THE MONGOL: A NEW EXPLANATION.

(Second communication.)

By R. M. Clark, M.B.Edin.,
Medical Superintendent, Whittingham Mental Hospital.

Further consideration of the theory that mongolism is caused by a fœtal hyperthyroidism ceasing at birth shows that much can be added to support this view.

Such a theory is in accord with the negative findings in the mongol infant, of bacteriologists, biochemists and serologists, and would explain why the mongol idiot is not benefited by any therapeutic agent. In a previous communication, in endeavouring to show that many of the changes which occur in and around the eyes of the mongol may be explained by the simple mechanics of elastic eyeball protrusion in the fœtus, I applied an explanation which has been given before by various authorities to account for many of the signs and symptoms which occur in the same region in Graves' disease, most of which are associated with the names of the authorities who described them. It may be asked what other explanation can be given to account for the following conditions so frequently found in mongol idiots—strabismus, rolling movements of the eyes, liability to polar cataracts, small eyes, ill-fitting eyelids, thin eyelids, ptosis, epicanthus, thinness of bones lining the orbital cavities, high arched eyebrows, wrinkled forehead, and, if another explanation be forthcoming, can it also explain why so many of these tend to become less pronounced as age advances? It is to be expected that, in the mongol idiot, as in the subject of Graves' disease, all the eye signs will not always be present; some will be more marked than others, and just as in the exophthalmic adult, the eyes may remain prominent during a remission and give a staring effect, so in the mongol infant a similar condition may result.

Sir A. Keith has shown that the thyroid may by its influence on growth cause retraction of the nasion and so bring about the characteristic concave profile of the Mongolian; this retraction may, by restricting the blood-supply in this region, assist in accounting for the absence or ill-development of the nasal bones; but as Sir Arthur's explanation of the defective growth at the base of the

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

skull only applies to bones developed in cartilage, it will not, of itself, explain the defective nasal bones, for they develop in membrane.

Two other conditions—"speckled irides" and "rosy cheeks"—occur with such significant frequency in the Mongol idiot that any explanation of mongolism should account for these conditions; two corresponding conditions occur in Graves' disease, and with somewhat equal frequency, namely, speckling of the eyelids with pigment, and flushing and paling of the cheeks. It is suggested that these two mongol signs may be accounted for by conditions existing in the fœtus such as give rise to the corresponding signs in adult hyperthyroidism. It is known that in a developing vessel the size, both diameter of cavity and thickness of wall, is determined by the amount of blood which is pumped through it, and by the pressure at which it is pumped (19). Hyperthyroidism, too, may explain the abortions and still-births which occur with undue frequency in families containing mongols, for it is known that thyroid fed to pregnant bitches causes death of the fœtus and abortion.

Numerous ætiological factors have been advanced to account for mongolism, *e. g.*, syphilis, alcohol, tuberculosis, procreative insufficiency of either parent, exhaustion, etc. While these may have a causal relationship, they do not help much towards an understanding of the disease, and something more is required to explain the peculiar nature of the growth-changes which have given the name to the condition; further, most of these "causes" are as frequently absent as present, and are too common in the family histories of normal children to be of any causal significance; in fact, each or all of them might be the cause of the hyperthyroidism which is here postulated. It is in favour of an endocrine theory that mongolism is more common at the beginning or end of the child-bearing period, for endocrine imbalance is more likely to occur at ages when endocrine readjustment is taking place. Again, hyperthyroidism may be the cause of a defective ovum, or a defective ovum may be over-susceptible to thyroid.

The only theories which offer an explanation of mongolism, other than an endocrine theory, are those of Jansen and Van der Scheer (7 and 8) and of Crookshank (9). The hyperthyroid explanation of mongolism will be supported if it can be shown to embrace both these theories. Fœtal hyperthyroidism may be found to explain not only mongolism, but also achondroplasia, dysostosis cleidocranialis, and anencephaly, for these diseases have a number of characteristic features in common: They are (1) congenital, and are associated with (2) dwarfism, (3) absence or ill-development of the nasal bones, (4) arrest of growth at the base of the skull, (5) defective

