A little girl was once asked what an elephant has that no other animal possesses. She answered “Little elephants” and thereby showed how the fundamental truth of heredity is accepted as a commonplace (Hurst, 1935, p.29). Last year the Curriculum Committee (1935) of the British General Medical Council stated that the medical course should include instruction in the principles of genetics, the science of heredity, that is, that medical men and women should learn more about the profound truth voiced by the little girl. This recommendation is in line with the great increase of interest in human heredity shown in the medical literature of the last two decades. Another tendency shown in the same period is discontent with the overburdening of the medical course, and the question naturally arises: Why should the rather conservative G. M. C. Committee recognize the weight of the present burden and yet recommend adding to it?

Perhaps the best answer to that question is by examples from the writings of Doctor Madge T. Macklin (1932b), a medical graduate and teacher in the University of Western Ontario, who has striven to impress on medical workers the practical value of a knowledge of heredity. The first case is that of a man who had in vain consulted many physicians for an ulcerated corn on his foot. In conversation with a neurologist he mentioned the incurable corn. To the man’s amusement the neurologist asked for a radiograph of his lumbar spine and there found the cause—an occult spina bifida. The neurologist remarked later, “I would never have thought of its being a trophic condition due to spina bifida had it not been that I had treated that man’s two brothers for trophic lesions . . . due to occult spina bifida”.

Another man had vomited a large amount of blood. “Ordinarily the diagnosis would have centred about gastric ulcer, Banti’s disease, hepatic cirrhosis with oesophageal varices, etc. But the father gave the history that he too had suffered from frequent and severe haemorrhages but they were all from the nose. . . . To the physician who knew his hereditary diseases the diagnosis of telangiectasia (a tumour composed of capillaries and small arteries) was simple and an inspection of the father’s nasal mucous membrane with its spiderweb vessels confirmed it. The son was operated upon and the large telangiectatic spot was excised (from the stomach). . . . There was no recurrence of haemorrhages over a period of five years, at which time the report was made”. Again, a patient is being treated for anaemia, which does not appear to be of the pernicious type. If the physician knows that a brother of the patient had pernicious anaemia, also that the patient has achlorhydria, that achlorhydria and pernicious anaemia are related and that such achlorhydria is hereditary, then he will recognize that this patient is really exhibiting a very early stage of pernicious anaemia and can institute treatment. “The diabetic offers the
opportunity of investigating other members of the family, of determining the potential diabetic and of instituting proper treatment and cure before the diabetes becomes outspoken". "The appearance of a disease, not dependent on an infection or trauma, in one member of a pair of identical twins, offers a brilliant opportunity for instituting preventive measures with the other twin".

These examples illustrate the value of a knowledge of heredity in diagnosis, treatment and prevention, but the term "prevention of disease" has a wider meaning than exemplified here. The more enlightened members of the public are already asking their doctors such questions as: "Ought I to get married?" "If I get married ought I to have children?" "If I get married and have children what are the chances of their inheriting my disease or a disease that occurs in my family?" The public will not continue to tolerate the response given by the physician in the following incident, again quoted from Macklin (1932a). Two doctors investigated the family history of a patient suffering from peroneal atrophy, a progressive, incurable and disabling atrophy of the peroneal muscles, and found twenty-one persons affected with the disease in five generations. The patient "had suffered sufficiently both mentally and physically from the disease to desire its eradication" and gave to members of his family and to relatives reprints of the article written by the two doctors. "One of his cousins who herself was affected went to a physician and asked whether she should refrain from having children in view of the fact that analysis of her family tree showed that the chances were even that her children would be affected. The physician heaped vituperations upon the two doctors who had published such an article. . . . The offering of advice that would stop the propagation of the disease caused the medical man to arise in his wrath against anyone teaching the layman about himself, and the hereditary nature of his affliction". A physician who in such a case replied: "Heredity is all nonsense. Go ahead and have all the children you want" might be acting from charitable motives, but very soon if a doctor cannot or will not give reliable information and advice on such matters, the intelligent patient will go elsewhere. To enable practitioners to give such advice there was published two years ago a book called "The Chances of Morbid Inheritance" (Blacker, 1934). This book was obtained by the Dalhousie Medical Library in October, 1934, and has since been taken out by three persons and few have sought to consult it in the library. Other books on human heredity have been similarly neglected, in marked contrast to the interest displayed by students and clinicians towards books and periodicals dealing with other branches of medicine, both clinical and non-clinical. This contrast suggests that it would be unjust to criticize either students or graduates for a lack of interest in heredity and nothing that is written here is intended to imply such criticism. The roots of the fault lie in medical education, and at first sight they appear rather hard to find, when one recalls the little girl's "baby elephants" or Aristotle's statement that "men are called healthy in virtue of the inborn capacity of easy
resistance to those unhealthy influences that may ordinarily arise’’ (Garrod, 1927), and especially when one recalls how general practitioners have for centuries recognized that certain families are particularly prone to certain diseases.

