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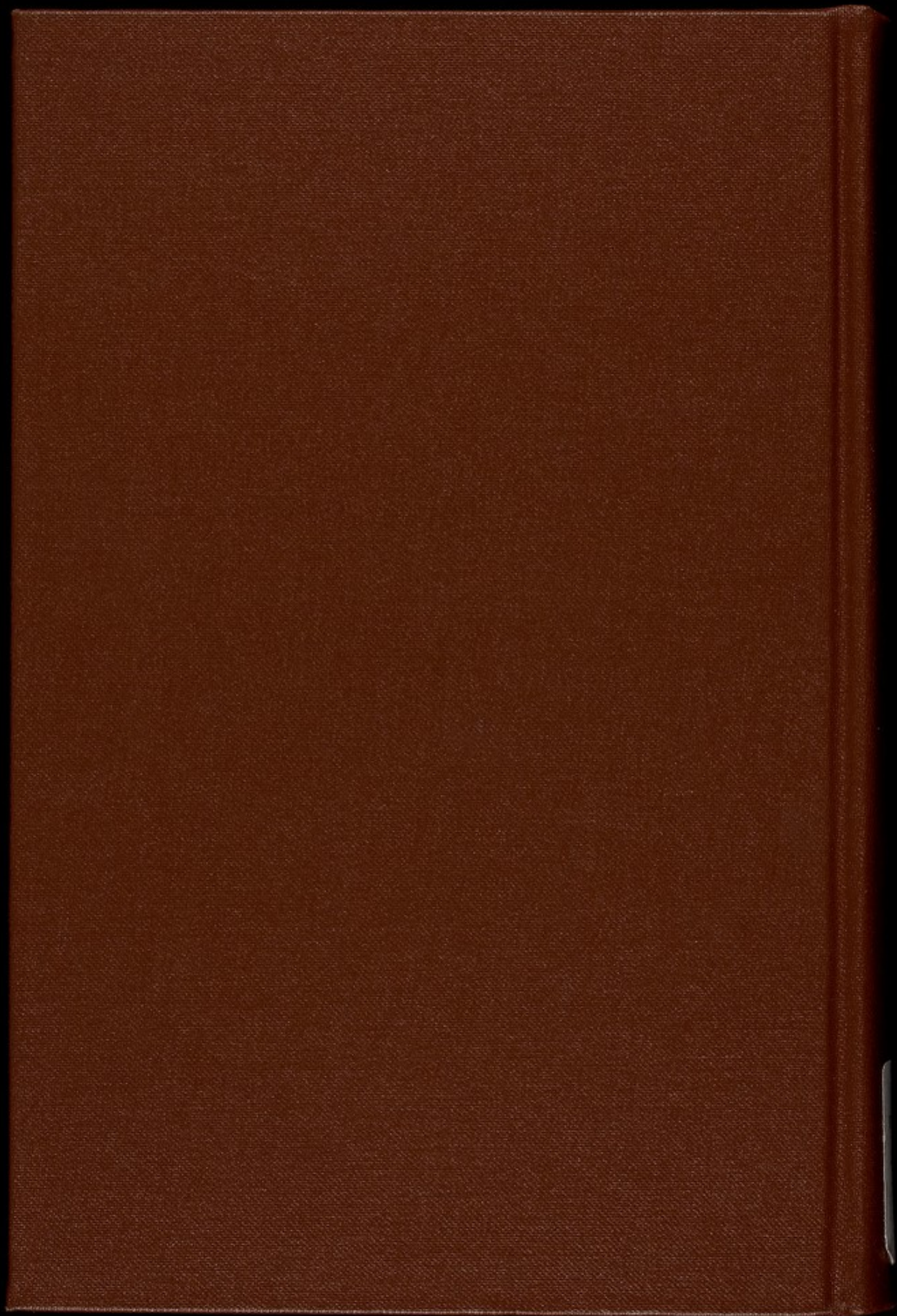
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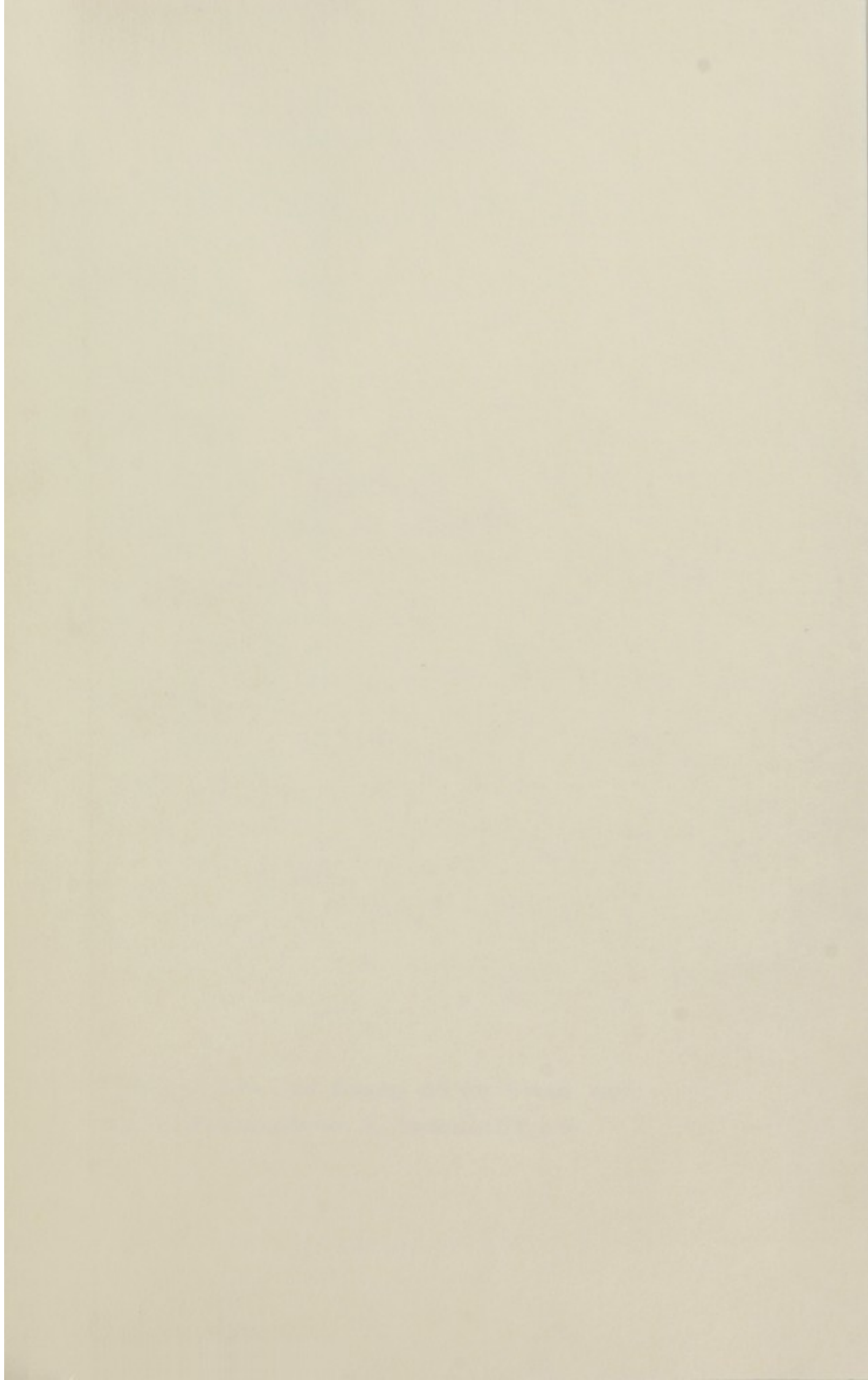
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HEREDITY  
IN BREAST CANCER

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*by*  
ROBERT FRASER



# HEREDITY IN BREAST CANCER

A GENETIC AND CLINICAL STUDY  
OF TWO HUNDRED PROBANDS

BY  
OLUF JACOBSEN



1946

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I thank the Chiefs of the different hospital services for kind permission to use the patient material, and the Probands for the readiness with which they placed themselves at my disposal and by their information furthered my researches.

The work has been done with support from the Danish National Anti-Cancer League and from H. M. King Christian the Tenth's Fund, for which I offer my respectful thanks.

Copenhagen,  
August, 1946

OLUF JACOBSEN

The following is a list of the names of the persons who have been appointed to the various positions in the Department of the Interior for the year 1900. The names are given in alphabetical order, and the positions are given in the order in which they are filled. The names of the persons who have been appointed to the positions of Assistant Secretary, Chief of Bureau, and Chief of Division are given in bold type. The names of the persons who have been appointed to the positions of Assistant Secretary, Chief of Bureau, and Chief of Division are given in bold type.

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John H. Hays, Secretary of the Interior.



## INTRODUCTION

For centuries attempts have been made to throw light on the causes of cancer, and especially within the last generation the problem has been the object of extensive systematic studies and experiments; still we have not come so far that it has been possible to establish a classification of the malignant tumors on an etiologic basis. Tumors occur in all living beings; their formation is thus a common biologic phenomenon; we must therefore take it for granted that their development depends on the laws applying in biology, among others the Mendelian laws of heredity. It therefore lies near to examine to what extent the incidence of malignant tumors is due to hereditary predisposition, and according to what laws they are inherited. Experimental genetic studies of this problem on animals, especially on mice, have shown that the tumors may be to a great extent, or even altogether, hereditarily determined; but in spite of good experimental conditions the problems have not been definitely solved.

It has long been known that cancer in the human species often occurs familiarly, and the older literature contains many descriptions of such cancer families. Also systematic genetic, biologic studies of cancer in man seem to show that the development of the tumors is controlled by hereditary factors; but researches of this kind, so far, have been of limited extent and have not been carried through with quite sufficient exactitude; and as, moreover, the methods employed have been somewhat defective, no clear conclusions can be drawn from them. Therefore, a more systematic study of the heredity

of every single form of cancer in man, carried out by exact methods, is needed.

In the present work I have attempted such an investigation with regard to cancer of the breast. To this end I have examined 200 non-selected probands and a number of controls with corresponding age distribution; and have registered their affected and sound relatives within the groups of parents, brothers and sisters, grandparents, and brothers and sisters of parents. Primarily I made sure that the age distribution in the different groups was the same for the relations in the proband- and control materials. Next, I have examined

(1) whether there is any demonstrable difference in the incidence of breast cancer in the groups of relations in the proband- and control materials;

(2) whether it is possible after calculation of the cancer risk in the different groups of relations to form any estimate of the mode of inheritance of the disease.

The second of these questions necessarily requires an examination also of

(3) whether there is any demonstrable difference in the total incidence of cancer of all sites in corresponding groups of relations in the proband- and control materials; and

(4) whether it is possible to demonstrate a genetic connexion between breast cancer and other forms of that disease, especially uterine and ovarian cancer.

When the material had been collected, it was found that the age distribution curve, contrary to expectation, showed two peaks. The age distribution in the proband material was therefore compared with the distribution in a larger material from the Danish Cancer Registry under the National Anti-Cancer League, comprising 1565 patients, and an anamnestic and statistical analysis was made of the age distribution curve for the 200 probands.

Outside the original scheme of the work, an examination has been made of a small material of males with breast cancer.

## *Chapter I*

### EARLIER WORKS ON HEREDITY IN CANCER

#### 1. EXPERIMENTAL GENETIC INVESTIGATION

Since it is from experiments on animals we know that hereditary factors are determining for the development of malignant tumors, it will be logical briefly to review the results of experimental researches into that subject before proceeding to discuss the literature dealing with the genetics of cancer in man.

For the study of the genetic origin of tumors it was of paramount importance that Morgan<sup>77</sup> in 1919 in the banana fly (*Drosophila melanogaster*) observed a mutation in the X-chromosome which, recessive toward the allelic gene, determined the development of a malignant melanotic tumor, which killed the individual in the larval stage. This proved beyond refutation that a malignant new growth may develop by mutation, and that the hereditary transmission of the character follows simple Mendelian principles.

The classic experimental animal for tumor research, the mouse, presents great advantages also from the genetic point of view; firstly because most of the tumor forms known from human pathology occur in this animal spontaneously, secondly because the mouse is comparatively shortlived, so that it is possible within a reasonable time to obtain large experimental series covering many generations.

In the last thirty-five years, systematic studies have been carried out with regard to cancer of the breast, which is the commonest tumor in mice; and by inbreeding it has been possible to obtain strains in which up to 100 per cent of the females develop this tumor. By experiments with cross-breeding with apparently cancer-free strains it has then been tried to find out by what laws the transmission was governed.

The results of these experiments have been so various, however, that there is great divergence of opinion with regard to the mode of inheritance. Thus, Lynch<sup>71, 72</sup> surmises a dominant Mendelian factor, Slye<sup>99</sup> a recessive, Little<sup>68</sup> a sex-limited dominant with homozygous lethal effect; and Dobrovolskaja-Zavadskaja<sup>33</sup> comes after extensive experiments to the conclusion that there exists a hereditary predisposition to cancer, and that the experiments seem to show that the different tumors are controlled by different, mutually independent genes, recessive toward the normal dominant ones. That the interpretation of the various experiments has been so difficult is partly because the supposedly cancer-free strains used for cross-breeding have not been surely free from the disease, partly that extra-chromosomal factors play a rôle for the development of cancer.