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

differentiation of cartilage into bone, (6) undue frequency of congenital deficiencies, *e. g.*, congenital heart affections, cryptorchidism, hernia, hare-lip, club-foot, etc. Van der Scheer considers that ischæmia and physical compression caused by a defective amnion at the 6th and 7th week of fœtal life can account for the characteristic features of mongolism; Jansen is of the same opinion, but goes further and explains achondroplasia by these same conditions occurring at the 5th and 6th week of embryonic life, dysostosis cleido-cranialis by their occurrence at the 8th week, and anencephaly by compression and ischæmia occurring at the 3rd week. Both these authorities consider that increased amniotic pressure from a defective development and expansion of the amnion can cause a general ischæmia which accounts for general dwarfism—the ischæmia especially affects fast-growing cell-areas—in addition they postulate an excessive infolding of the fœtus occurring in its long (embryonic) axis, compressing the glabellar and nasal regions of the face on to the chest in such a way as to produce the characteristic skull, face and spine changes of achondroplasia and mongolism. In dysostosis cleido-cranialis the infolding is assumed to be in a transverse direction as well as in the embryonic axis, pressing the shoulders upwards, forwards and inwards, and thus compressing and narrowing the base of the skull and lower part of the face and preventing ossification of the clavicles. This theory involves the view that ischæmia and physical compression cause, by chance, remarkable resemblances between the mongol idiot and the racial Mongolian, or that the features of the racial Mongolian have been brought about in a similar manner by a defective amnion, and this is highly improbable. Jansen's view is that ischæmia of a few hours' duration can prevent the differentiation of cartilage into bone and so cause the absence or ill-development of the clavicles in dysostosis cleido-cranialis. This, however, is not in accordance with the fact that if a bone be removed from a child and periosteum grafted in its place a new bone results. Van der Scheer accounts for the dorso-lumbar kyphosis in the mongol idiot by an excessive infolding of the fœtus on its embryonic axis, and he asks, how else can this condition be accounted for? The answer is—by defective differentiation: kyphosis in acromegaly is not caused by excessive infolding. The flexed attitude of the fœtus *in utero* would appear to have little effect on the curves of the spinal column of the infant, for normal infants may be born with umbilical cords only an inch long; such cords must have been even shorter in early fœtal life, and must have prevented a flexed attitude of the fœtus *in utero*. Jansen accounts for the Mongolian appearance of the eyelids by supposing that there is dwarfism or absence of the nasal bones and that the

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

frontal bones compensate for the defect by sending processes in a medial and downward direction, the covering tissues following the direction of the underlying parts. To be effective these processes must extend below the inner canthus, and yet in many cases these processes cannot be demonstrated; moreover, if Jansen's explanation were correct, the condition would become worse as age advances, whereas on the contrary improvement takes place. Sir Arthur Keith (10) has said that it is impossible to give any satisfactory explanation of achondroplastic skulls by postulating abnormal development of the amnion or abnormal amniotic pressure. On the other hand he has recorded much that supports the theory here enunciated, for he holds that a reduction or alteration of the thyroid has been a factor in determining some of the racial characters of the Mongolian race which the idiot under discussion so much resembles. He has further recorded (2) that "two forms of dwarfism, achondroplasia and mongolism, must be regarded as due to a defect in the growth-regulating mechanism of the thyroid," and his description of how the cranial and facial features in achondroplasia and mongolism come about fits in well with a fœtal hyperthyroidic explanation, as the following extracts from his writings show. "Achondroplasia (10) is essentially a disease of ossification . . . stunting of the growth of the base of the skull occurs; the basi-occipital and basi-sphenoid are shortened, causing the contraction of the naso-pharyngeal space, the presphenoid ossification is also arrested, and the distance between the pituitary fossa and the foramen cæcum is reduced so that the nasion is drawn inwards and the forehead bulges owing to the brain's seeking compensatory space in this region; the essential feature is that the cartilage cells do not undergo the rapid division, columnar arrangement, vacuolation and hypertrophy which normally precedes ossification." "This passive resistance of the cartilage cells is probably due to absence of the secretion of one of the ductless glands." The same author, in his presidential address (11) on the differentiation of mankind into racial types, has recorded that racial characters may have been brought about by differences in the glandular balance, *e. g.*, "there is evidence of preponderance of pituitary in the gland-balance of the gorilla, Neanderthal man, and the European, as shown by the pronounced nasalization, eyebrow ridges, and extension of areas for muscular attachments; on the other hand, and contrasting with these features, there is evidence of preponderance of thyroid in the gland-balance of the orang and the racial Mongolian." "The influence of the thyroid on the development of the other systems of the body, particularly on the growth of the skull and skeleton, is equally profound . . . the arrest

