THE INHERITANCE OF A DISEASE OF THE ACCESSORY NASAL CAVITIES.

By HANS GRÜNEBERG.

(*Department of Zoology, University College, London.*)

(With One Text-figure.)

In recent years, investigations concerning heredity in laryngo-oto-rhinology have been directed towards elucidating the causes of the many anatomical variations (2, 3, 4, 6, 7). In connection with this subject there have been few investigations dealing with the connection between pathological processes and their hereditary causes. As a matter of fact in otology the investigations of Bauer and Stein (2) have brought a considerable number of interesting results to light. As compared to this very little seems to be known about the importance of hereditary factors in the origin of inflammatory diseases of the accessory nasal cavities. The only reference to this, so far as I know, is to be found in the paper of Schwarz (7), who observed a pair of monozygotic twins, both of whom had an exactly similar diffuse polyposis. Therefore it may be justifiable to communicate here a pedigree of a family, which shows very clearly the importance of the genotype.

The family to be described is a Jewish one of Western Germany, which lives (or better now: lived) under favourable economic conditions. It consists of the offspring of two brothers, both having thirty-two descendants, one in three, the other in two generations. Only the first of these two lines shows the disease to be described below; the other one, which does not contain the disposition of this illness, is to be mentioned only a few times. The whole family is living in different towns and villages of the Rhineland and in Berlin.

The investigations were made by means of detailed query-sheets, and most of them were completed by a thorough verbal inquiry. The family being well educated, the author could expect to get reliable answers by using this method, inasmuch as the extremely chronic disease is known to the family as a hereditary evil and therefore is a matter of careful observation. The repeated recurrence of the illness forced most of these patients to take the advice of specialists. All these specialists were asked

in writing for all particulars about the course of the disease[1]. Thus several statements controlling each other were obtained concerning nearly all the patients. The few cases where it was difficult to get sufficient data are given below separately. The statements of the patients coincide so completely with those of the various specialists, that the foundation of this paper seems to be well established. It was impossible for the author to examine all the members of the family in person owing to the fact that they lived far apart; besides, such an examination would probably not have been very successful, as the investigator would have found at any given date only a part of the patients with actual symptoms, and thus have been dependent on the history of the patient as given by himself. Moreover, the original anatomical situation has mostly been modified more or less by various therapeutical measures. Thus in this case the chosen way of investigation seems to be the best one. It is hardly necessary to mention that beside the direct descendants also the relatives by marriage have been investigated.

The disease alluded to is a chronic relapsing inflammatory affection of the accessory nasal cavities, most of the cases being empyemas. Most of the persons suffer from inflammation of the frontal and maxillary sinuses and of the ethmoidal air cells, as shown in the extracts of the histories of the illnesses; some members of the family also suffer from an infection of the middle ear. Periods of moderate well-being alternate with times of acute exacerbations, which compelled the patients to keep to their beds or at least interfered with their business. Neither medical nor surgical measures finally eradicated the trouble; even the slightest rhinitis always causes relapses.

The history of the ancestor of the family who died in 1887 (I, 1 of the pedigree, Fig. 1) was given to me by his wife and by one of his sisters, who told me that he suffered for many years from violent frontal headaches, and a purulent discharge from his nose. These symptoms began in youth in spite of the fact that he was otherwise of a strong constitution. The whole history of the case leaves no doubt that there was a very chronic disease of one or more of the accessory nasal cavities lasting at least for 25–30 years.

There is no sign that any similar disease occurred among his ten brothers and sisters. On the contrary he appeared remarkable among the family by virtue of his illness. The offspring of one of his brothers,

[1] The author is indebted to all the practitioners and specialists for putting the data at his disposal. He has also to thank his colleague P. A. Gorer, who corrected the English manuscript of this paper.

the other line mentioned above, consisting of eleven children and twenty-one grandchildren, were examined by query-sheets. In this line there were no chronic diseases of this kind. However, one young man, who died at about 23 years of age, is said to have suffered from a "catarrh of the frontal cavity," and another individual is said to have had an acute otitis media. Some of the other sibs died unmarried, and about some others the author could get no information. Now follow short extracts of some of the histories of the illnesses, the figures of the pedigree serving as references.