After Murray & Little<sup>78</sup> had shown that cancer of the breast contrary to the Mendelian principle is oftener inherited through the mother than through the father, Bittner<sup>13, 14, 15</sup> made his interesting experiments with exchange of broods, young ones from strains carrying the taint being suckled by mothers from cancer-free strains and conversely. Since it was found that the incidence of cancer of the breast in these broods was in the first cases reduced, in the second increased, there is reason for believing that the mother-milk must contain a cancerogenic factor of unknown nature. At the same time, the experiments showed, however, that this factor is not alone in determining the result, and an inherited, constitutional predisposition must therefore still be reckoned with. When it was shown by Lacassagne<sup>60, 61, 62</sup> and others that breast cancer could be developed in male mice of tainted strains by continuous

dosage with estrone, it became evident that the sex-limitation observed could not be of chromosomal character, but must be due to a factor connected with the internal secretion of the ovaries.

During the experiments it was found, however, that also other factors play a rôle for the development of breast cancer. Thus, virginal mice get cancer more rarely than mice that have brought forth and suckled young ones. The incidence increases with the number of pregnancies, and stopping of the milk, whether by ligature of the nipples or by removal of the brood, increases the incidence also in strains in which spontaneous occurrence of the tumor is comparatively rare (Adair & Bagg<sup>1</sup>). The animal experiments have thus shown that a number of factors besides the inherited disposition contribute in determining the development of cancer of the breast.

In this connexion, the latest Danish investigations, by Lefevre<sup>65</sup>, are of interest. He thinks that in mice it is impossible to produce other tumors of the internal organs than those to which the animal has a hereditary disposition; that tumors appearing after a carcinogenic influence has been brought to bear must therefore be considered as accelerated, and that this acceleration may express itself both by an increase of the tumor incidence and by a lowering of the tumor age. Though animal experiments like these have taught us much about hereditary factors in relation to the development of cancer, and have shed light on interesting details, a final elucidation of the problems has not been arrived at.

## 2. STUDIES IN GENETICS OF HUMAN CANCER

Cancer of the breast has been a well-known disease since the earliest times of medical science; already from about year 100 of our era we find in the Roman medical literature a good description of the late stages of the familiar pathologic picture with the ulcerating tumor and the metastases to the axilla.

While there is nothing in the antique or medieval literature to show that any precise ideas were held with regard to its

etiology, we see in more recent times every fresh biologic discovery being seized upon and employed in attempts to explain the cause of this mysterious disease.

The theory that cancer might be a hereditary constitutional anomaly seems to have been first put forward about the year 1700, by Hoffmann<sup>50</sup>, who related an instance of familial occurrence of the disease. His idea seems to have been widely discussed, and to get the controversy settled the Academy of Lyons offered a prize for the best paper answering the question: *Qu'est-ce que le Cancer?* The prize was won in 1773 by Bernard Peyrilhe<sup>86</sup>, who concluded by denying that cancer could be hereditary and expressed the opinion that an extraneous agent (? virus) was necessary for its development. The clinicists continued to find, however, that malignant tumors often accumulated in certain families, and in a work by Johan Nepomuk Rust<sup>94</sup>, from 1811, we find the opinion of that day expressed when the author says:

"It is impossible to deny the existence of a certain predisposition to cancer, the nature of which is certainly unknown, but which is probably due to some aberrant structure of the glands, which favors the sooner or later development of this specific contagium; because it without the acceptance of such a hypothesis is impossible to explain why this evil so often transmits itself from parents to children, especially from mothers to daughters, and persists through entire generations; of which I have had occasion to make some important, incontestable observations."

In the following hundred years, until Roger Williams<sup>116</sup> in 1908 published a considerable material compiled by himself, the literature consisted of a series of case reports, lesser statistical studies and a few collective reviews.

Instances of familial, hereditary occurrence of breast cancer have been reported by the following authors:

Velpau<sup>112</sup> (1854): two sisters, whose mother died from breast cancer, both got cancer of the left breast at the age of 35 years.

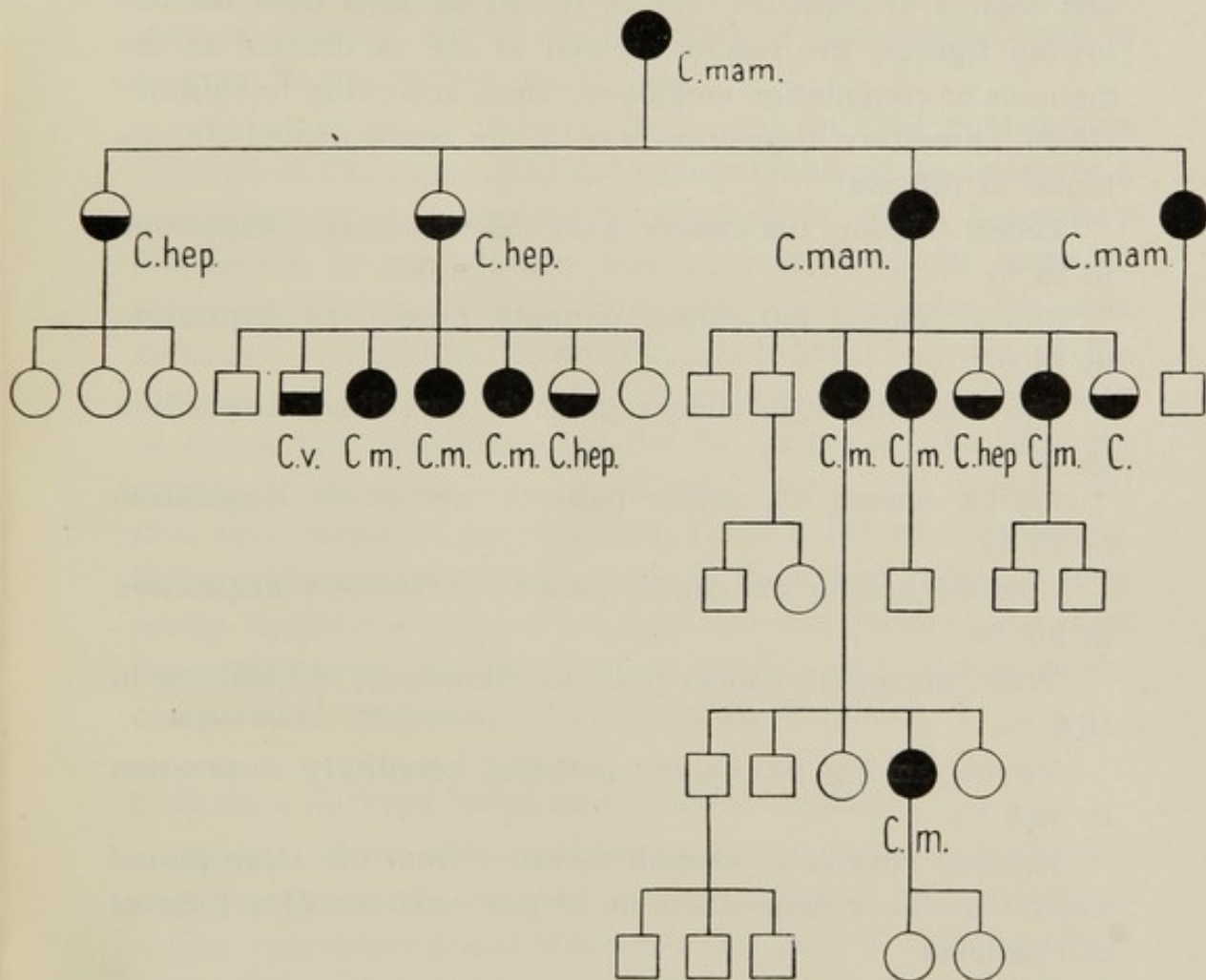
Warren<sup>106</sup> (1856): A man who died from cancer of the lip

had 3 daughters, who all died from breast cancer; and two of these each had a daughter who was treated for the same disease.

Laurence<sup>63</sup> (1858): A woman who died from breast cancer had 3 daughters, all with the same disease.

Sibley<sup>98</sup> (1859): A mother and her 5 daughters all died from cancer of the left breast.

A pedigree published by Broca & Lugol<sup>18</sup> in 1866 is unique for its time. The family was Broca's own, and all its members are registered in the years 1768 to 1856, with statement of age at death and cause of the same.



As the pedigree chart shows, 1 man and 15 women out of the 38 members of the family in five generations died of cancer, and 10 of the cases were cancer of the breast.

*Statistics.*

In 1802 an attempt was made to collect a material that would be sufficiently large to form the basis for an estimation. The Society for Investigating the Nature and Cure of Cancer sent out a inquiry to all physicians in England, one of the questions being: Is cancer hereditary? The response to the enquête does not seem to have been great, however; at least, the committee was dissolved four years later, and no result of its work is to be seen to-day. Publications by several older authors contain statistics to elucidation of the rôle of hereditary factors in the development of cancer, based on hospital journals and replies to inquiries; but as it will be seen from the following figures, the results arrived at are as diverse as the methods of compilation employed. Thus, according to Guillot<sup>43</sup> (1889), hereditary disposition was by the below named authors found as follows:

Lebert, among 102 cancer patients, hereditary disposition in 13 %.

Sibley, among 160 cancer patients, hereditary disposition in 16 %.

Snow, among 1075 cancer patients, hereditary disposition in 11 %.

Piorry, among 83 cancer patients, hereditary disposition in 23 %.

Combes, among 256 cancer patients, hereditary disposition in 9.7 %.

West, among 49 cancer patients, hereditary disposition in 16.6 %.

Veyne, among 106 cancer patients, hereditary disposition in 18.8 %.

Kristian Poulsen's<sup>88</sup> Danish statistics from the same period show hereditary disposition in 17 per cent out of a total of 210 patients.

From this time are also two papers by English authors, which differ from the others by dealing only with breast cancer. One of them is by Paget<sup>80, 81</sup>, who found familial occurrence of cancer in 16 out of 80 patients with scirrhus of



the breast. He is convinced that cancer is partly due to inherited disposition, an opinion which he after a lifetime's study of the disease expresses as follows: "The fact of frequent inheritance is sure in this as in many other diseases, but its method is so mysterious; it is so utterly impossible to conceive the form of the material in which the impregnated ovum contains that which will become or be made cancerous, that it cannot be safe or useful to think that we can deduce anything from the bare fact. We are apt to speak of potentiality, tendency and predisposition as if they were forces independent of matter or of structure; but when we try to think of the very things on which they depend, we find ourselves in a cloud-land of mystery, where the difficulty of discovering truth is as great as the facility of guessing."

The other paper is by Butlin<sup>21</sup>, who in 1887 published a material of 184 cases of breast cancer collected by means of a questionnaire. It comprises 68 families in which hereditary disposition to the disease was present, with 99 cases of malignant tumors, in all. Unfortunately, the schemas are often defective as regards information about the character of the tumors; but cancer of the breast clearly preponderates, with 34 cases. The distribution of the 99 tumors on the different groups of relations was as follows: father, 11; mother, 21; sibs, 10; children, 6; grandparents, 7; more distant relatives, 44. Butlin feels convinced that cancer of the breast is due, at least partly, to inherited disposition, both because cancer often can be demonstrated in the direct line of descent and because of the comparative frequency of the homologous tumor.

#### *Collective Surveys based on the older Literature.*

Several of the older authors try to get nearer to a solution of the continuously debated problem, oftenest on the basis of earlier case reports and statistics. The general opinion seems to be that cancer must be considered a constitutional diathesis, and therefore hereditary (Recamier<sup>90</sup>), while the location, anatomic appearance and development of the tumor must be due to secondary causes (Verneull<sup>113</sup>); and Fabre<sup>37</sup> points out

that there are variations as regards the different tumor forms; thus only between 5 and 10 per cent of patients with cancer of the skin can tell of familial occurrence of cancer, whereas the corresponding percentage of patients with cancer of the breast is as high as 33 per cent.

In 1885, Henri Puig<sup>89</sup> after a critical survey of the literature says that the investigations are faulty, that the value of the different clinical materials is made questionable by the want of controls, and that each tumor form should be the object of separate genetic study. He is himself convinced, though, that cancer is hereditary, and he finds signs which seem to indicate that hereditary tumors often have a homologous location. Finally, in 1903, Wienberg<sup>115</sup> sums up the situation and declares that all the earlier case reports and statistics are without value, owing to disparate methods of investigation and wanting control material. As regards the question of hereditary disposition he is doubtful; he will not exclude the possibility that cancer may be conceived as an infectious disease, and that the susceptibility to infection may depend on an inherited tendency.

A large material was published in 1908, by Bashford<sup>5</sup>. Reports on 2932 patients suffering from malignant new growths had been received by the Imperial Cancer Research Fund, and to these questionnaires were sent. Only from 669 of them could reliable information about their family history be obtained, and out of this number 311 were able to tell of cancer having occurred among their relatives, the father being attacked 58 times and the mother 114 times, or 1 in 11.5 for fathers and in 1.6 for mothers, corresponding to the 669. The mortality statistics for persons above 35 years of age showed a death rate from cancer for men of 1 in 11, for women 1 in 8. After this comparison, Bashford concludes that there is no reason to believe that cancer is hereditary.