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

of growth falls mainly on the basal part of the skull with the result that the root of the nose appears flattened and drawn backwards between the eyes . . . the face appears flattened and the forehead bulging." "The features just enumerated give the Mongolian face its characteristic aspect." In addition to the experimental work done on the action of thyroid on frog tadpoles, further light has been thrown on the nature of the influence of thyroid on development by the recent observations of Champy, Ebeling, Carrel and Torrey on the effect of thyroid on cell-division and differentiation. Torrey (12) has studied the effect of different concentrations of thyroxin on the fertilized eggs and embryos of *Echinometra* and *Phallusia*, and has shown that neither cleavage nor differentiation is accelerated, on the contrary both are retarded. He concluded, "Thyroxin depresses cell-division in such widely different organisms as *Paramecium*, *Echinometra* and *Phallusia*; it may well be that it is a depressant of cell-division throughout the animal kingdom . . . cell-cleavage and embryonic development are retarded." Differing then from Jansen and Van der Scheer, I think that the arrest of growth and the malformations in the skull and face in the mongol can be better explained by the depressing effect of hyperthyroidism on cell-cleavage, cell-differentiation and embryonic development. This action would also explain how those signs in the mongol which have led to its being called an unfinished child are brought about. In one lot of eggs, following fertilization, Torrey found many embryos wholly unable to free themselves from their membranes, their form became irregular and they failed to become normal larvæ. This abnormality only occurred twice in his experience, and on both occasions Torrey had reason to suspect a departure from the normal standard of thyroxin. This action might account for a defective amnion as is postulated by the Jansen—Van der Scheer theory.

Recent work on the toxæmias of pregnancy suggests the possibility of changes being brought about in the thyroid hormone, either in the placenta or uterus. In this connection it is unfortunate that while the incidence of mongol idiots in the case of twins is often carefully recorded (13), yet mention is seldom made of whether a common placenta or separate placentæ are present. Torrey further found that the retardation of cleavage and differentiation caused by thyroxin varied in degree with the concentration of thyroxin, and this fact may be correlated with the known facts that (1) a gland-balance with preponderance of pituitary can account for the racial characters of the European, the Neanderthal race and the gorilla, and a higher concentration of pituitary, as in acromegaly, converts the racial characters of the European into those of Neanderthal man;

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

(2) a gland-balance with preponderance of thyroid can account for the racial characters of the Mongolian and orang. It is suggested, then, that a higher concentration of thyroid, as in fœtal hyperthyroidism, may substitute for the racial characters of a European those of the Mongolian race, as occurs in the mongol idiot. In making the above analogy it is noted that acromegaly and mongolism are pathological conditions, while the racial characters of the European and Mongolian have been brought about by their respective gland-balances under favourable conditions of natural, environmental, and sexual selection. Crookshank (9) was the first to show the correlation between mongolian imbecility and thyroid gland-balance, and he also pointed out that the homologies between the mongol and the racial Mongolian might be explained by there being a similar gland-balance in each case, and with this view Sir Arthur Keith (10 and 11) seems to be in agreement. An explanation of mongolism by fœtal hyperthyroidism is in agreement with these views.

Since thyroid may bring about the skull and face features common to the mongol and Mongolian, it can also account for other homologies pointed out by Crookshank, *e.g.*, if stunting of the base of the skull occurs, the space beneath the tentorium cerebelli is restricted, and this by compression leads to relative inferiority of the cerebellum, pons and medulla; the occipital bone above the tentorium is also stunted and permits relatively less expansion of the brain than does the vault, the bones of which are developed in membrane. Development of the occipital lobes is therefore interfered with—they are small and allow the underlying cerebellum to be seen between them. Again, inferiority of the cerebellum, pons and medulla and hyperthyroidism may be correlated with muscular hypotonus and lax joint-ligaments and so account for the Buddha posture as compared with the non-Mongolian or negro posture. Other homologies pointed out by Crookshank could be explained in a similar way.

