(2) Roentgen therapy is never safe prior to surgery except in chiasmal and pituitary adenomas, where diagnosis can be certain. Edema increase is possible. Medulloblastoma is the only additional type favorably influenced.

(3) Angiomas call for no surgery. Radiation may help.

(4) Hemangioblastomas, commonly cystic, call for removal of nodule and cyst.

(5) Tumors of skull require extirpation.

Etiology:

The problem, like in all tumors, is still obscure. Gliomas do not metastasize, except those which involve the retina.

Heredity: Only in neurofibromata, cerebellar hemangioblastomas and hemiangiomas do we find familial incidence.

Embryonic rests may cause:

(a) Chordomas

(b) Cholesteatomas from squamous epithelial cells

(c) Craniopharyngiomas develop from epithelial rests near the pituitary gland

Trauma has been stressed but there is no proof that it causes brain tumor.

More recent researches:

Intraperitoneal injections of saline emulsions of gliomas of brain tissue into guinea pigs and intravenously in rabbits have been found to produce specific antibodies. (Weil and Liebert.) The same has been shown for glioblastomas.

Irradiation:

Medulloblastomas, ependymomas and astrocytomas have been shown to indicate radio sensitivity. (Frazier and Alpers.)

(Some illustrative cases were reported.)

Mr. Carlgren: I want to thank you, Dr. Michael.

Most of you have met the next speaker, Dr. Engberg, our Superintendent of the State School for Feeble-Minded. Dr. Engberg will speak to us on the subject, "Heredity and the Transmission of Hereditary Characteristics." Dr. Engberg.

HEREDITY AND THE TRANSMISSION OF HEREDITARY CHARACTERISTICS

E. J. Engberg, M.D.

By heredity is meant the transmission to individuals of certain physical or mental qualities in parents or more remote ancestors. Biological laws operate to make this possible.

An individual offspring results from the meeting of two "Gametes," the egg or female cell and the sperm or male cell, each carrying hereditary units which appear in the resulting offspring to determine the physical and mental characteristics except as they be influenced by good or bad environmental factors.

The term genotype is used to describe an individual's hereditary equipment which is the total sum of the hereditary units, called genes, received and this was determined irrevocably the moment the mature sperm and egg cells met. A personality, or individual, is, however, the product of two sets of forces, that of internal ones carried by the genes which he could not control and the external forces about him, or the environment which can be influenced to some degree.

It is important to know what conditions appearing to be inherited are truly so, as many earlier ideas were wrong. We now know that syphilis and tuberculosis are not inherited but are the results of direct infection. Congenital syphilis is the result of infection and not of inheritance even if the disease is evident at birth. The female type of plumage might readily be considered due to inheritance but is due instead to the effect of hormone activity as the removal of the ovaries result in the appearance of male plumage.

Environmental conditions may greatly influence inherited characteristics such as the harmful effects of x-ray radiations on eggs and larvae to be mentioned later and as demonstrated by the existence of certain plants which are either terrestrial or aquatic in form depending upon whether grown in dry or moist surroundings.

Harmful effects in the environment may impair the individual's efficiency and if sufficiently severe the result is called sickness while harmful effects resulting from internal inherited agencies result in defects. Medical investigations have tended to focus attention in the reaction of the individual to changes in the environment and not to recognize the important role played by inheritance in causing disabilities or freedom from them.

All living organisms consist of multitudes of minute microscopic cells consisting of two types of protoplasm or living matter, the cytoplasm and nucleus. All organisms with a sexual form of reproduction develop from a single cell called the zygote which results from the union of one mature sperm cell with a mature egg cell. The fertilized egg or zygote immediately divides in two cells and each of these into two others successively until the various parts of the completed offspring results. Each time before cell division occurs, the nucleus of the cell changes from a spherical form to a definite even number of rod like structures called the chromosomes and it is know that these carry the inheritance units. Before each cell division occurs, however, each chromosome splits lengthwise and one of each of the resulting pairs of chromosomes shift to opposite ends of the dividing cell. Because of this after cell division each resulting daughter cell has not only the same amount but the same qualities of chromosome material as had the parent cell. The number of chromosomes is constant for a given species, man having 48, the horse 60, etc.

The mature germ cells differ from all other body cells in that they have only half the number of chromosomes characteristic of the species. This is because instead of splitting lengthwise as do the chromosome pairs of other body cells, the two members of each chromosome pair separate and pass undivided to opposite ends of the dividing sex cell with the result that each of the two daughter germ cells has one of each pair of chromosomes. Thus applied to a species with six chromosomes, we have the egg cell and the sperm cell each with three chromosomes so that on fertilization six chromosomes are present in the zygote which starts again body cell growth with each cell having the characteristic number of chromosomes for the species and in each successive generation half of the chromosome material is that furnished by the father and the other half by the mother.