The reason why the science of heredity has not yet reached its proper place in medical practice and teaching is to be found partly in the history of genetics itself and partly in the concurrent progress of medical science. Four salient dates in the history of genetics are (Crew, 1925)—

1866: Foundation of modern knowledge and theory of inheritance—Mendel’s article on experimental breeding of peas (size, pod-colour, etc.). This article passed unheeded until 1900.

1902: William Sutton, a young student in the laboratory of E. B. Wilson (Columbia University) suggested the material basis of Mendelism—the germ-cells.

1909-10: T. H. Morgan (Columbia University) first used Drosophila, a fruit-fly—correlation between chromosomes and the results of breeding experiments, leading to a drawing of chromosome maps showing what position the genes (factors responsible for the hereditary transmission of qualities) must occupy in order to account for the results of breeding experiments. Morgan’s work yielded a great amount of information regarding the general working of heredity, applicable to almost all species of plants and animals. (It may be noted in passing that the gene has until recently been something postulated, just as an electron is something postulated, but within the last year or so there have been indications that certain visible parts of the chromosome can be shown to correspond to genes.)

The most fundamental genetic investigations have thus been carried on in a field remote from human medicine, and necessarily so, because they had to be done with few and easily visible chromosomes (four pairs in the ordinary body-cells of Drosophila) and on animals that would produce generation after generation in a short time. In mammals chromosome work is much more difficult, but extensive breeding experiments have been carried on and genetics is now recognized by governments and private firms as perhaps the most important aspect of research in dairy-farming and agriculture. In the human species neither long-term breeding experiments nor extensive chromosome analysis is possible and one must depend on careful observation of Nature’s experiments. Much information has been gathered, but little of it comes into the medical course, partly because the experimental geneticist and the medical worker (practitioner, research-worker or teacher) commonly speak, as it were, different languages, and appear to be dealing with unconnected subjects. Lack of interest in genetics can therefore be easily understood in the medical graduates of some years ago, but the student of today still labours under a disadvantage. There is less obvious connection between Drosophila chromosomes and human disease than there is between the skull of a cat and the skull of a man, and genetics is apt to suffer more than other branches in the
general discarding of knowledge that follows the passing of the pre-medical biology examination.*

Those teachers who try to capture students’ interest by examples from human diseases are handicapped by the complexity of human heredity and by the students’ lack of acquaintance with the disease referred to.