Crookshank eventually definitely rejected a gland-balance theory in favour of his descent theory and atavistic explanation of mongolism on the ground that the latter is necessary to explain all the facts, for he asks: "Now if mongolism in Western Europe is explicable on the grounds of (i) a special gland-balance similar to that of the racial Mongols, (ii) determining all the anatomical, physiological and psychological homologies that have been described, how, unless we adopt some theory of common descent, are we to explain the fact that, as can be definitely shown, Mongolian ancestry more or less remote is at least probable? How explain why mongolian imbecility and non-racial mongolism do not occur where, as amongst the negroes and Hindus, there is not any

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

probability of common descent from a Mongolian or orangoid phylum?"

Now, even if what these questions imply be admitted, this does not conflict with a fœtal hyperthyroidic theory of Mongolism, for it is reasonable to hold that it is not the homologies themselves but the cause of these homologies (a thyroid type of gland-balance) that is the unit character inherited, and if Keith is right the European has inherited a pituitary and the Mongolian a thyroid type of gland-balance. Nor is it difficult to suppose that hyperthyroidism must have a greater influence on a thyroid than on a pituitary type of gland-balance, and would therefore more likely provide the necessary preponderance of thyroid to bring about mongolism in a Mongolian, or a European with Mongolian ancestry, than in a pure European or a negro. Crookshank's difficulty in explaining the sporadic occurrence of occidental mongolism, of Mongoloid and orangoid children in Western Europe, then disappears, for the inheritance of a thyroid gland-balance in Europeans is obviously limited to those Europeans with a Mongolian ancestry, and the occurrence of fœtal hyperthyroidism is sporadic in the same way as Graves' disease is sporadic in Western Europe. Sir Arthur Keith has recorded facts about acromegaly which can be applied in the elucidation of the origin of mongolism. He refers to the skeleton of a Chinese giant who died in London some years ago—the subject of excessive action of the pituitary gland—the gland which he regards as playing a predominant part in shaping the face and bodily form of the European. The skeleton shows recognizable Chinese features, but the nasal region and supraorbital ridges of the face have assumed the more prominent European type. Have we not just the opposite of this taking place in mongolism?—excessive action of thyroid (a gland which Sir Arthur regards as playing a predominant part in shaping the face and skull of the Mongolian) on the fœtus causing dwarfism, and substituting Mongolian features for European. A comparison of the mongol and the acromegalic shows remarkable contrasts, especially in regard to those features which Sir Arthur has shown give us the key to acromegaly. He has shown that the key to the growth-changes in acromegaly is as follows: some secretion from the pituitary gland renders the osteoblasts hypersensitive to stimuli, *e. g.*, of pressure or tension, and growth results. Pressure on the alveoli during mastication causes increase in depth of the alveolar ridges, stimulated by the masseters, and the malars and zygomatic arches increase rapidly. True growth increases the base of the skull, giving better leverage and power for muscles of mastication and head movements. The area of origin of the temporal muscle is extended forwards, backwards

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

and upwards towards the sagittal suture, preceded by a wave of bone, and a strong sagittal bony arch is built up, beginning first in the frontal region and extending backwards to the external occipital protuberance, thus giving a strong fulcrum for muscles. The fronto-parietal suture is sometimes elevated. In the occipital region a wave of thickened and strengthened bone forms in front of the extending attachment of neck muscles. There is growth and thickening of the supraorbital regions and the superciliary ridges, the nose becomes long and prominent, the mastoid elongated, joint-ligaments all over the body are tightened. The skull resembles that of Neanderthal man in being low in proportion to length of base. Acromegaly occurs at the end of growth. Now the growth-changes in the mongol are in marked contrast to the above: the base of the skull is diminished, and the zygomatic arches, malars, superciliary ridges, mastoids and occipital bone are reduced and show a smoothing down of muscle attachment areas. The sagittal crest is weakened by defective closure of the fontanelles and sutures.