II, 1. Shows for at least 25 years, during attacks of catarrhal diseases of the upper air passages, a chronic relapsing frontal sinusitis, on the

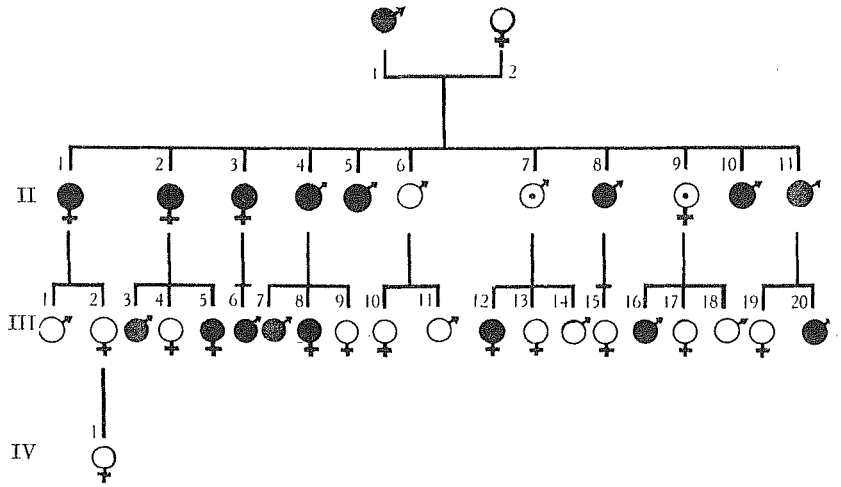

Fig. 1. Explanation in the text.

left more than on the right. No operations. Decrease in power of vision of the left eye. Disease first occurred at the age of 28 years.

II, 2. Chronic relapsing frontal sinusitis (? also maxillary) for 20 years, first occurring at the age of 35 years. In addition to conservative therapeutics the "vegetations of the nose and the upper jaw were removed." In 1929 she again had headaches and dull feeling in the ear. State: right side of the nose, in the middle nasal duct purulent secretion; left side of the nose, clear. Diagnosis: suppuration of the frontal cavity on the right, bilateral catarrh of the Eustachian tubes. No operations.

II, 3. In March, 1910, at the age of 34 years, an acute otitis media followed a rhinitis. In June, 1910, paracentesis on the right; in July,

1910, surgical opening of the mastoid process on the right; inflammation of the auditory canal and temporary defect of hearing on the right. Since the operation no further trouble of the ear, also cessation of the heavy periodical bleeding from the nose, from which the patient had suffered previously. Also empyema of the right frontal cavity; congenital narrowness of the right ductus nasofrontalis.

II, 4. Chronic otitis media on the left side for 35 years, first manifesting itself at the age of 17 years.

II, 5. For 25 years chronic relapsing suppuration of the frontal cavity and the ethmoidal cells, first occurring at the age of 26 years. No operations. In 1902 hemilateral acute otitis media. Paracentesis.

II, 6. At the age of 23 years "enlargement of the upper nasal duct." Except bleeding from the nose, no symptoms leading to surgical operation is known. There being no signs of any disease of the accessory nasal cavities, the patient is not marked as a carrier of the disposition in the pedigree.

II, 8. Purulent inflammation of the frontal and maxillary cavities, first appearing at the age of 27 years (1910). In 1911 radical operation of the maxillary cavities followed by complete healing; simultaneously emptying of the right frontal cavity. Half year later removal of a part of the nasal wall. In December, 1923, surgical opening of a big abscess within a frontal cell (sinus strikingly partitioned into smaller cavities); the temporal cells largely extending above the orbit were also opened (Killian's operation). Minor relapses when the patient catches a cold still occur.

II, 9. In 1903 probably "enlargement of the upper nasal duct." No further information by the physician is available now; for the rest see II, 6. In this case it must be assumed that the patient is a carrier of the disposition, one son (III, 16) showing the typical disease.