Owing to fundamental difficulties, all these early studies thus brought only slight results, and by the beginning of the present century we therefore see the researchers turning their attention from the clinic in order to occupy themselves altogether with experimental investigation of cancer in

animals. There is still, however, some interest in the study of heredity in human cancer, and communications about cancer-families have continued to appear (Peiser<sup>84</sup>, Auvray<sup>2</sup>, Ewald<sup>36</sup>, Cholewa<sup>24</sup>, Paulsen<sup>82</sup>, Koerbler<sup>59</sup>, Frykholm<sup>41</sup>, Clemmensen<sup>28</sup>). But even the most compendious and most carefully investigated pedigrees (Warthin<sup>108</sup>) have added nothing to what was already known, namely that cancer,—especially certain forms of the disease,—often occur with particular frequency in certain families; nor do the larger materials, based on hospital journals or inquiries (Häberlin<sup>52</sup>, Warthin<sup>107</sup>, Peller<sup>85</sup>, Letulle<sup>66</sup>, Chaton<sup>48</sup>, Deelmann<sup>32</sup>) widen this experience.

#### *Newer Studies on Heredity in Cancer.*

In modern cancer literature, attempts to throw light on the problems are made through studies of (1) statistical reports on the population, (2) the occurrence of cancer in twins, (3) familial occurrence of cancer; all of which are methods usually employed in genetic research; and further through investigation of special, rare categories of patients, in whom it may be thought that particular conditions play a part in furthering the manifestation of the tumor; namely, young cancer patients and patients with multiple primary carcinomas.

#### *Studies of statistical Reports on the Population.*

The object with these investigations is to find out if deaths from malignant tumors are more frequent among relatives of cancer patients than among the general population. They are often based on material from the life insurance companies, and show an absolute excess mortality from cancer among those insured who have given information of cancer in their families. In a numerically very large material of 85,000 insured with 22,000 deaths, Florschütz<sup>40</sup> found that the cancer mortality in families carrying the taint is twice as great as in families without it.

In 1923, a large material from the United States was published by Little<sup>67</sup>. He compares the frequency of cancer in sibships where (1) the father has died from cancer, (2) the

mother has died from cancer, and (3) a cancer death has already occurred among the sibs, with an incidence of cancer among the general population calculated on the basis of mortality statistics. In all three groups he finds a statistically significant excess mortality from cancer, and he therefore concludes that the development of the disease is due to inheritance of a predisposition. Unfortunately his work deals with all forms of cancer collectively, despite the fact that both clinical experience and animal experiments seem to show that genetically there are great differences between them.

From Norway there appeared in 1931 a similar, but much more comprehensive and better analysed material, published by Waaler<sup>102, 103</sup>.

In the years 1908 to 1928 reports on 6000 patients suffering from malignant new growths had been received by the Norwegian Cancer Committee. The replies to the inquiries sent out contained information about the relatives—parents, brothers and sisters, children and consort—of the patients, and in most cases this information was supplemented by means of a follow-up carried out by medical students, who were sent out to interview relatives still living. The object with the investigation was to show that cancer as cause of death is more frequent in brothers and sisters of cancer patients than in the population as a whole. As controls were used on the one hand the consorts of the patients, on the other the general mortality statistics. The mortality from cancer was calculated in ratio to the total number of deaths in the different age groups, whereby a possible uneven age distribution was equalised.

The sibships comprised in the investigation were divided into an F-series, in which all the individuals had died, and their fate therefore was fully known, a U-series, in which a number of individuals still were alive at the time of the investigation in 1929, and a G-series, comprising sibs who had not been searched for or found, so that only the information given at the notification of the case was available. The result of the investigation showed in the F- and U-series an indubitable excess mortality from cancer both among brothers and sisters.

Waalder also found that the percentage of cancer incidence was much higher among children whose father or mother, or both, had died from cancer, than among children of sound parents. This is contrary, however, to the result of an investigation carried out in Switzerland, in 1943, by Hanharte<sup>46</sup>. He examined a group of individuals, all over 50 years of age and children of parents who both had died from cancer, and found a cancer mortality rate of 13.28 per cent, a figure lower than for the corresponding age class of the population as a whole. He therefore concludes that heredity is of no etiologic significance for the development of cancer.

After dividing the cancer material according to the location of the tumor, Waalder found that whereas cancer of the esophagus, the stomach, the breast, the uterus and the ovary seem to be hereditarily determined, the development of cancer of the tongue depends on exogenous factors. Moreover, he found that when the cancer of the patient in whom the taint first manifested itself was either mammary, uterine or ovarian, the frequency of the disease would be much greater among her sisters than among her brothers, and that this excess was due precisely to an increase in cancer of the same sites.

After working up his material statistically, Waalder says that in all probability there are two mutually independent hereditary factors, each of which is present in 16 per cent of the population. One of them disposes males and females in equal degree, the other occurs only in females. Waalder himself points out that there are considerable elements of uncertainty connected with his investigation, and as regards these it seems to me that there are two points, especially, on which criticism may justly be levelled. One of them is the want of uniformity of method in the collection of the material, the original information to which was given by numerous physicians and hospitals and the supplementary obtained through over one hundred examiners; the other is the want of certainty about the diagnoses, both those in the general mortality statistics and the unverified ones in the material.

*Investigations concerning the Occurrence of Cancer  
in Twins.*

Since enzygotic twins are genotypically identical and, besides, owing to like traits of character, may be supposed to live under more similar conditions than other pairs of sibs, so that peristatic factors get the least possible influence, the more frequent, concordant occurrence of a disease or quality in them both will indicate that it is determined by hereditary disposition.

Concordant occurrence of tumors in enzygotic twins is known from many case reports, and in a review of 20 pairs collected from the literature McFarland & Meade<sup>38</sup> found that cancer of the breast, the uterus and the ovary occur concordantly, whereas squamocellular carcinomas showed discordance. In non-selected, but small materials, three investigators, Weitz<sup>110</sup>, Habs<sup>44</sup> and Kranz<sup>58</sup>, found that cancer even in enzygotic twins oftenest occurred discordantly, that enzygotic twins showed concordance oftener than fraternal, and that full concordance with regard to the character, site and age for the manifestation of the tumor was seen only in the former, never in the latter.

The conclusion with regard to the investigation respecting twins must therefore be that hereditary factors must play a part in determining both the character and the site of the tumor, but that peristatic factors in a great measure contribute to determining its manifestation.

*Investigations concerning Probands.*

So far as I have been able to find, there are in the more recent literature five studies on this subject, namely by W. Roger Williams<sup>116</sup> (1908), E. Lane-Claypon<sup>25</sup> (1926), I. M. Wainwright<sup>105</sup> (1931), W. Wassink<sup>109</sup> (1935) and Martynova<sup>75</sup> (1937). Williams investigated a non-selected series of 136 breast cancer probands and found the hereditary taint in 33 (= 24.2 per cent), with 48 cases of cancer, in all, 19 of which were cancer of the breast. One hundred and one females with benign tumors

served as basis for comparison; among these, hereditary disposition was found only in 15.8 per cent. Incidentally, the investigation seemed to show that hereditary cancer is most frequent in females, and that the risk of getting cancer is greater for individuals whose parents have died from the disease.

Lane-Claypon's report on the subject has unfortunately not been available to me, but according to Wainwright the material consists of 508 breast cancer probands, and the control material of 509 sound females. By means of this material, light has been shed on many etiologic problems, and also the question of heredity is touched upon, in so far as the author by an investigation of the incidence of cancer among the parents of the patients found a slight, but indubitable excess mortality from cancer in these.

In a parallel work on a larger American material, Wainwright tested the British results. His material was collected with the aid of a number of physicians and trained nurses, and from the varying number of patients in the different series of investigation it is evident that it was wanting in homogeneity. The investigation into the heredity seems to comprise 784 females treated for cancer of the breast, with a control material of 576 sound females in ages between 45 and 70 years. In both series, information is given about the parents and brothers and sisters of the probands.

Like Lane-Claypon, Wainwright found a slight excess mortality from cancer in the parents of the individuals in the proband-series (11.4 per cent as against 8.5 per cent for the controls), and also that the incidence of breast cancer was four times as great among the mothers of the former as among the mothers of the controls. The investigation of the brothers and sisters of the two series showed only a slight excess mortality from cancer among the brothers of the cancer series; but the figures with regard to the sisters proved to be more interesting.

From the following Table it will be seen that cancer as cause of death was twice as frequent among sisters of breast cancer patients as among sisters of sound females, and that the

homologous tumor occurred in an unexpected large percentage of cases.

	No. of deaths among sisters	No. of deaths from cancer of the breast	No. of deaths from cancer of other sites	TOTAL
784 Probands	160	16	25	41 (= 25.5%)
576 Controls	151	7	14	21 (= 13.6%)

This was further emphasised by the investigation of the morbidity from cancer among the living sisters of the two series, which showed

	No. of living sisters	Treated for cancer of the breast	Treated for cancer of other sites
784 Probands	510	6	1
576 Controls	560	0	1

The results of the investigations are summed up by Wainwright as follows:

1) The American study, like the British, showed a slightly higher incidence of cancer in parents of breast-cancer patients.

2) A study of the American brothers and sisters consistently showed a higher incidence of cancer among the brothers and sisters of the cancer series, both for breast cancer cases and for cancer as a whole.

3) Grouping of 3 or 4 cases of cancer in a family was found in only the cancer series, not in the controls.

4) There is a suggestion that cancer is inherited more often by women than by men.

Unfortunately, Wainwright's study suffers from some fundamental shortcomings, which somewhat lessen its value. Thus, the method employed in the compilation of the material is too loose, the sureness of the diagnoses doubtful, and the control



material far from being in statistical agreement with the proband material.

A Dutch study by Wassink<sup>109</sup> from 1935 comprises a long series of investigations of cancer patients with data respecting their parents, brothers and sisters, grandparents and first cousins male and female. The total figures for cancer found among these relations are designated as "rendement total", while the figures for cancers with the same localisation as those in the probands are designated as "rendement homotope". If cancer is not due to inherited disposition, it will be expected that the percentage of "rendement homotope" in proportion to "rendement total" must be the same as in the population as a whole. As basis for comparison, Wassink uses the mortality statistics, though quite aware that this introduces an element of uncertainty. After dividing the probands into groups according to the site of the tumor, he found with regard to breast cancer that among 660 patients cancer was familial in 207 with a total of 311 cases, 109 male and 192 female, and that cancer of the breast, with 112 cases ("rendement homotope") represented 59 per cent of the total cancers in women. When the proband had cancer of the breast, there was thus a considerable increase of cancer among the female relatives, and this increase was due precisely to the homologous form of tumor. Studies on cancer of the uterus gave a similar result, whereas the conditions with regard to cancers of the digestive tract were less easy to make out, and skin- and lip cancers did not seem to deviate from the "normal figures". Wassink concludes that breast cancer and cancer of the uterus must be supposed to be conditioned by hereditary endogenous factors, and that several signs point to cancers of the digestive tract being to some extent hereditarily determined. This apparent disposition of the organs to cancer might just as well be thought, however, to be due to a disposition of the tissues, so that a genetically conditioned tendency to the development of cancer in cylinder epithelium may give rise to cancer in the stomach just as well as in the colon. If we extend the hypothesis of such a hereditary tissue proclivity, it is also possible to imagine that, for example,

breast cancer in woman has its genetic equivalent in cancer of the larynx, the mouth or the bladder in man. These thoughts give wide scope for the imagination, but do not, as yet, rest on any very solid foundation.

Wassink recommends the continuation of comprehensive proband investigations in order to shed light on the problems, and Martynova's<sup>75</sup> study, from 1937, is such an attempt at systematic familial investigation of a selected series of 201 breast cancer probands, all treated at the Central Oncological Institute in Moscow and examined by the author herself. The 201 pedigrees included 7173 persons, in all. It does not seem that any limits were set to the degree of collateral relationship required for inclusion; thus, one pedigree comprises as many as 105 persons. Only those cases which had been diagnosed by a physician were considered as sure cases of cancer, while all anamnistically suggestive histories were included in the category of "suspected cancer". As control material, Martynova used 796 patients of the State Dental Clinic, all beyond the age of thirty.

In this way she found that the percentage of cancer was distinctly higher among parents and brothers and sisters of the cancer probands than among those of the controls. The data respecting the incidence of breast cancer among the female relatives are presented in the following Table.

	No. of mothers	Mothers with breast cancer	No. of sisters	Sisters with breast cancer
201 Probands	128	6	274	6
796 Controls	768	2	395	0

According to this, cancer of the breast was thus eighteen times as frequent in mothers of the breast cancer patients as in the mothers of non-cancer females. Finally, Martynova found that in her material 28.75 per cent of the female relatives with a history of cancer had cancer of the breast, a much larger

proportion than expected, especially when compared with Novoselsky's Russian mortality statistics, according to which only 4.7 per cent of cancer deaths in woman are due to cancer of the breast. On the basis of 6 pedigrees from her material, in which both parents had died of cancer and all the offsprings were unaffected, though seven of them were over forty years of age, she thinks it very unlikely that general disposition to cancer is determined by a recessive gene substitution.

Martinova's work suffers from great shortcomings. The figures in themselves indicate that the investigations have not been conducted with sufficient thoroughness; at least it is strange that 201 probands only could give information with regard to 128 mothers, and that the same probands have 274 sisters, while 796 controls had only 395. The correctness of the diagnoses is extremely problematic, and the age distribution in the control material does not correspond to that in the proband material.