In the mongol, pressure on the alveoli is not responded to by the osteoblasts, for the alveolar ridges are diminished in depth (15), the growth of the teeth fails to stimulate the osteoblasts and is not responded to by an increase in the area of the palate, on the contrary the palate is small and narrow, the two latter features being in part responsible for the tongue's appearing too large for the mouth (it has been shown that the area of the palate has a relation to the nature and quantity of food masticated). The area of the palate in acromegaly is not increased for the reason that after adolescence the stimulus to its growth (growth of teeth) is absent. In contrast again to acromegaly pressure at joints fails to stimulate growth, lax ligaments and joints resulting. The contrasts between acromegaly and mongolism are such that one seems justified in assuming that if acromegaly is caused by endocrine imbalance so also is mongolism. It is as if the osteoblasts were rendered hypo-sensitive to pressure and tension stimuli in mongolism, and this might be accounted for by the retarding action *in utero* of thyroxin on cell-cleavage, differentiation and development, as is described by Torrey. An antagonism suggests itself between the pituitary hormone and the thyroid hormone, as if pituitary brought about large skull base with relatively large capacity for the muscle control centres, extension of muscle attachment areas, strengthened fulcrums for leverage for muscles, and small skull vault, whilst thyroid brought about the opposite with small skull base and large vault for expansion of the neopallium—as if thyroid advanced the evolution of mind, and pituitary of muscle.

Against Dr. Crookshank's theory of descent (16) the following

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press

facts have been adduced. In man the sphenoidal angle of Virchow diminishes from the time of birth, whereas in the ape it is always increasing, and a similar contrast is observed in the brain itself, for in the simian brain the convolutions of the middle lobes appear first and are completed before the convolutions of the frontal lobes appear, whilst in the human brain, on the contrary, the frontal convolutions appear before the convolutions of the middle lobe. From these data it has been argued that " man cannot be a descendant of a being whose development is in inverse order to his own." This deduction, however, does not seem justified, for since thyroid (and it has played a part in evolution) can bring about shortening of the base of the skull, and retraction of the nasion, it may also have altered the angle of Virchow, and, since it can bring about constriction of the base of the skull and expansion of the vault in the frontal region it may well bring about a reverse order of the development of the convolutions of the middle and frontal lobes of the brain. Support for my views confronted me recently quite by chance. On looking up a representation of mongolism in an Ethiopian infant (17), I found alongside it the picture of an anencephalic monster; the text states that " the fœtus was delivered at the beginning of the seventh month and was alive when half delivered . . . the eyes protruded about three-fourths of an inch." In one of the few clinical accounts in this country of the rare disease cleido-cranial dysostosis (18) many signs common to this disease and mongolism are mentioned and, in addition, from the text and the accompanying photograph, the following signs which it is held are caused by the mechanics of fœtal eyeball protrusion can be made out, *viz.*, high arched eyebrows, wrinkled forehead, prominent eyes, slight degree of double ptosis, and scanty eyebrows and eyelashes.

References.—(1) Berkeley, *Endocrine Medicine*, p. 75.—(2) Keith, Sir Arthur, *Lancet*, 1919, ii, p. 555.—(3) Sherlock, E. B., *The Feeble-minded*, p. 209.—(4) Shuttleworth, G. E., and Potts, W. A., *Mentally Deficient Children*, London, 1923.—(5) Stewart, R. M., *Proc. Roy. Soc. Med.*, January 12, 1926.—(6) Pighíni, G., *Policlin.*, 1925, xxxii, sez. med., pp. 334–337.—(7) Jansen, Murk, *Feebleness of Growth*, ii, p. 51.—(8) Van der Scheer, W. M., *Over Mongolismus*, 1918, and *Beitrage zue Kenntnis der Mongoloiden Missbildung*, 1927.—(9) Crookshank, F. G., *The Mongol in our Midst.*—(10) Keith, Sir Arthur, *Journ. Anat. and Physiol.*, 1913, xlvii, pp. 188–206.—(11) *Idem*, *Lancet*, September 27, 1919, pp. 553–556.—(12) Torrey, H. B., *Endocrinology*, 1928, xii, No. 1, pp. 65–80.—(13) Borovsky, M. P., *Journ. Amer. Med. Assoc.*, xc, No. 6, p. 459.—(14) Keith, Sir Arthur, *Medical Society's Transactions*, xxxiv, pp. 81–118.—(15) Greig, D. M., *Edin. Med. Journ.*, xxxiv, Nos. 5 and 6.—(16) Cock, Reg., *Brit. Med. Journ.*, 1927, January 15, p. 120.—(17) *Journ. Amer. Med. Assoc.*, lxxxiv, No. 14, p. 1041.—(18) *Met. Asylums Board Annual Report*, 1924–25, pp. 261–262.—(19) Haldane and Huxley, *Animal Biology*, p. 189.—(20) Clark, R. M., *Journ. Ment. Sci.*, April, 1928.

https://doi.org/10.1192/bjp.74.307.739 Published online by Cambridge University Press