II, 10. Patient fell ill of suppuration of the maxillary and frontal cavities after having been frequently treated before for "adenoids," at the age of about 23 years (1908). In 1913 radical operation of the left maxillary cavity; no healing took place; troubles with maxillary and frontal cavities still existing with frequent relapses.

II, 11. Patient, who always had a strong disposition to rhinitis, fell ill in 1911 (24 years old) of purulent inflammation of the ethmoidal cells, frontal and maxillary cavities. In the beginning conservative therapeutics. In 1914 radical operation of all the three cavities in a field hospital; after the surgical treatment renewed violent trouble; oedema and redness of the region of the frontal cavity caused a second radical

operation in 1915; a tampon forgotten at the first operation was found as the cause of these troubles. Afterwards neuralgia occurred. Even now there still exist troubles of the accessory cavities in attacks of catarrhal diseases of the upper air passages; now conservative therapeutics.

In the case of the grandchildren some individuals are still so young that the development of a disease of the accessory nasal cavities is not to be expected as yet. It seems therefore possible, that here corrections may be necessary in the course of time[1].

III, 3. Inflammation of the maxillary cavity, first arisen at the age of 18 years (1927). State: right side of the nose, mucous membrane extremely red, hyperplasia of the lower turbinate bone; left side, strong hyperplasia of the lower turbinate bone, some mucus. Radiograph: both frontal cavities clear; right maxillary cavity obscured, left clear. Radical surgical operation of the right maxillary cavity; in the upper part of the cavity several cysts filled with viscous mucus, the mucous membrane itself having a muco-purulent secretion. Since the surgical operation practically without trouble. Besides this the patient states that before the surgical operation mentioned above, "adenoids" of the nose have been removed twice by means of a galvano-cautery knife.

III, 5. At the age of 11 years (1924) disease of the left maxillary cavity. At present no trouble. If she has a rhinitis, suppuration out of the nose, and headaches. Information from the specialist not to be obtained as he is now dead.

III, 6. Slight catarrh of the right frontal cavity and dull feeling in both ears, first occurring at the age of 16 years (1929). Since this time chronic relapses in all cases of even slight rhinitis. Conservative therapeutics.

III, 7. For three years chronic relapsing empyema of the left frontal cavity, caused by a congenital narrowness of the ductus nasofrontalis; disease first appeared at the age of 19 years. Conservative therapeutics (aspiration of the pus, radiant heat, menthol-paraffin-suprarenin-drops, etc.).

III, 8. Slight inflammation of the frontal cavity first occurred at the age of 17 years (October, 1931). Since this time, on the occurrence of

[1] The age of the members of the third generation without actual symptoms was at the time of investigation:

III, 1	22 years	III, 10	11 years	III, 15	18 years
2	34 „	11	6 „	17	22 „
4	22 „	13	16 „	18	14 „
9	10 „	14	12 „	19	15 „

The child IV, 1 was 9 years of age.

rhinitis, suppuration out of the nose and heavy headaches. Conservative therapeutics.

III, 12. Inflammation of the left frontal cavity and catarrh of the Eustachian tube occurred at the age of 16 years (1930). Since this time chronic trouble from the frontal cavity.

III, 16. Empyema of the ethmoidal cells and of the frontal and maxillary cavities first occurred at the age of 13 years (1921). At first conservative therapeutics; in the autumn of 1921 and 1923 surgical operations have been performed, each time one ductus nasofrontalis being enlarged. No further information about the surgical treatment of the ethmoidal cells and the maxillary cavity could be obtained, owing to the death of the surgeon. At present there is only a chronic suppuration out of the frontal cavities. Conservative therapeutics.

III, 20. Simple inflammation of the frontal cavity (first occurred at the age of 6 years in 1925). Since this time several relapses; no operations. The beginning of the disease at such an early age as 6 years is striking. In the rhinological literature however, several cases of frontal cavity diseases are described, the occurrence of which is equally early. Moreover the diagnosis seems to be confirmed by the typical symptoms found in the history of the illness as given by the patient and his parents, and by the information given by the treating specialist for children's diseases, a specialist for laryngo-oto-rhinology and finally by the further course of the illness.