This gap between genetics and medical teaching is, of course, being bridged at many places, but, apart from the difficulties mentioned, there is an important reason why the bridges were not built earlier, and made larger and more numerous, namely the direction in which medicine progressed in the nineteenth and early twentieth centuries. The great success of bacteriology, of surgery and public health measures naturally inclined medical men to think that the seeds (bacteria) were more important than the soil (the patient’s constitution) and that environmental changes (the actions of the doctor or public health legislator) were more important than the inherited reactions of the patient. There is now however a tendency to change the outlook and this tendency should be strengthened by presenting to students and practitioners the information now available on inherited tendencies to disease and to immunity, and by showing how this information can be increased by practitioners themselves. In trying to determine how and where such information should be presented it will be noted that pre-clinical instructors are in general either scientists with some training in non-medical genetics or medical men with little or no regular training in genetics at all. To the latter class belongs the present writer, but, like others of his generation, he has acquired for himself an acquaintance with genetics—an understanding of its principles and an appreciation of its bearing on medicine. What has been thus acquired by personal effort, any reader of these pages can acquire nowadays even more easily. He need not be entirely ignorant of genetics, in spite of the fact that a place in the curriculum is, at many schools, not yet found for a study of the subject. In the pre-clinical field the most appropriate place to introduce genetic discussion would be the anatomy course, because human heredity is a morphological and observational rather than an experimental science. Special difficulties arise, however, first because little or nothing is known about the heredity of most of the normal anatomical features, such as arterial patterns, and secondly, where more is known, for example regarding bodily dimensions, eye and hair colour, the heredity mechanism is complicated. Again, anatomical abnormalities, such as the occurrence of extra fingers, while simpler to follow, are apt to give the student the impression that heredity deals with oddities and rarities.

The main object of this paper is not, however, to discuss ways and means, but to stimulate interest, and for that purpose further reasons can be mentioned why medical men and women should pay attention to genetics. Thus, a knowledge of its principles is now necessary if a practi-

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*If this article should fall into the hands of a pre-medical student, he or she should take the advice to absorb and retain as much knowledge of non-medical genetics as possible. One cannot understand medical genetics without such knowledge.
tioner is to have a critical understanding of articles that appear in the medical and non-medical press. The medical man is expected to have competent views on such questions as sterilization of the mentally defective, and he should certainly be aware of the effect that modern medical treatment is likely to have on succeeding generations, because such treatment of hereditary disease, for example the use of insulin in diabetes, tends to preserve the victims of the disease longer than formerly and give them a better chance of transmitting it to the next generation. Moreover, it is the general practitioner, rather than the hospital physician or laboratory worker, that is in a position to increase and correct the present knowledge of human heredity. Even for diseases in which the hereditary mechanism seems well known, new records are valuable. The records must, of course, be accurate, and persons in the family that fail to manifest the disease are as important as those that do manifest it. The records must be as complete as possible and must be intelligible to other people.

"The Chances of Morbid Inheritance" contains a schedule with standard symbols and instructions regarding the filling-in of pedigrees, and the instructions can be understood by an intelligent non-medical man, say the patient himself. Copies of the schedule can be obtained (price 6d.) from the Secretary of the Eugenics Society, 69 Eccleston Square, London, S. W. 1, England, and "if any person desires further information on how to fill in his pedigree or if any medical man wishes to have an opinion upon a given pedigree, these will be furnished on application to the Secretary of the Eugenics Society" (Blacker, 1934, p. 439).

In its original form the present paper took up the consideration of a few conditions such as varicose veins, haemophilia (bleeder's disease) and albinism (defect in eyeball pigment), and showed first how, by a simple juggling of chromosome diagrams, with the aid of fundamental principles, it is possible to prophesy the ratios of normal and diseased in the offspring when the genetic constitution of the parents is known. Secondly it was shown that clinical knowledge was necessary to appreciate how these expected Mendelian ratios might be modified, and thirdly it was pointed out how careful consideration of a few examples reveals many of the things that have always to be borne in mind in dealing with human genetics. Lack of space, however, confines the discussion to more general questions, and prominent in these is naturally the question: How does one determine that a hereditary element is present in a disease? The most obvious method is to compare the frequency with which the disease occurs in a family where one sufferer is found, with the frequency of the disease in the population as a whole, and the following quotation is apposite: "Since about 10% of all persons who survive childhood ultimately die of malignant tumours, among which cancer of the stomach is the commonest, we should naturally expect to find, in accordance with the doctrine of chances, an occasional run of cases in particular families. But when there is such a run of cases in a single family as is shown in one after another of the genealogical trees published here, we can no longer doubt that heredity must play its part in the origination of cancer" (Baur, Fischer
and Lenz, 1931, pp. 394-5). (It should be noted, of course, that this quotation does not contain the whole argument, which must involve the elimination of environmental factors, such as infection.) The second method of tracing heredity is more precise and penetrating—the examination of the sufferer's family-tree, to show whether the sequence of cases fits a Mendelian scheme and particularly whether it fits that scheme more closely than can be accounted for by chance.