It is surprising that before the knowledge of fertilization, the fundamental law of inheritance was disclosed by experiments conducted and analyzed by Gregor Mendel, a monk and later abbot of a monastery in Brünn, Austria. His work was published in 1866, but no one grasped its tremendous importance and he died unknown in 1884. In 1900, however, three botanists working independently rediscovered Mendel's work and demonstrated that his basic principle of heredity was active through the entire plant and animal kingdom and in man. The first human case was reported in 1905 and was that of a hereditary shortening of fingers and toes. Shortly before this the late Dr. W. A. Sutton while still a medical student at Columbia University, demonstrated brilliantly the distribution of chromosomes providing an adequate explanation for the marvelous numerical consistency of the Mendel law of inheritance. Mendel worked with various types of garden peas, but it is easier to cite an experiment in animal life as described by Dr. Otto L. Mohr, Professor of Medicine, The Royal Frederiks University, Oslo, in his book, "Heredity and Disease." If we breed a pure bred black rabbit with a pure bred white, all the offspring in the first generation will be black. If we breed these black rabbits together, however, we obtain in the next generation both black and white rabbits and these in a fixed ratio of three black and one white. Furthermore when these white rabbits are bred together all their offspring are white, but the black if bred together act differently as one of them by imbreeding gives black only while the other two black by imbreeding give black and white offspring, and again in the ratio of three black and one white. Furthermore if these two last described black are bred with their white brothers or sisters, they yield equal numbers of white and black. The fundamental principle demonstrated in this experiment is that though the genes from the parents meet in the offspring, they do not blend to give some color other than black or white and when the germ cells of the offspring ripen, the parental genes will disjoin and segregate again without having had any modifying influence upon each other. The ratio in which the hereditary traits reappear in later generations are a direct result of the segregation of the corresponding genes.

The explanation for the color present in the various rabbits in the experiment is that in the pure black there is in each member of one particular chromosome pair a gene for black coloring while in the pure white there is in each member of the corresponding chromosome pair an antagonistic gene causing the lack of color or albino state. The mature germ cell of the hybrid black parents contains only one representative of the chromosome pairs formed in the process of forming daughter germ cells or one black gene in one and one white gene in the other. The resulting rabbits were all black which is explained by the black gene being dominant rendering the white or recessive gene inactive. The recessive gene can determine color only when one recessive unit in fertilization combines with another mature germ cell also carrying that particular recessive gene. Therefore, only pure white bred with pure white results constantly in white offspring, as then only recessive genes for color are present in each parent. The pure black rabbit has two genes for color dominant for black while hybrid blacks have one dominant and one recessive gene so in breeding them together there results the combination of genes: black—black 25%, black—white 50%, white—white 25%, or the first 25% carry the gene of color in two units or are called pure, homozygous, for this gene and therefore are colored; 50% carry one unit for black and one for white but black being dominant results in these offspring also being black; while 25% carry two units of white resulting in white offspring. Accordingly, an individual may carry a particular gene in double or single dose having received it from one or both parents. The germ cells, however, are genetically pure and will have a particular gene in single unit only. This discovery made by Mendel is one of the greatest ever made in biology.

The same rule applies with reference to the color of the eyes in man. Brown is dominant, blue is recessive and brown eyed or blue eyed individuals are born according to the Mendel formula for inheritance.

A simple dominant human case reported by Dr. Mohr, is that of finger shortening effecting the second phalanx of the second finger and toes only in which the dominant inheritance was traced back six generations to a Norwegian woman born in 1764. Of her ten living and seven stillborn children, the family record stated: "Every second child had, as she has herself, a shortened crooked forefinger with one joint only."

Consanguineous marriages favor the appearance in offspring of recessive traits and the defect may not have been apparent for several generations. The data on albinism is very extensive and illustrates this tendency well as extensive studies have been made showing consanguinity in the production of albinotic children in 50% of one series and 33% in another. Theoretically such a mating will result in 25% being albinotic but in human families with a small average number of children, many instances will show no effected children in spite of the theoretical three and one ratio. Thus among sixteen two children families, nine might have two normal children, six families one normal and one albinotic child, while in only one family both children will be expected to be albinotic.