#### *Genetic Studies respecting young Cancer Patients.*

When the question is of cancer, "young" patients means patients in the age group 0-30. According to the larger statistics, they constitute only between 1 and 2 per cent of all cancer cases. This remarkably small percentage suggests the existence of special, perhaps hereditary factors as determining for the early manifestation of the disease. Schnorrbusch & Kujath<sup>96</sup> (1938) have attempted to throw light on the problem by a genetic investigation, but failed to confirm the theory. They examined the pedigrees of 30 young cancer patients, but did not among their relatives,—159 persons, in all,—find a higher mortality from cancer than among the population as a whole. Therefore, they conclude that hereditary disposition (increased gene dose) has nothing to do with the earliness of the manifestation.

#### *Statistical Studies respecting the Occurrence of multiple primary Carcinomas.*

While multiple primary carcinomas were formerly regarded

as curiosities and their occurrence as quite fortuitous, it is now commonly agreed that they are much more frequent than hitherto supposed, that in some individuals there seems to be a disposition to the formation of several malignant tumors, and that these often are localised to some particular organ or organ system (Lefevre<sup>54</sup>).

We know, both from clinical experience and from investigations on animals, that the localisation of cancers is genetically controlled, and the fact that multiple carcinomas group themselves within certain organ systems therefore supports the theory of the heredity of the tumors. In 1942, Engelbreth-Holm<sup>34</sup> published a material from the Radium Center in Copenhagen, of 87 patients who besides breast cancer had some other malignant tumor. One of the interesting facts brought out was that the distribution of the complicating neoplasms deviated greatly from the expected, 75 per cent being localised to the breast, the uterus or the ovary. Besides, it was found, after an estimate of the morbidity risk among the population in general, that the risk of a breast cancer patient getting a malignant tumor in any of the other sites just named is considerably greater than for a non-cancerous woman in the same age class; and finally there was an indubitable displacement of the age distribution toward the left for patients with multiple tumors. It seems to me that the results of this investigation point to a genetic relationship between certain forms of tumor and suggest that these genetically controlled cancers manifest themselves in the younger age classes. Genetic study of a larger material of patients with multiple primary carcinomas may throw further light on these problems.

The study of the genetics of malignant neoplasms in man has thus given us a number of experiences but no facts, inasmuch as nothing has been forthcoming which uncontrovertibly proves that the development of cancer is conditioned by hereditary disposition, and we absolutely ignore according to what Mendelian laws the disease is inherited. Still, all the studies of breast cancer seem to indicate that this form of cancer is at least partly determined by hereditary factors, and

that it,—and perhaps also the other cancers of the female genitals,—thus hold a place apart in the etiologically variegated mosaic of malignant neoplasms. The question then is if it, in view of the difficulties attaching to genetic studies of cancer in man, is possible, at all, to prove that cancer is a hereditary disease, or if the problem, after the vain attempts made, must be considered as insolvable, and that all that can be done is to analogise with experiments on animals, and perhaps supplement these with examples from clinical experience.

Since all the studies of these questions hitherto have been more or less vitiated by flaws in the materials, especially in the control materials, which makes the figures arrived at unsuitable for statistical treatment and thus makes it impossible to prove anything with regard to the heritability of cancer or the mode of transmission of the disease, it is necessary, before one adopts the negative view that genetic research on human cancer is futile, to make a separate, systematic investigation of every form of cancer, with special attention to the control material, every group of relations in which must answer, statistically, to the corresponding group in the proband material.

## *Chapter II*

### AUTHOR'S MATERIAL

#### 1. COLLECTION AND VERIFICATION OF THE PROBAND MATERIAL

For the reasons stated in the foregoing chapter I have chosen to make a statistical-genealogic investigation of a number of probands with breast cancer, picked at random, and the diagnosis of whose cases had been verified by histologic examination of the tumor. In the files of the Danish Cancer Registry I found a series of over 300 patients, all domiciled within the area of Greater Copenhagen and treated in Copenhagen hospitals, half of them at the Radium Center, the rest distributed among the State Hospital (services C, D and the roentgen clinic), the Municipal Hospital (services 1 and 5), the Bispebjerg Hospital (services A and D), the Sundby Hospital (surgical service), the Frederiksberg Hospital (service A) and the Hospital of the Deaconesses' Institution (services A and B).

Between October, 1942, and November, 1943, I got in touch with 262 of these patients. Sixty-two of them had to be eliminated, however; 22 because they were born out of wedlock, 8 because they were born in Sweden and had never had any contact with their relatives there, 4 because they had lived so long abroad that they knew nothing about their family, 17 because they knew nothing about their relations, of whom they believed that none were alive, 6 because they refused to lend their aid to the investigation, and 5 because the information they were able to give was so slight that they after vain attempts to get it supplemented had to be counted

out, too. As regards the distribution by age of these sixty-two, it was not restricted particularly to one or a few (older) groups, but was even through all age classes; therefore the elimination of the comparatively large number did not affect the age distribution curve of the material.

There thus remained 200 probands,—197 females and 3 males,—a material which was deemed sufficiently large to serve as basis for statistical investigation and analysis. After obtaining and making a record of such personal data as name, address, year and date of birth, occupation and marriage, I tried to secure the fullest possible anamnestic information, especially respecting such facts as might be thought to have an etiologic bearing on the disease; thus (1) exogenous etiologic possibilities:

- a. traumas, with details of their nature and the time elapsed from the trauma was sustained until the tumor in the breast was discovered;
- b. benign tumors of the breast;
- c. the number, duration and course of nursings, especially with a view to affections of the breast during the lactation, notably mastitis and galactophoritis;
- d. treatment with estrogenic hormones, with statement of name of preparation, magnitude of doses, duration of treatment and length of time from the institution of the latter until the tumor in the breast was diagnosed.

(2) endo- and exogenous possibilities: number of pregnancies and deliveries, and information about menstruation.

From the case records of the hospitals information was obtained about the date of operation (trephine biopsy by Christiansen's method, bio-assay or radical operation), that is to say the time, as near as it can be ascertained, when the diagnosis of malignant new growth was established with certainty, and the result of the histologic examination of the tumor.

#### *The Family of the Proband.*

The first problem that presented itself was to what groups of the proband's family the examination should be extended.

For several reasons I chose to follow the pedigree chart C of the Danish Institute of human Genetics, which comprises the following: parents, brothers and sisters, children, father's and mother's parents and parents' brothers and sisters.

In the first place it may be expected that detailed information about these rather near relatives will be obtainable, and that it will be possible to test the correctness of the information. What information is obtained about more distant relatives, —cousins, grand uncles and -aunts,—will as a rule be more or less a matter of chance; so that one is very liable to get a number of cancer cases registered without getting it clear how many individuals, ill and sound, the family group really comprises; consequently, the material will be without value for comparison with the morbidity in the population as a whole.

Next, I judged it unnecessary in an investigation into a disease so frequent as cancer to include distant relations, such as one would do in the case of a rare disease with possibly recessive inheritance. And, finally, it would be impossible for one investigator within a reasonable number of years to carry through a proband- plus control examination, with registration of relatives, of larger compass than the one here chosen.

I therefore with the proband went through the list of all the relatives, in the order named, and began by noting the name, occupation, address, year and date of birth, and, for the deceased, the year, date and place of death. My reason for this roundabout procedure instead of beginning by asking if there had been any cases of cancer in their family, was that many of the patients were happily ignorant of the real nature of their affection, and that a too marked interest in the question of cancer on the questioner's part might arouse their suspicion and tear them out of the confidence in which they lived. Besides, I knew both from the literature and from own experience that cancer patients, though they may have an inner absolute feeling of the malignancy of their disease, yet try to avoid facts, and therefore, feeling that the disease may be hereditary, will hide or explain away analogous cases in their nearest family. In other words, they lie, consciously or



unconsciously, both to themselves and to the questioner. I tried to guard against potential errors due to that mental attitude in the patients by speaking with them about the history of illnesses of each of their relatives, showing just as much interest, for instance in tuberculosis, heart disease and accidents, as in cancer, until I had formed a definite idea of the cause of death or the diagnosis. Verification of the diagnoses required, however, so precise information that none of the probands were able fully to meet those considerable demands on their memory; therefore it became necessary to supplement all the pedigrees by means of inquiries to relatives and to keepers of census- and parish registers in all parts of the country.

When the collection of the material was finished, I was in possession of 200 pedigrees, in which the registration of the number of individuals within the family groups, and the anamnestic information about the morbidity in each of them, was as complete as it might reasonably be expected. Information had been obtained about 3130 relatives of the 200 probands, while 171, or 5.2 per cent, could not be traced.

There was still wanting one documentation, however, without which the value of the results would be very problematic. The most important was, of course, to examine the 347 patients presumably suffering from cancer, but in addition to these I included, as control for my diagnostic estimate, 118 individuals supposed to have died from other causes than that disease. The possibilities for getting the diagnoses confirmed were (1) inquiries to practicing physicians, provincial hospitals and parish-register offices, (2) examination of case records and necropsy journals of hospitals in Copenhagen and (3) examination of death certificates. Unfortunately, no ordered system of such certificates exists for the rural areas of the country prior to 1920, which made it impossible through this means to trace individuals who have died before that time. Therefore, there were, of the 465 cases searched for, only 419 which there was any possibility of finding, and much beyond expectation I succeeded in finding them all.

In 398 (= 95 per cent) of these 419 cases, there was full accordance between my tentative diagnosis and the one found on verification. But death certificates, considered as documents, are not always quite satisfactorily filled out; and I feel convinced that among the ten in which heart disease, pneumonia or apoplexy were stated as cause of death, there may very likely have been hidden some formerly treated (? cured) cases of cancer. The causes of death given in the other eleven were such as ectasis of the aorta with compression of the esophagus, tumor of the ovary, ileus, gangrene of the abdomen and cholecystopathy,—all diagnoses which make a mistaken estimate understandable. In 46 cases, my diagnosis could not be verified by reference to death certificates, because the patients had died in rural districts before 1920. As none of them had been treated in hospitals, also that way to documentation was closed; but as the percentage of error in the much larger, verified part of the material is so small, I have felt justified in relying on the diagnoses arrived at on the basis of my examinations. As additional precaution I made it a condition for including these cases in the material that there should be concordant information about them from at least two relatives of the proband. In the family notes accompanying the pedigree charts I have, where these non-verified cases occur, added a short description of the disease, in order that the reader may judge for himself of the reliability of the diagnosis.

## 2. COLLECTION AND VERIFICATION OF THE CONTROL MATERIAL

Morbidity statistics of cancer in the general population might be a good standard with which to compare the results of the proband investigation, but until the registration of malignant tumors by the Cancer Registry shall have been going on for yet a number of years this morbidity cannot be calculated, and an estimate of it must rest on mortality statistics, which are quite unsuitable as basis for comparison.

To obtain a control material suitable for direct comparison,

the following criteria had to be set up. The controls must be from the same social level as the breast cancer probands, they must belong to the same age groups as these, the investigation respecting them must be carried out with the same minuteness and comprise the same groups of relatives, and, finally, the verification of the diagnoses must be just as thorough as in the case of the others.

After dividing the breast cancer probands into five-year age groups, I examined a series of likely controls with corresponding age distribution, who had been admitted to surgical wards of various Copenhagen hospitals for exogenous surgical diseases such as appendicitis, fractures or hernias. The older age groups, which are not so well represented in the surgical hospital services, I found in the municipal "Old People's Town". These were all sound, and had shortly before passed through the local hospital ward for routine examination prior to being transferred to the nursing home, so that the chance of their having occult cancer could with reasonable certainty be excluded.

In this investigation I interrogated, with regard to their family, 273 persons. Of these, 73 had to be eliminated, however; 28 because they were born out of wedlock, 11 because they refused to lend their aid to a genetic investigation, 5 because they knew nothing about their family, 4 because they were born in Sweden and knew nothing about their relatives there, 19 because they knew nothing about their family, none of whom were alive; and 6 because the information they were able to give was so slight that they, too, after a vain attempt to obtain supplementary data, had to be counted out.

There thus remained a total of 200 controls, 110 females and 90 males, with, in all, 3181 relatives, 241 of whom (= 7.6 per cent) could not be traced, owing to lack of information about their fate. I have not deemed it necessary that the sex distribution should be the same as for the breast cancer group,—197 females and 3 males,—because it is immaterial so far as the total figure for the investigated groups of relatives and the morbidity are concerned. The verification comprised 68

cases of cancer, which were all found and showed accordance between the presumed diagnosis and the actual one. Thirteen relatives, whose deaths were stated to have been due to cancer, had died in the rural districts before 1920, and as none of them had been treated in hospitals it was therefore impossible to get the diagnosis verified, but like the corresponding ones in the proband material I have counted them as sure and included them in the calculations.

### *Chapter III*

## ANALYSIS OF THE PROBAND- AND CONTROL MATERIAL

In the following analysis of the case histories of the 197 female and 3 male probands, I deal first with such anamnestic factors as may possibly have had an influence on the development of the cancer; next I review the incidence of the disease among the relations of the probands as compared with the incidence among the relations of the controls.

### 1. ENDO- AND EXOGENOUS FACTORS IN THE ANAMNESIS OF THE PROBANDS WHICH MAY HAVE CONTRIBUTED TO THE DEVELOPMENT OF THE BREAST CANCER

The material is too small to serve as basis for a general estimate of the significance that may be attributed to exogenous—perhaps also endogenous, non-genetic—factors as causes of breast cancer. Nevertheless it is possible on the basis of the case histories to form an idea of whether these factors have played an essential part in the development of the disease in the two hundred probands examined. Briefly reviewed, the previous affections appearing in the case histories, which may be thought to have any causative relation to the subsequently developed malignant new growth are the following.