IV, 1. Bilateral otitis media following influenza at the age of 5 years (1928). Paracentesis. Antrotomy. The connection of this case with the other ones seems doubtful; therefore it is not marked in the pedigree as having the disposition for the illness.

The pedigree shows at once that the disposition for the inflammatory diseases of the accessory nasal cavities is a hereditary one. Such an accumulation of chronic cases, which are not found so frequently amongst the population as a whole, is not to be explained otherwise. The unusual concentration of cases in the family is apparently not caused by external factors, such as the climate, for instance, as members of the family lived in several distant towns; moreover in the second generation all the brothers and sisters fell ill after leaving their native town. Another control is the second line; here the disease is missing though the members of this family are living in the same towns as those of the family who have the disposition to the illness.

The hereditary behaviour seems to correspond best to an irregular dominance. The character can be followed in most of the cases in an

unbroken line from the ancestor to the descendants. Only II, 7 and II, 9 have not been manifestly ill, the malady nevertheless reappears in their offspring; in the case of II, 9 it is true that a small surgical operation on the nose seems to have been performed, as mentioned above; symptoms definitely caused by an illness of the accessory cavities were never observed. In II, 7[1] there is no sign of any disease at all.

Therefore it seems, that those two cases (II, 7 and II, 9), where the regular dominance is not apparent, are not due to any inadequacy of the method used, but that there are real fluctuations in the manifestation of the gene.

Both sexes seem to be attacked in about the same manner. The eight sick persons of the second generation fell ill between their 17th and 35th years of age, on an average 27 years old. In the third generation, however, the first signs of these diseases to be found in the eight persons who have been attacked as yet appeared between their 6th and 19th years, on an average at 14·5 years. So we find apparently some sort of "anticipation," this phenomenon often described in human pedigrees, namely that the time onset of the illness becomes somewhat earlier in later generations.

SUMMARY.

A family is described in which the disposition to inflammatory diseases of the accessory cavities of the nose and ear is caused by an irregularly dominant gene.

REFERENCES.

(1) BAUER, J. (1923). *Vorlesungen über allgemeine Konstitutions- und Vererbungslehre.* Berlin: Julius Springer.

(2) BAUER, J. and STEIN, C. (1926). *Konstitutionspathologie in der Ohrenheilkunde.* Berlin: Julius Springer.

(3) BILANCIONI, G. (1927). *Ueber die morphologische und pathologische Familienerblichkeit bei Nasennebenhöhlenerkrankungen.* Beitrag zum Studium der Wichtigkeit des morphologischen Faktors in der Pathologie. Reference in *Zentralblatt für Hals-, Nasen- und Ohrenheilkunde,* **10**.

(4) LEICHER, H. (1928). *Vererbung anatomischer Variationen der Nase, ihrer Nebenhöhlen und des Gehörorganes.* München: J. F. Bergmann.

(5) —— (1928). *Innere Sekretion und Krankheiten des Ohres und der oberen Luft- und Speisewege.* Leipzig: Curt Kabitzsch.

[1] In the families of the wives and husbands of II, 4, II, 7 and II, 9 respectively only one case of an acute otitis media and one of a frontal sinusitis (both completely healed) could be found. No other maladies of this kind were detected in these families.

(6) SCHWARZ, M. (1928). "Die Formverhältnisse der Nasenscheidewand bei 84 Zwillingspaaren." *Archiv für Ohren-, Nasen- und Kehlkopfheilkunde*, **119**.
(7) —— (1930). "Die Bedeutung der Zwillingsforschung für die Hals-Nasen-Ohrenheilkunde." *Zeitschr. f. ind. Abst.- u. Vererbgsl.* **54**.
(8) SIEMENS, H. W. (1924). *Die Zwillingspathologie.* Berlin: Julius Springer.
(9) —— (1923). *Einführung in die allgemeine und spezielle Vererbungspathologie des Menschen.* Berlin: Julius Springer.