Certain inheritance defects are sex linked. The best example of this in man is that of red-green blindness in which case vision is normal but the individual cannot distinguish between red and green. The observation has been made that they are bad strawberry pickers or railroad trainmen. We shall not discuss the scientific facts in the transmission of the defect but extensive studies show in the general population a frequency of 8% color blind men and 0.5% of color blind women. Hemophilia is another sex linked defect. No established cases of hemophilia in women are known. This has been explained by the assumption that if the gene for hemophilia is present in double dose as would be necessary in a female fetus, changes leading to death in utero result.

Hereditary defects in the organs of special sense are very striking. Hereditary deafness is due to recessive genes and even the deafness in later life due to otosclerosis seems in a number of cases to be best explained by the presence of inheritance of a recessive gene carrying this defect. Some of the most striking and most destructive inherited defects are those affecting the eye. Congenital night blindness is one of the best examples of single dominant inheritance. In one French family this defect has been present through ten generations. Of more serious eye lesions are certain cases of glaucoma which may be dominant or recessive sex-linked; a large number of hereditary cases of cataract, mostly dominant but of very different types and time of onset. Microphthalmia is a condition in which there is an undevelopment of the eye ball in which blindness may result and this may be associated with coloboma or "clift iris," and in some cases with cataract, opaque lens or lens luxation. In this condition a number of dominant and recessive inherited types have been observed.

It is generally agreed that about 50% of the feeble-minded are so because of inherited defect. Mongolism is not. Nor are cases due to damage to the brain by disease or accident before or at birth or in early infancy, or due to early endocrine disorders such as cretinism. The hereditary type of feeble-mindedness generally shows also defective physical development while the non-hereditary cases tend to show only mental retardation. Goddard concluded from his extensive studies that normal-mindedness as opposed to feeble-mindedness behaves like a dominant unit character and is transmitted in accordance with Mendel's law. When both parents are feeble-minded, there is a distinct tendency for all of their children to be feeble-minded. Infantile Amaurotic idiocy is due to the effect of sublethal recessive genes.

In our institution for the feeble-minded at Faribault some interesting studies have been made bearing out the observation that feeble-mindedness is hereditary. Dr. A. C. Rogers showed this in his very interesting publication, "Dwellers in the Vale of Siddem."

A Chart prepared for the Children's Bureau of the Board of Control in February, 1937, is very interesting, and shows the social burden resulting

from intermarriage between the families named as Callerquist and Larkeson. As a result of this union sixteen descendants have been in our institution. A study made by Miss Perkins of our Social Service Department of the B. Family shows the same result in social burden with the particularly interesting fact that as the result of the union of two feeble-minded, three were dead and mental state undetermined while the other four living children were inmates of our institution, as were the parents. Dr. A. R. T. Wylie kindly prepared a list for me to use in this presentation showing various instances of several members of the same family now in our institution. Of these families, in one instance we have eleven members and have had sixteen; another instance fourteen; five instances of four members still in institution and in one of these cases this consists of the father, mother and two children; another instance where we had four and still have two remaining, the other two having died; one instance of five of the same family; two instances of six of the same family; and one family of eight, including father, mother, two sons and four daughters.

The exact status of inheritance in the psychoses is not clear except that one considers, as do the English particularly, that the defect is one showing varying psycho-neurotic states such as psychoses, feeble-mindedness, epilepsy, migraine, etc. However, inheritance has been shown to be of a great deal of importance in the etiology of manic-depressive psychoses and schizophrenia. Of all the types of psychoses studied, the manic-depressive have shown the greatest frequency of hereditary taint and this predominately with psychoses and more frequently in the direct line.

In the field of neurology many hereditary diseases are found among which may be mentioned different hereditary types of muscular dystrophy, Fredreich's Ataxia, Huntington's Chorea, which is typically dominant; Wilson's disease in which the brain and liver are involved and which defect is of recessive type; and Idiopathic Epilepsy which stands on a definite hereditary recessive basis. Quincke's angio-neurotic edema results in sudden swelling of the skin or mucous membranes. In one study it showed as a clear cut dominant inheritance through five generations resulting fatally in fifteen of twenty-eight affected family members.

Diabetes mellitus appears to be inherited as a recessive defect while diabetes insipidus is a clear cut dominant defect when inherited and is due presumably to hereditary dysfunction of the pituitary gland.

Alkaptonuria, a condition in which the urine turns black on exposure to air, is considered a clear cut recessive defect.

The four blood groups in man are inherited. This fact is employed in tests for paternity which cannot be used to pick out a particular man as the father of a given child, but in one-third of the cases can exclude a particular man as being the father of the child. In two-thirds of the cases the blood group tests will not be of help.

The hereditary mechanism of tumor susceptibility has not been demonstrated with any degree of certainty. The somatic mutation theory has been advanced but at present is looked upon by careful students as a guess only.