#### *Trauma.*

The rôle which earlier authors have attributed to traumas, —both to the severe, isolated lesion and to repeated minor

insults,—as cause of breast cancer, is no doubt considerably exaggerated. But among laymen the belief in their significance is so rooted that the patient will keep searching her memory in efforts to remember some previous accident; therefore, it is easy to understand why trauma in some works on the etiology of breast cancer appears in the anamnesis of up to nearly 75 per cent of the patients questioned on the subject.

Of the patients in my material, only 31 (= 18 per cent) stated anything about previous injury to the affected breast; in 6 of them it had been a question of repeated minor insults, in 25 of a single, severe injury. As regards the interval from the time the trauma was sustained until the tumor was first observed, it was in 6 cases from one to six months, in 8 about a year, in 9 from one to five years, in 8 from ten to thirty.

#### *Benign Tumors of the Breast.*

These are sparsely represented, only 4 probands having at an earlier period been treated for a benign growth in the breast which later became the seat of the cancer. In three, the diagnosis had been given as fibroadenoma, in the fourth as chronic, cystic mastitis.

#### *Treatment with estrogenic Hormones.*

Whether treatment with estrogenic hormones in therapeutic doses can give rise to the development of malignant tumor in the breast, or cause it to become manifest in an individual in whom the latent disposition is present, is a problem which lies outside the scope of the present investigation, but among my first probands there was one (Pedigree 56), the history of whose case awakened my interest in the question, and in going through the rest of the case histories I found that 18 of the patients had been treated with estrogenic hormone preparations for climacteric troubles. On the whole, the dosages seem to have been very moderate, and considering the rather considerable extent to which this therapy is now employed it

is perhaps not very remarkable that 18 women out of a total of 96 in the age class 40-55 years should have received this treatment. On the basis of so small figures it is not possible, however, to draw any conclusions with regard to the rôle of the estrogenic hormones as cancerogenic agent, and for the present we must believe that in therapeutic doses it is of no significance for the development of cancer of the breast.

The question whether the physiologic functions of the breast associated with the sexual function of the females contribute to determining the development of cancer in that organ is still unsolved, despite analyses of very large materials; but it seems to be generally agreed that pregnancy and subsequent normal nursing have a certain prohibitive effect (Lane-Clayton<sup>25</sup>; Wainwright<sup>105</sup>). The present investigation cannot furnish any contribution to the discussion, but its results may be stated, and seem to support the theory.

The ages for onset and cessation of the catamenia were within the physiologic limits. Of the 197 females, 41 were single, 156 married; 127 had had normal pregnancies and deliveries. Fifty-three were primiparae, 31 secundiparae, 20 terti-, 16 quadri-, 2 quinti-, 1 sexti-, 2 septi-, and 2 octiparae.

Only 77 of the 127 mothers had carried through a normal nursing of their children; the other 50 had not nursed, the causes being in 36 cases hypogalactia, in 5 agalactia, in 9 social reasons or early death of the child. Suppurative mastitis in the breast which later became the seat of cancer occurred in 6 patients. Galactophoritis, which is of much greater interest etiologically, is difficult to define, but had only been present with certainty in 6 patients if the criteria—infiltration in the breast, milk stasis and temperature to about 38° C.—are to be adhered to.

So far as any estimate can be formed on the basis of this small material, respecting an influence of the exogenous factors mentioned on the development of cancer of the breast, it must be that none of them, except perhaps the protective influence of the lactations, can be supposed to play any determining rôle.

2. OBSERVATIONS OF FAMILIAL OCCURRENCE OF  
CANCER IN THE PROBAND- AND CONTROL  
MATERIALS

THE PROBAND MATERIAL

Cancer was found in 154 (= 77 per cent) of the 200 families investigated, while in 46 (= 23 per cent) there were no cases of the disease. In 61 there were cases of cancer of the breast, in 28 cancer of the uterus or the ovary. In 10 of the families in which breast cancer was present, there were also cases of cancer of the two last named sites. In the 65 others there were cases of nearly every form of the disease except the otherwise so frequent skin- and lip cancers, which were not represented at all. In this connexion it must be remembered, however, that persons with cancers of these sites are often entirely unaware of the nature of their affection, which is therefore paid little heed to by the patient herself, and still less by the relatives. With a view precisely to this question, I asked both the probands and the controls, though, if any of their relatives had ever been treated at the Radium Center.

In 66 pedigrees, cancer was present only in the mother's family, in 24 only in the father's, in 46 both in the mother's and father's families, in 8 in brothers and sisters of the proband.

TABLE I

*Showing the Number of Cancer Cases among the Relations of the Probands.*

	Number	Total number of cases of cancer	Per cent	Number of cases of cancer of the breast
Mother .....	200	55	27.5	21
Father .....	199	40	20.1	1
Sister .....	381	30	7.87	13
Brother .....	377	16	4.24	—
Mother's mother ....	183	23	12.57	4
"    father.....	168	17	10.12	—
Father's mother .....	157	11	7.01	4
"    father .....	160	13	8.13	1
Mother's sister .....	316	51	16.14	17
"    brother .....	238	24	10.08	1
Father's sister .....	224	30	13.39	12
"    brother .....	236	15	6.36	—



The distribution of the total number of cancer cases on the different sites is shown in Table III.

Tables I and II show the cancer incidence among the relatives respectively of the probands and the controls. It will be seen that the incidence percentage, as would be expected if the disease is hereditary, is highest among the parents of the probands, considerably lower among the grandparents and the brothers and sisters of the parents, and lowest among the brothers and sisters of the probands themselves, which is due, of course, to the comparatively young age of the latter group. An evaluation of these frequencies is only possible after correction has been made for the age distribution, as it has been done in the calculation of the cancer risk in Chapter IX (see particularly Table XXIX).

In Table II it will be seen that also among the relatives of the controls the cancer incidence is highest among the parents of these. This is, in fact, rather surprising, since it, if we do not take into account the difference in frequency that may be due to different age distribution in the different categories of relatives, might be expected that the incidence would be the same in them all. I have been unable to find any explanation of this, unless perhaps the information of the controls respecting the occurrence of cancer in their families has been less exact than that of the probands; but as to that I can only say that the compilation and verification of the proband- and control materials has been done in the same manner and with the same thoroughness (cf. p. 35). A direct comparison of the the results shown in the two Tables can therefore only be of limited value, and that the chief importance must be attached to the conclusions that can be drawn from the calculated cancer risk figures.

#### THE CONTROL MATERIAL

Cancer was found in 58 (= 29 per cent) of the 200 families investigated, while in 142 (= 71 per cent) there were no cases of the disease. In 9 families there were cases of cancer of the

breast, in 8 of cancer of the uterus or the ovary. In none of the families were cancer of these different sites present together.

In 25 pedigrees, cancer was present only in the mother's family, in 23 only in the father's, in 4 both in the mother's and father's families, in 6 in brothers and sisters of the control.

TABLE II

*Showing the Number of Cancer Cases among the Relations of the Controls.*

Relationship	Number	Total Number of cases of cancer	Per cent	Number of cases of cancer of the breast
Mother .....	200	19	9.5	2
Father .....	199	19	9.5	—
Sister .....	433	8	1.84	2
Brother .....	389	4	1.31	—
Mother's mother ....	172	4	2.32	—
"    father.....	134	6	4.48	1
Father's mother .....	162	3	1.85	2
"    father .....	129	5	3.88	—
Mother's sister .....	312	6	1.92	—
"    brother .....	224	3	1.35	—
Father's sister .....	223	3	1.35	2
"    brother .....	305	1	0.33	—

The distribution of the total number of cancer cases on the different sites is shown in Table IV.

TABLE III  
Showing the Localisation of the 325 Cases of Cancer found in the Pedigrees of 154 of the Proband.

	Breast	Uterus	Ovary	Vulva	Mouth	Tongue	Esophagus	Stomach	Small intestine	Colon	Rectum	Pancreas	Liver	Gall bladder	Kidney	Urinary bladder	Prostate	Larynx	Lung	Maxilla	Brain	Nasopharynx and brain	Eye	Sarcoma of mesenteric gland	Sarcoma of shoulder blade	Pelvis	Leukemia	Myelomatosis	Unspecified	TOTAL		
Mother .....	21	9	3	1			13		2	2	2		2		1																1	55
Father .....	1						3	20	3	1	1	1	5			1	1	3						1							40	
Sister .....	13	8					4					2	1												2						30	
Brother .....							1	3	4	4	4				1				2		1										16	
Mother's mother ..	4	3	1		1	1	2	4		2	2		3	1			1														23	
" father ..					1		1	9	1		1		1			1												2			17	
Father's mother ..	4	1					1	1					1							2							1				11	
" father ..	1						1	7			1		2			1															13	
Mother's sister ...	17	4	6			1		10	2	1	2		2		1					1		1			1	1	1				51	
" brother ..	1						2	10		1	2		1		2	1			2			1				1					24	
Father's sister ....	12	6	2				5		1	1	1		2										1								30	
" brother ..							1	6		1	1	1				1	2			1								1			15	
TOTAL .....	74	31	12	1	2	2	12	92	3	13	17	4	20	1	5	4	2	6	4	4	4	1	1	1	1	1	1	1	6		325	

TABLE IV  
Showing the Localisation of the 81 Cases of Cancer found in the Pedigrees of 58 of the Controls.

Mother .....	2	2	1			4	1	1	1	2		1		1					1		1			1			1			1				1			19
Father .....					3	5	1	1		1	2		1	1	1																			1		1	19
Sister .....	2	2	1		1				1																								1			8	
Brother .....						1		1	1																											4	
Mother's mother .....						3																														4	
"    father .....	1			1		2				1		1																								6	
Father's mother .....	2										2																									3	
"    father .....					1	2																														5	
Mother's sister .....		2	1		1																															6	
"    brother .....						2																														3	
Father's sister .....	2		1																																	3	
"    brother .....					1																															1	
TOTAL.....	9	6	4	1	7	19	2	3	6	3	3	3	1	4	1	1	1	2	1	1	1	1	2	2	2	1	1	2	2	1	1	1	1	81			

*Chapter IV*

STATISTICAL METHODS EMPLOYED

1. EVALUATION OF THE INCIDENCE  
DISTRIBUTION

My object with a statistical analysis of the collected material is to obtain the best possible objective estimate of the relative frequency of carriers of the disposition to cancer in a number of families, because this is the only basis on which an investigation of the mode of hereditary transmission by comparison with the Mendelian figures can be made. As we here have to do with a disease which is not manifest at birth, but only becomes so later in life, the estimate respecting any particular family group must therefore take into account the age distribution within the latter, and the observed frequency must be corrected with regard to this distribution.

It must first be examined, however, if there can be any question of heredity, at all; that is if an indubitable increase in the frequency of the disease in the family groups of the proband can be demonstrated. Also here the age distribution is of primary importance, because the significance of an excessive number of cancer cases in the family can only be evaluated by comparison with the observed frequency of the disease in corresponding proband- and control groups when it is certain that the age distribution in this comparatively small material is the same within those groups.

The so-called  $\chi^2$  test (see Kemp<sup>55</sup>: *Statistiske Metoder i Medicin og Biologi*, p. 112) is a good objective measure for the degree of accordance between two distributions of frequency.

The principle of this test is that assuming the distributions to be the same (i.e. from the same population) the observed frequencies are compared with those calculated on the basis of that hypothesis, with the use of the formula  $\chi^2 = \sum \frac{(x_i - a_i)^2}{a_i}$ , in which  $x_i$  and  $a_i$  are respectively the observed and the calculated frequencies in class "i", and  $\sum$  the sum of all the classes.  $\chi^2$  is a collective, standardised expression for the difference between the observed distribution and the one calculated on the basis of the hypothesis, and the expression for  $\chi^2$  shows that the less agreement there is between the observed distribution and the calculated, the higher is  $\chi^2$ . What the value of  $\chi^2$  (i.e. the difference) should be before the hypothesis of agreement between the two observed distributions is rejected, must be determined by the law of distribution for  $\chi^2$ , which is presented in tabular form, for instance in Fisher & Yates's "Statistical Tables"<sup>39</sup>, where  $\chi^2$  is given as  $\chi^2 = \chi^2 (P, f)$ , and in Pearson's "Tables for Statisticians and Biometricians"<sup>83</sup> which give  $\chi^2 = \chi^2 (P, f + 1)$ ,  $P$  being the probability that the value of  $\chi^2$  will exceed the value observed, and  $f$  the so-called degree of freedom, which in the present investigations is determined by the number of age classes minus 1. In the present work I have used the Tables of Fisher & Yates.

The agreement is considered as satisfactory if the value found for  $\chi^2$  lies within the limits of 5 and 95 per cent; if it lies beyond the 1 per cent limit it must be supposed that the distributions are really different. It is important to remember, however, that the value obtained for  $\chi^2$  depends in a great measure on the division into classes, for any alterations in the compass of these or displacement of their limits may result in essential changes in the value. In important investigations where the classification according to age is not clearly defined, the  $\chi^2$  test must therefore be repeated with one or several other groupings (cf. p. 57).

The  $\chi^2$  distribution is also calculated with use of methods of approximation, which requires that in practical application it must be seen to that no  $x_i$  is smaller than 5. With series of

observations as small as those of which there is question here, this will often be the case, however, especially in the youngest and oldest age groups; but if so the difficulty may always be overcome by combining two or more groups into one. Of course, this cannot be done if there are only two age groups, but in such cases one may either use Fisher & Yates's correction or, better, the following exact solution, which is based on the elementary binomial theorem.