For those who may have been stimulated to increase their knowledge of genetics the following advices and cautions, taken at random and dogmatically expressed, may be of use:

Be sure to understand the meanings of terms, e.g. be careful to distinguish between "congenital" (literally "born with") and "hereditary". Congenital syphilis is an infection transmitted from the mother's circulation, not via the germ-cells. Congenital hernia, if appearing after birth, would be more accurately described as hernia due to congenital weakness. Such weakness may, of course, be hereditary, i.e. transmitted by the germ-cells, but a congenital weakness is not necessarily hereditary. A hereditary disease may not appear for years, e.g. high blood pressure.

Be sure to get the most up-to-date information on human genetics. Do not be content with a book that is ten years old.

Do not distrust genetic laws because disease is absent when the Mendelian scheme leads you to expect it to be present. Environmental factors may also be necessary. Vein weakness may be present, but varicose veins may appear only under occupational strain, e.g. pregnancy.

Be sure of your diagnosis. All people who bleed exceedingly are not haemophiliacs. If you are not absolutely sure about other cases in the family, make this clear in your records.

Note than an expected Mendelian ratio may not be found in certain diseases because the disease is fatal at an early date. Most haemophiliacs die before begetting offspring.

Remember that in human heredity a disease may follow one Mendelian plan in one family and another plan in another family. Find out if this is apt to happen, e.g. from Blacker (1934) or Baur, Fischer and Lenz (1931), and, if so, draw your conclusions from your patient's own pedigree or submit it to an expert.

Do not distrust genetics because it involves mathematical tests. These tests are called statistical and are therefore looked at askance by those who think statistics is a mass of data, often inaccurate, collected by insurance companies and other organizations. Mathematics as a whole is distrusted by those who forget that it is the basis of all modern mechanical inventions from the X-ray outfit to the George Washington Memorial Bridge.

Do not think that because a disease is to be expected in children in the ratio of, say three diseased to one normal, therefore a family of four will present this ratio. The ratio represents the average that should be expected if an extremely large number of families could be investigated. If the expected ratio is three diseased to one normal, and ten thousand
families, each of four children, could be investigated, there should be expected the following:—

<table>
<thead>
<tr>
<th>Diseased</th>
<th>Normal</th>
<th>No. of Families</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>0</td>
<td>3164</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>4219</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2109</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>469</td>
</tr>
<tr>
<td>0</td>
<td>4</td>
<td>39</td>
</tr>
</tbody>
</table>

Do not be hopeless because a disease is hereditary. There are several important hereditary factors in tuberculosis, but recognition of this should cause us, not to close our sanatoria, but rather to redouble our efforts to protect people with a hereditary predisposition.

Do not think of human heredity solely in terms of disease. Strength is inherited just as much as weakness.

Do not become a "heredity crank".

Finally, a few comments on books are included:

Gates (1929): A valuable introduction and a great deal of information on all aspects of human heredity.

Hurst (1935): Short and interesting introduction; shows a tendency towards speculation.

Blacker (1934): Contains a short very practical introduction to genetic principles, and each subsequent section supplies information in a particular field in the form in which the practitioner is most apt to need it.

Baur, Fischer and Lenz (1931): A standard work of reference, but very readable.

Clendening (1930): Not a book on genetics, but discusses heredity and many other medical topics in a very interesting manner. Provides a sane reaction to the depressing fatalism created by knowledge of heredity.

LITERATURE


