function of the nervous system and of the manifestations of the intellect. In favorable conditions of nutrition, however, *neuroblasts may become transformed into elements of a superior order*, that is to say, nerve-cells. In the layer of neuroblasts there are sometimes found polymorphic cells. Thus the neuroblasts, which for a certain time preserve their embryonic forms, and which are in a state of functional lethargy, may, under the influence of a propitious impulse, become transformed into nerve-cells and help in reinforcing the activity of the cerebral functions. It is perhaps in this way that are to be explained the cases of profound and apparently hopeless idiocy in which there sometimes occurs a marked improvement of the intellectual faculties. The idiot seems to wake from a long sleep while, nevertheless, retaining permanently the stamp of his mental infirmity, though in a less marked degree. It is this process of repair which organotherapy tends to promote.

What are the stigmata which enable us to recognize that the adrenals are functionally defective in these cases?