TABLE V

	Cancer	No Cancer	TOTAL
Probands	$\alpha$	$\beta$	$n_1 = \alpha + \beta$
Controls	$\gamma$	$\delta$	$n_2 = \gamma + \delta$
	$n_3 = \alpha + \gamma$	$n_4 = \beta + \delta$	$n = n_1 + n_2 = (n_3 + n_4)$

With  $P$  as expression for the (unknown) probability of finding one individual with cancer, the probability of finding  $\alpha$  with the disease among  $n_1$  individuals (and  $\beta = n_1 - \alpha$  without it) is  $\frac{n_1!}{\alpha! \times \beta!} \times p^\alpha (1-p)^\beta$ , where  $n_1!$  is, for instance,  $1 \times 2 \times 3 \times 4 \dots n_1$ . In the same way, the probability of finding  $\gamma$  with cancer among  $n_2$  is  $\frac{n_2!}{\gamma! \times \delta!} \times p^\gamma (1-p)^\delta$ . From this we get, by means of the multiplication formula of probabilities-calculation, that the chance of finding exactly the distribution  $\alpha, \beta, \gamma$  and  $\delta$  shown in Table V is

$$\frac{n_1!}{\alpha! \times \beta!} \times p^\alpha (1-p)^\beta \times \frac{n_2!}{\gamma! \times \delta!} \times p^\gamma (1-p)^\delta = \frac{n_1! \times n_2!}{\alpha! \times \beta! \times \gamma! \times \delta!} \times p^{n_3} (1-p)^{n_4} \quad (\text{a})$$

If we now keep to  $n_1, n_2, n_3$  and  $n_4$ ,—i.e. if we consider only groups of individuals representing those values, and only consider variations in  $\alpha, \beta, \gamma$  and  $\delta$ , the same formula (a) will

hold good for the probability of the possible distributions, only with the corresponding values for  $\alpha, \beta, \gamma$  and  $\delta$ .  $\frac{1}{\alpha_i! \beta_i! \gamma_i! \delta_i!}$  is thus, except for a constant factor  $k^*$ , a measure for the probability of finding a group with the distribution  $\alpha_i, \beta_i, \gamma_i$  and  $\delta_i$  among those with the marginal sums  $n_1, n_2, n_3$  and  $n_4$ . The probability  $P$ , which we are seeking, is (according to established convention) the probability of obtaining the existing distribution or one even more extreme, and is given by the equation

$$P = \frac{n_1! \times n_2! \times n_3! \times n_4!}{n!} \sum \frac{1}{\alpha_i! \beta_i! \gamma_i! \delta_i!}$$

and, also in accordance with convention, we will say that if  $P = 0.01$  the difference between the proband material and the control material is significant.

## 2. EVALUATION OF THE CANCER RISK

Since a satisfactory calculation of the risk of getting the disease is closely bound up with its manifestation, and since no evidence of the latter is obtainable, recourse can only be had to methods of approximation, with the use of a considerable material as basis for comparison. With  $P$  and  $P_s$  denoting respectively the cancer risk sought for and the risk in the material used for comparison, we have

$$\frac{P}{P_s} = \frac{a}{l_1 \times p_1 + l_2 \times p_2 \dots} = \frac{a}{\sum l_i p_i} \quad (1)$$

where  $a$  denotes the observed number of cancer cases,  $p_1, p_2, p_3 \dots$  the proportion between the number of cancers and non-cancers in the the respective age classes in the material used for comparison, and  $l_1, l_2, l_3 \dots$  the number of non-cancers under observation in the middle of the classes.  $p_i$  then covers both the incidence of latent carriers and the degree of

\* The factor  $k$  is determined by the sum of the probabilities of the possible result as 1; whereby we obtain  $k = \frac{n_1! \times n_2! \times n_3! \times n_4!}{n!}$



manifestations.  $\sum l_i p_i$  denotes the number of cancers expected in the observation material when the conditions in the material used for comparison are made to apply to the latter.  $P$  can then be calculated by means of (I), since we by approximation get  $P_s = p_1 + p_2 + p_3 \dots = \sum p_i$ , so that

$$P = \frac{a (p_1 + p_2 + p_3 \dots)}{l_1 \times p_1 + l_2 \times p_2 \dots} = \frac{a \sum p_i}{\sum l_i p_i}$$

The formula shows that  $p_i$  only enters with the proportional relation; that is so say that in using it is not necessary to determine the actual frequencies, but the proportional values will suffice. The fraction  $\frac{l_1 \times p_1 + l_2 \times p_2 \dots}{p_1 + p_2 \dots}$  is usually termed the reduced proportional value ("Bezugsziffer"). It follows as a matter of course that the values found for the cancer risk cannot be subjected to any calculation of standard error.

This method of calculating the risk will be explained in greater detail in Chapter IX, with an example of its application.

## Chapter V

### ESTIMATION OF THE DISTRIBUTION OF BREAST CANCER ACCORDING TO AGE AT FIRST MANIFESTATION OF THE DISEASE

Age distribution curves for breast cancer materials have hitherto oftenest been worked out on the basis of mortality statistics, though these are, in fact, unsuitable for the purpose because the length of survival, even for untreated cases, varies from a few to many years and a number of the patients are cured and thus disappear from the materials.

In 1932, Taylor<sup>101</sup> worked out a morbidity curve based on 6085 cases collected from the literature, which he divided into 10-year groups according to the patients' ages at the time of operation. As it will be seen from Fig. 1, he thereby obtained a single-peaked curve with its greatest height in the age group 40-50. Similarly, Wainwright obtained, with an age distribution of 608 patients into 5-year groups, a single-peaked morbidity curve with its greatest height at 50 years. These 608 were, however, only a part of a material collected for other purposes, and it is not stated why a selection was made; neither is it possible to see whether they were cases that had been treated only once, or if there were recurrences included among them.

I chose to arrange my own material according to the age of the patients at the time when the first treatment was instituted and the histologic diagnosis established with certainty. The ideal choice would of course have been the

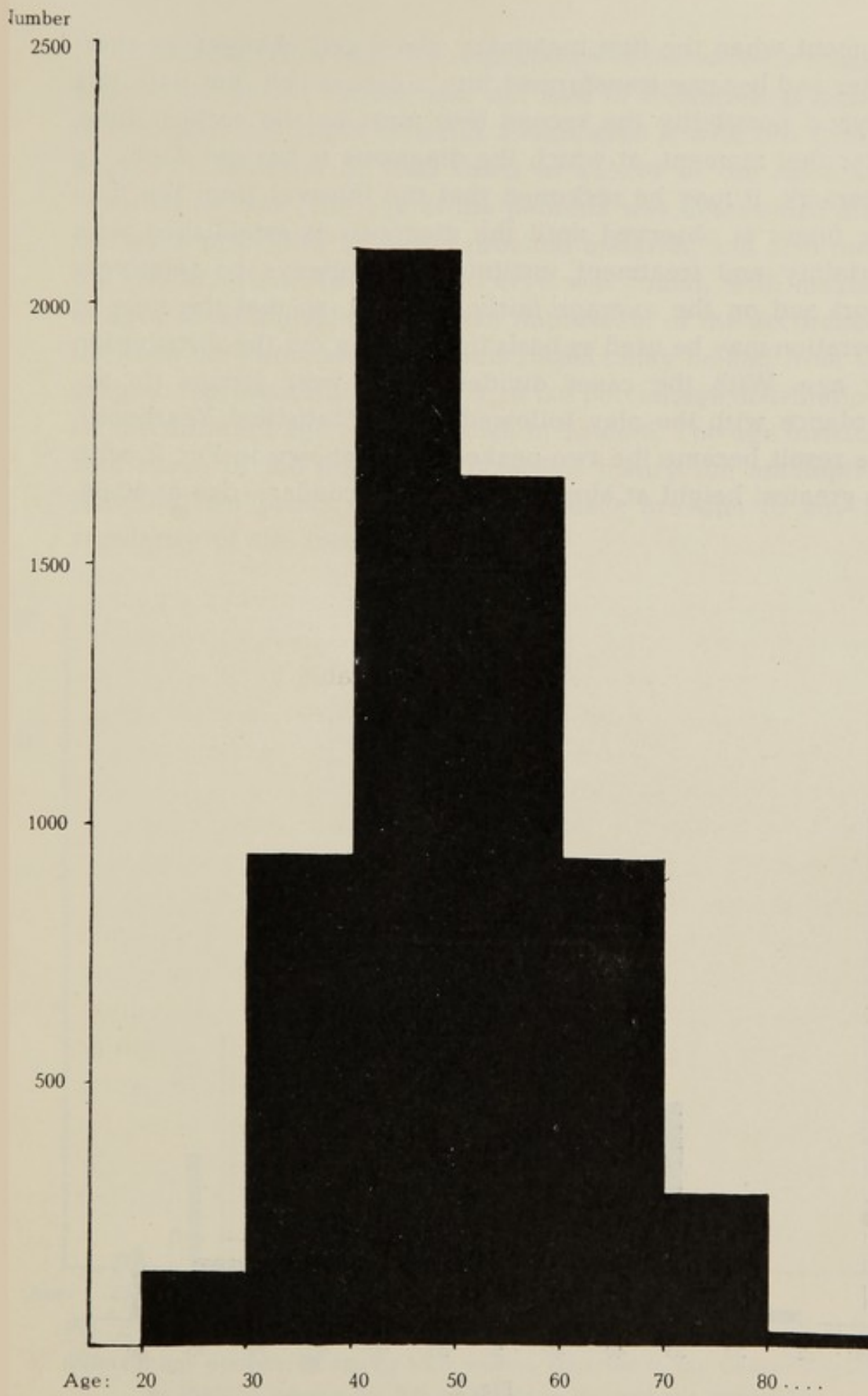


Fig. 1.

moment when the first mammary gland cell changes its character and became transformed into a cancer cell; but with this beyond possibility the second best must be the earliest time, after that moment, at which the diagnosis is beyond doubt. In Denmark, it may be reckoned that the interval from the time the tumor is observed until the diagnosis is established with certainty and treatment instituted will always be relatively short and on the average fairly constant, so that the time of operation may be used as basis for working out the distribution by age. With the cases divided into 5-year groups (in accordance with the plan followed in the Statistical Yearbook), the result became the two-peaked curve shown in Fig. 2, with its greatest height at ages 45-49 and a secondary rise at 60-64.

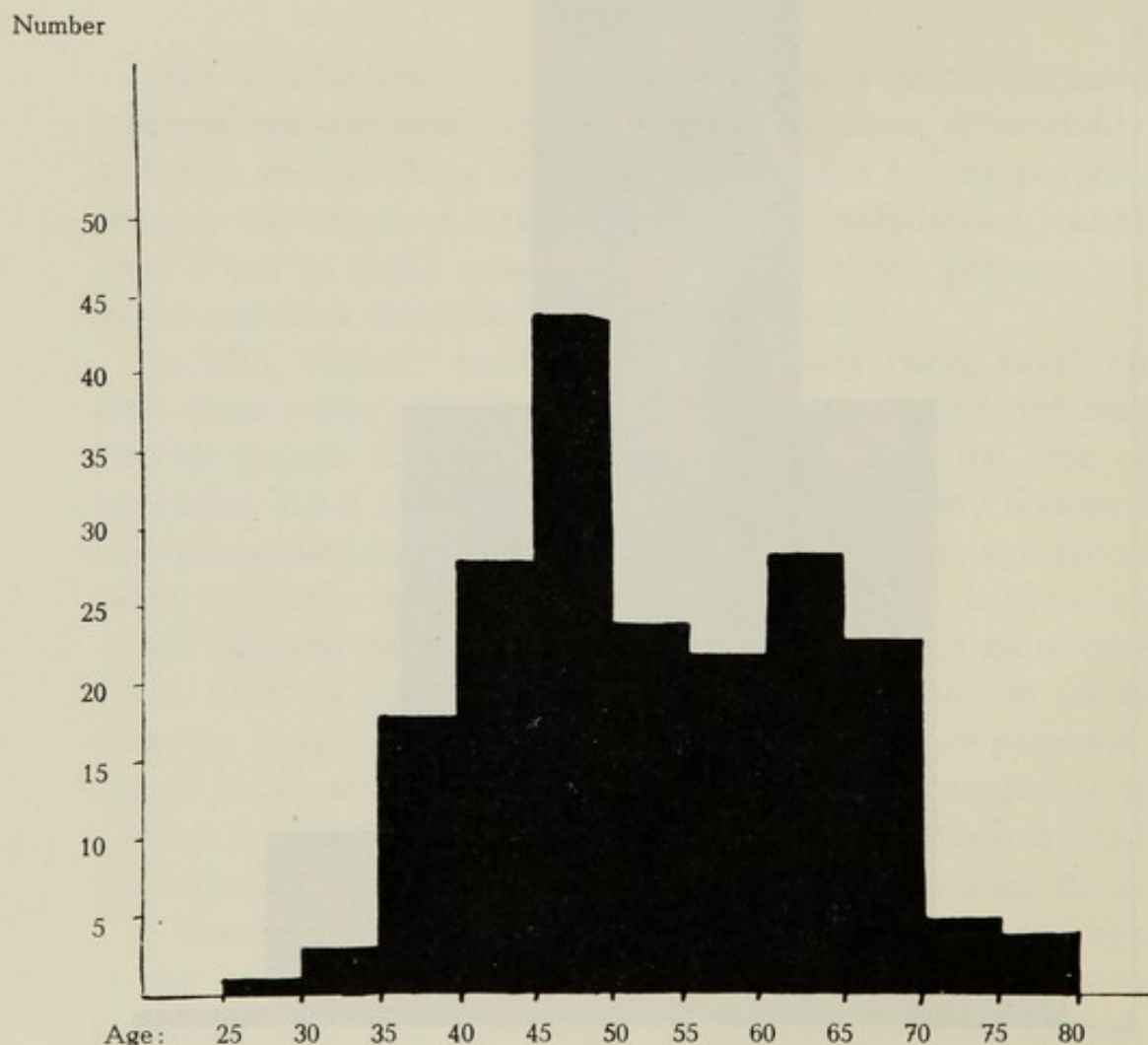


Fig. 2.

In order to show that this appearance of the curve is characteristic for breast cancer and not due to fortuitous selection in the relatively small material, I compared it with the Cancer Registry's material of 1565 cases of cancer of the same site reported in 1942. The age of the patients was determined after the same principles as in my proband material, and also there the characteristic two-peaked curve was found, with maxima at ages 45-49 and 60-64. A direct impression of the accordance between the two materials in this respect may be had from the graphic representation, in Fig. 3, of the percentage distributions on the different age groups shown in Table 6. The age distribution curve of the population does not justify the assumption that the two peaks of the present curve are due to any irregularity of the former.

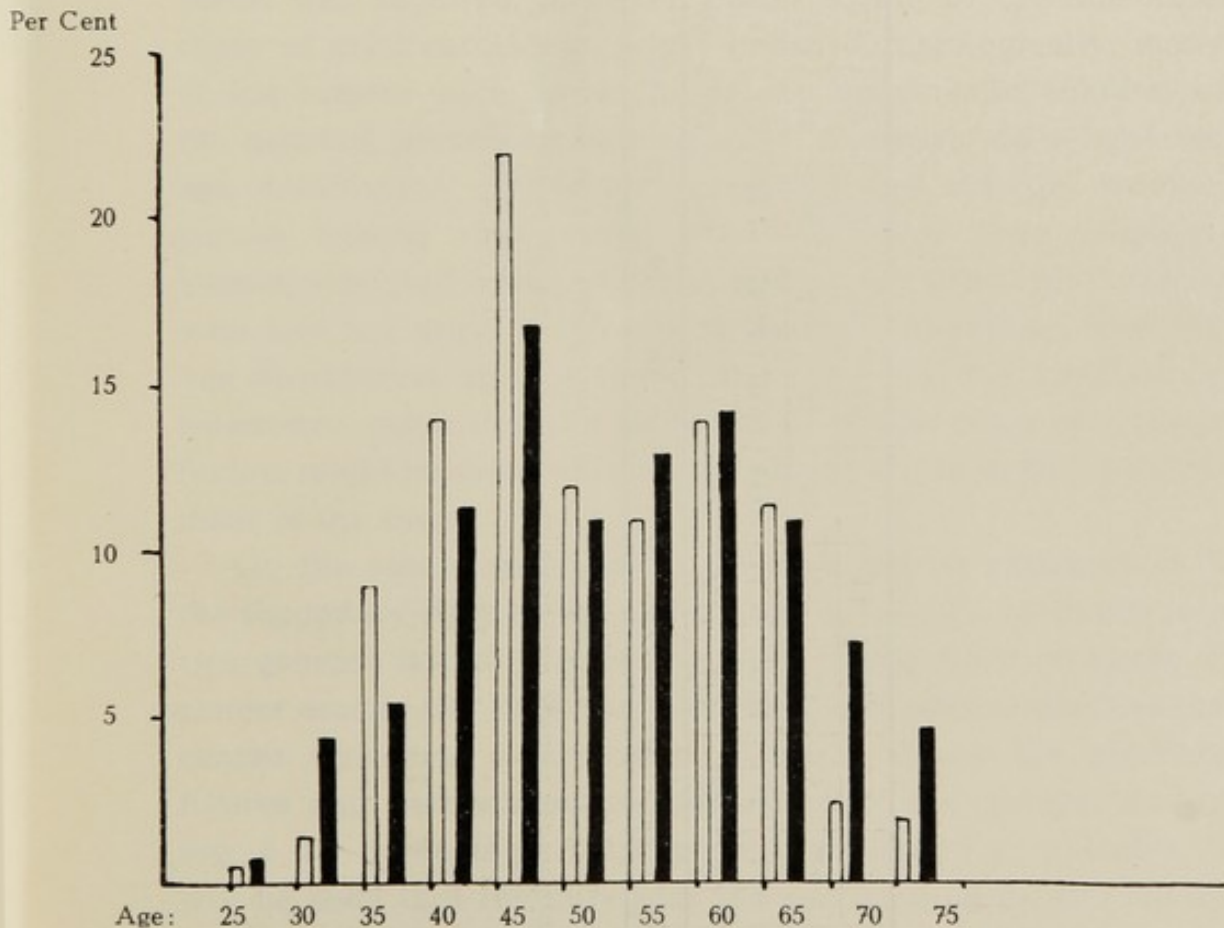


Fig. 3.— Diagram showing the relative frequency of breast cancer at the different age periods: ■ among 1565 women reported to the Cancer Registry in 1942; □ among the 200 probands in the author's material.

TABLE VI  
 Showing the absolute and relative Frequency of Breast Cancer at different Age Periods in the Author's Material of 200 Probands, as compared with a Material of 1565 Cases from the Cancer Registry.

Age	0	25	30	35	40	45	50	55	60	65	70	75	TOTAL	
1565 Patients from the Cancer Registry	Absolute	.3	8	69	87	175	262	172	204	223	171	115	76	1565
	Per Cent		0.70	4.41	5.56	11.18	16.74	10.99	13.04	14.25	10.98	7.35	4.86	100.06
200 Probands	Absolute	0	1	3	18	28	44	24	22	28	23	5	4	200
	Per Cent		0.5	1.5	9	14	22	12	11	14	11.5	2.5	2	100

A numerical expression for the accordance is obtained if we merge all the age classes under 40 into one group and all those above 65 into another, and thus working with 7 age groups apply the  $\chi^2$  test. We then find  $\chi^2 = 8.923$ ,  $f = 6$ , and thus  $0.20 > P > 0.10$ .  $P = 0.18$ , which is to say that there is good accordance between the two materials.

The distribution curve Fig. 2 being two-peaked, the question arose whether this is characteristic for cancer of the breast or is due to overlapping of two single-peaked curves. Clinically, it is estimated that scirrhous carcinoma of the breast occurs at a later age than the medullary, more malignant forms of cancer; I therefore tried to separate the curves by sorting out the cases belonging to each according to the histologic diagnoses given on the filing-cards of the Cancer Registry. The result was negative, however, partly owing to the numerous cases of solid carcinoma, partly because, histologically, many of the tumors were mixed forms. An anamnestic analysis of the material proved equally negative. Comparisons of separate age distribution curves for unmarried and married women, parous women and women who had never been pregnant, women who had borne children and nursed them, and women who had not nursed, showed no marked deviations from the age distribution already found. The same was the result of an estimation respecting the probands in whose cases exogenous factors might be supposed to have played a rôle in the development of the tumor.

On the other hand it seems that we get an explanation of the secondary peak of the curve if we divide the probands into two groups: the 46 in whose families there were no cases of cancer among the relatives, and the 154 in whose families the cancer tendency was present. Table 7 shows the absolute figures and percentages for the different age groups, and in Fig. 4 the percentage distribution is presented graphically. It will be seen that the curve for the probands of cancer family has a single high point at age 45-50, whereas the curve for probands of non-cancer family is two-peaked, with maxima at ages 40-44 and 60-70. The last peak reaches at least the same

TABLE VII  
 Showing the absolute and relative Frequency of Breast Cancer in 154 Proband's with hereditary Predisposition to Cancer, as compared with 46 in whom no hereditary Taint had been ascertained.

Age	25		30		35		40		45		50		55		60		65		70		75		TOTAL
	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	Absolute	Per cent	
Taint	Absolute	1	2	17	20	37	21	18	18	13	4	3											154
	Per cent	0.65	1.3	11.04	12.99	24.03	13.64	11.69	11.69	8.44	2.6	1.95											100.02
No taint	Absolute	0	1	1	8	7	3	4	10	10	1	1											46
	Per cent		2.17	2.17	17.39	15.22	6.52	8.70	21.74	21.74	2.17	2.17											99.99



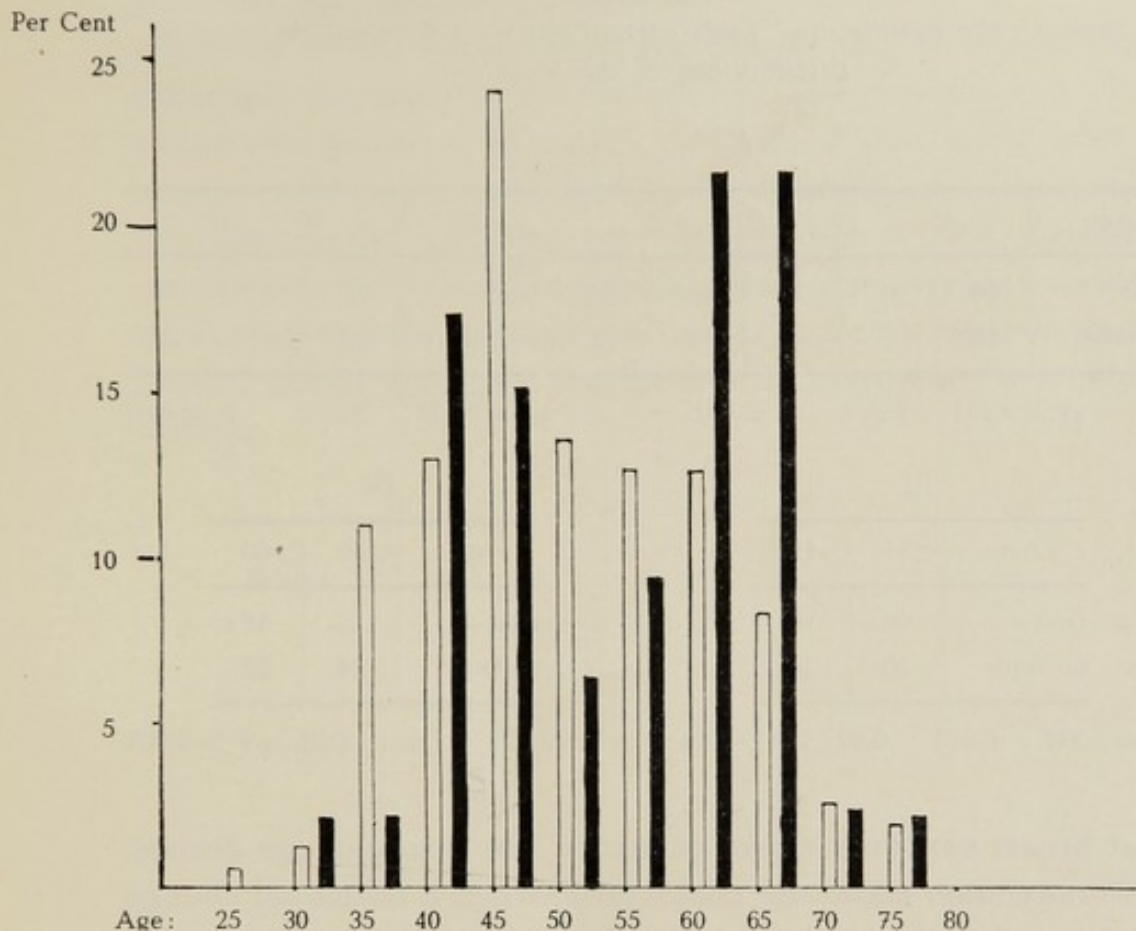


Fig. 4.—Diagram showing the relative frequency of cancer at the different age periods: □ in 154 families in which hereditary predisposition to cancer was present; ■ in 46 families in which there was no hereditary predisposition.

level as the first, and must be supposed to be the cause of the secondary rise demonstrated for the material as a whole.

In order to find out if this deviation in the picture is significant, I applied the  $\chi^2$  test. In accordance with what was said on p. 46, I made it with diverse divisions into age groups, and as it will be seen from Table 8, the results seem to show that the difference is real.

This observation, made on a small material collected for another purpose seems to me interesting, and similar analyses of age distribution and inherited susceptibility in future genetic studies on cancer must be awaited before the cause of the differences can be finally explained.

The curve for the probands with cancer in the family shows

TABLE VIII  
 Showing the Results of  $\chi^2$  Tests carried out with different Age-Group  
 Distributions of the Material.

I						II			
Age	0	45	50	60	65 . . . .	Age	0	50	60 . . . .
taint	40	37	39	18	20	taint	77	39	38
no taint	10	7	7	10	12	no taint	17	7	22
$\chi^2 = 9.431$ $f = 4$ $P = 0.05$						$\chi^2 = 9.182$ $f = 2$ $P = 0.01$			
III			IV						
Age	<55	>55	Age	<60	>60				
taint	98	56	taint	116	38				
no taint	20	26	no taint	24	22				
$\chi^2 = 5.949$ $f = 1$ $0.02 > P > 0.01$			$\chi^2 = 9.039$ $f = 1$ $0.01 > P > 0.001$						

that breast cancer in these occurs in the younger age groups, with maximum about the climacteric, when a hormonal change sets in; while the curve for those with no cancer in the family shows that in these breast cancer oftenest occurs at two periods, the first about the climacteric, the second and principal one about the age of 60 to 70. The question is whether the cancer in these individuals of no-cancer families has developed unconditioned by any hereditary tendency, or whether the absence of the hereditary factor is only apparent, due to the fact that the familial investigation has not extended far enough; in other words, whether cancer of the breast should be considered, pathogenetically, as one or two diseases.

The question is important because the calculations of the frequency of carriers of the taint hinges upon it. Since there is no certainty that the families of the apparently untainted are surely cancer-free, they cannot be eliminated genetically; therefore they are also included in the following calculations. The displacement of the apparently untainted toward the right in the age-distribution curve can be explained, too, if we

presume that cancer of the breast is dependent on inherited tendency. If the development depends in the first place on an inherited disposition, but besides on the intervention of an exogenous factor, it is readily understood that those with the heavier taint become grouped in the younger age classes, while the apparently untainted live longer before the neoplastic growth manifests itself. In genetic terms, this may be expressed by saying that the tainted are homozygotic as regards one or several genes, whereas the apparently non-tainted are heterozygotic.

Chapter VI

COMPARISON OF THE AGE DISTRIBUTION FOR CORRESPONDING GROUPS OF RELATIVES OF PROBANDS AND CONTROLS

The individuals of each group of relatives, both of the cancer patients and the controls, were divided into 5-year groups, based for the living on the age at time of examination, for the dead on the age at time of death. The  $\chi^2$  distribution was used as means of testing the agreement between the corresponding groups of the two materials. The result was as follows

TABLE IX

MOTHERS

Age	0	30	35	40	45	50	55	60	65	70	75	80	85	Total
Probands	2	5	5	6	5	15	16	12	27	41	36	15	15	200
Controls	1	7	6	7	6	8	19	17	23	46	21	19	20	200

$$\chi^2 = 9.312 \quad f = 11 \quad 0.70 > P > 0.50$$

Very good agreement.

TABLE X

FATHERS

Age	0	30	35	40	45	50	55	60	65	70	75	80	85	Total
Probands	1	4	8	4	11	17	11	19	31	30	30	23	10	199
Controls	3	1	9	10	13	8	14	19	29	35	30	17	11	199

$$\chi^2 = 7.110 \quad f = 9 \quad 0.70 > P > 0.50$$

Very good agreement.

TABLE XI

## SISTERS

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	25	9	27	35	52	46	51	53	41	19	13	4	3	3	381
Con-trols	44	15	35	48	51	50	64	39	47	25	11	3	1	0	433

$$\chi^2 = 13.235 \quad f = 10 \quad 0.30 > P > 0.20$$

Very good agreement.

TABLE XII

## BROTHERS

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	22	12	30	35	50	53	49	48	42	21	9	4	1	1	377
Con-trols	29	10	34	32	54	46	58	41	37	22	20	4	2	0	389

$$\chi^2 = 7.804 \quad f = 11 \quad 0.80 > P > 0.70$$

Very good agreement.

TABLE XIII

## MATERNAL GRANDMOTHERS

Age	0	30	35	40	45	50	55	60	65	70	75	80	85	Total
Probands	5	6	7	6	4	8	7	11	14	37	24	22	32	183
Controls	5	10	6	5	1	3	3	4	11	49	22	27	26	172

$$\chi^2 = 11.384 \quad f = 7 \quad 0.20 > P > 0.10$$

Good agreement.

TABLE XIV

## MATERNAL GRANDFATHERS

Age	0	30	35	40	45	50	55	60	65	70	75	80	85	Total
Probands	0	7	4	14	3	13	6	13	16	31	19	25	17	168
Controls	2	5	1	4	2	6	7	7	3	50	12	18	17	134

$$\chi^2 = 16.840 \quad f = 5 \quad 0.01 > P > 0.001$$

No agreement.

The difference is greatest in the age groups 70-75, but as the control material is the largest, numerically, in this group, the comparison of the observed frequencies of cancer in the two materials will not be compromised.

TABLE XV

## PATERNAL GRANDMOTHERS

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	0	1	11	7	4	2	5	2	7	17	43	20	19	19	157
Controls	1	1	9	3	4	1	3	3	6	5	53	30	23	20	162

$$\chi^2 = 9.372 \quad f = 7 \quad 0.30 > P > 0.20$$

Good agreement.

TABLE XVI

## PATERNAL GRANDFATHERS

Age	0	30	35	40	45	50	55	60	65	70	75	80	85	Total
Probands	1	15	2	7	4	3	5	18	8	46	21	21	9	160
Controls	2	5	4	4	2	2	1	3	7	53	15	19	12	129

$$\chi^2 = 12.427 \quad f = 7 \quad 0.10 > P > 0.05$$

Agreement.

TABLE XVII

## MATERNAL AUNTS

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	19	7	5	7	9	10	16	24	28	32	65	44	35	15	316
Controls	19	13	5	7	5	6	17	21	39	40	69	42	19	10	312

$$\chi^2 = 12.983 \quad f = 13 \quad 0.50 > P > 0.30$$

Very good agreement.

TABLE XVIII

## MATERNAL UNCLES

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	17	2	5	2	5	5	15	22	26	33	61	24	13	8	238
Con-trols	15	4	5	4	10	5	16	19	22	28	40	37	14	5	224

$$\chi^2 = 10.768 \quad f = 9 \quad 0.30 > P > 0.20$$

Very good agreement.

TABLE XIX

## PATERNAL AUNTS

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	20	5	5	5	5	3	13	18	21	21	44	24	28	12	224
Con-trols	11	4	4	2	7	5	8	13	25	31	65	26	11	11	223

$$\chi^2 = 17.866 \quad f = 10 \quad 0.10 > P > 0.05$$

Agreement.

TABLE XX

## PATERNAL UNCLES

Age	0	25	30	35	40	45	50	55	60	65	70	75	80	85	Total
Pro-bands	25	2	3	8	8	5	8	11	19	31	57	26	20	13	236
Con-trols	12	3	4	4	8	10	13	23	29	39	99	40	13	8	305

$$\chi^2 = 22.488 \quad f = 10 \quad 0.02 > P > 0.01$$

No positive agreement.

NOTE.—If the age group 0-25 is left out, we get  $\chi^2 = 13.858$  and  $f = 9$ , with  $0.20 > P > 0.10$ , and thus good agreement between the age distributions in the groups of the two materials. In the proband material, the youngest age group is the largest, numerically; therefore the figures for observed cancer cases become minimum figures.

*Chapter VII*

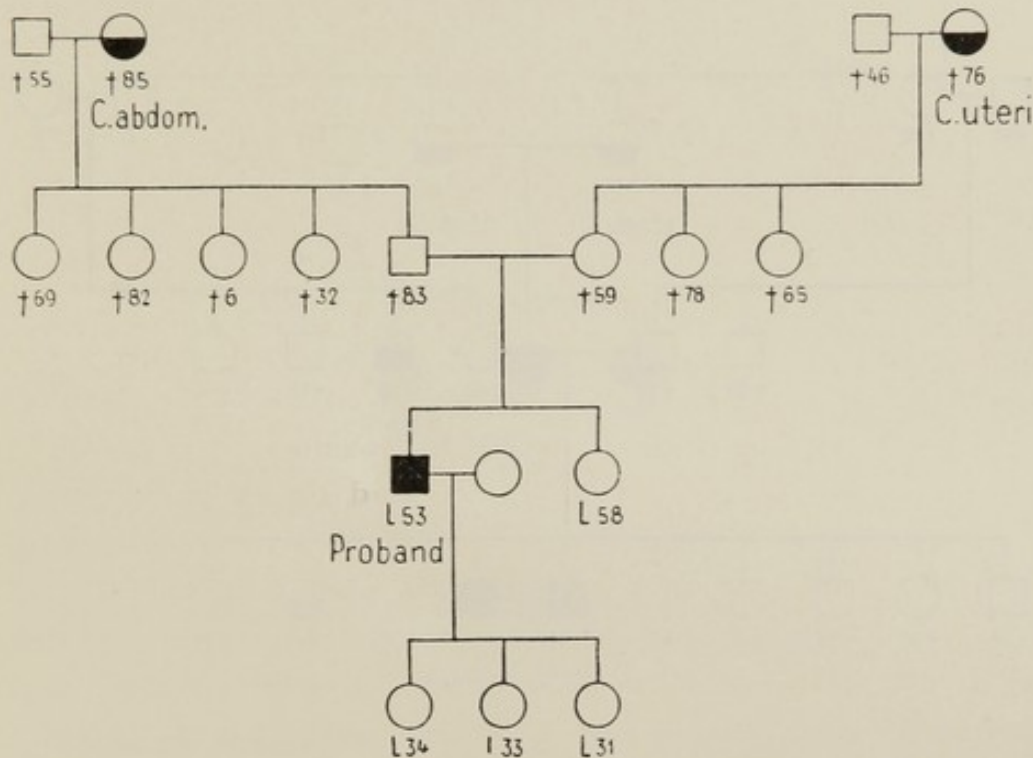
BREAST CANCER IN MALES

Breast cancer in males is comparatively rare. Kristian Poulsen<sup>88</sup> says in his study on mammary tumors that the frequency is about 1 per cent, and in all recent considerable materials it is stated to be between 1 and 2 per cent. That cancer with this localisation is so uncommon in men is undoubtedly because the mammary gland of the male has no actual function and does not undergo the cyclic changes due to the action of the female sexual hormones. In this connexion it must again be mentioned that experiments on animals have shown that the injection of folliculin in male mice of cancer strains may result in the development of malignant mammary tumors; i.e. that the multiplication of hereditary disposition and folliculin together may be the cause of the disease manifesting itself.

If the theory of the rôle of heredity in the etiology of breast cancer holds good, it must, since one of the factors determining the onset of the disease is absent in the male, be expected that the taint in these is correspondingly severer; and if genetic research can prove this to be the case, it will have some weight as proof of the correctness of the theory. In my proband material there are 3 males with cancer of the breast (pedigrees nos. 8, 30 and 58), and in their families there were not only subjects with other cancers, but also cases of breast cancer. This caused me to extend the investigation by a search for other male cases, but I was only able to find 5, all living in,



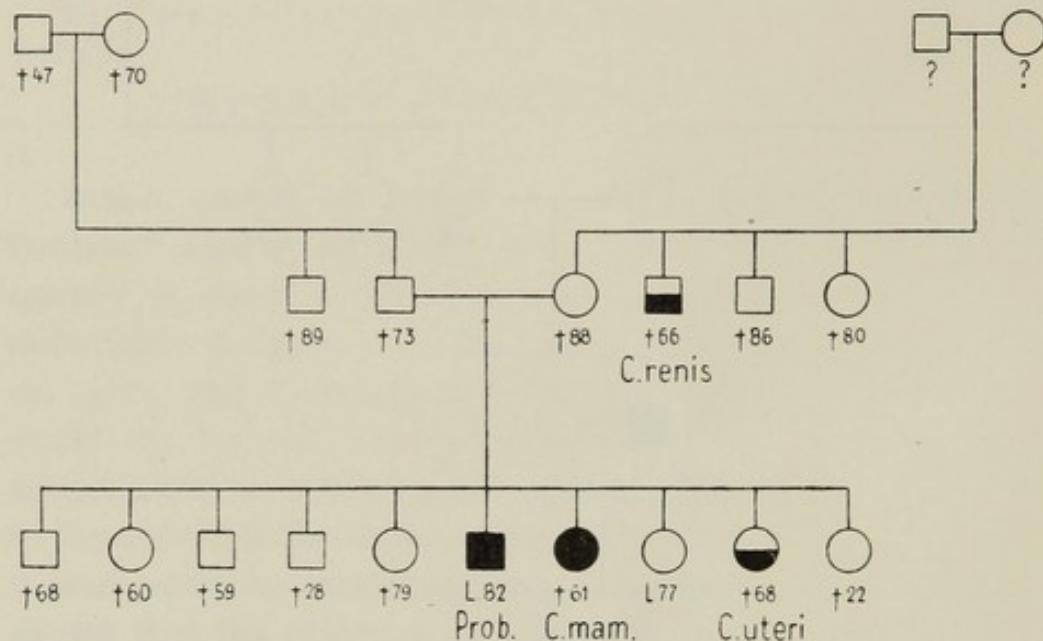
or near Copenhagen; and of these, 2 were unfortunately of no use for the investigation, because they knew little about their family and had no relations living. The results of the examination of the other three were, however, so interesting that I shall briefly give their case histories and pedigrees.



*Proband* (Radium Center, no. 12775):  $\square$  Born in Copenhagen Feb. 6th, 1882. Piano-mover. Married. Died March 3rd, 1937. Formerly well, father of three children. No previous affection of the breast. Two years before he noticed a swelling there, a piano had fallen over him and had pressed hard against the right side of his thorax. There had come large extravasations of blood about the right nipple. During the following four months he had been aware of a slowly growing lump under the latter, and when a suppurating eczema developed there he had consulted a physician and had been treated with compresses. Histologic diagnosis of the specimen from the operation: Adenocarcinoma.

*Father's mother.* ○ Born Nov. 7th, 1828. Widow. Died in Copenhagen Feb. 7th, 1914, of cancer of the abdomen. The diagnosis verified by death certificate.

*Mother's mother.* ○ Born 1828. Widow. Died in Copenhagen Oct. 24th, 1905, of uterine cancer. The diagnosis verified by death certificate.

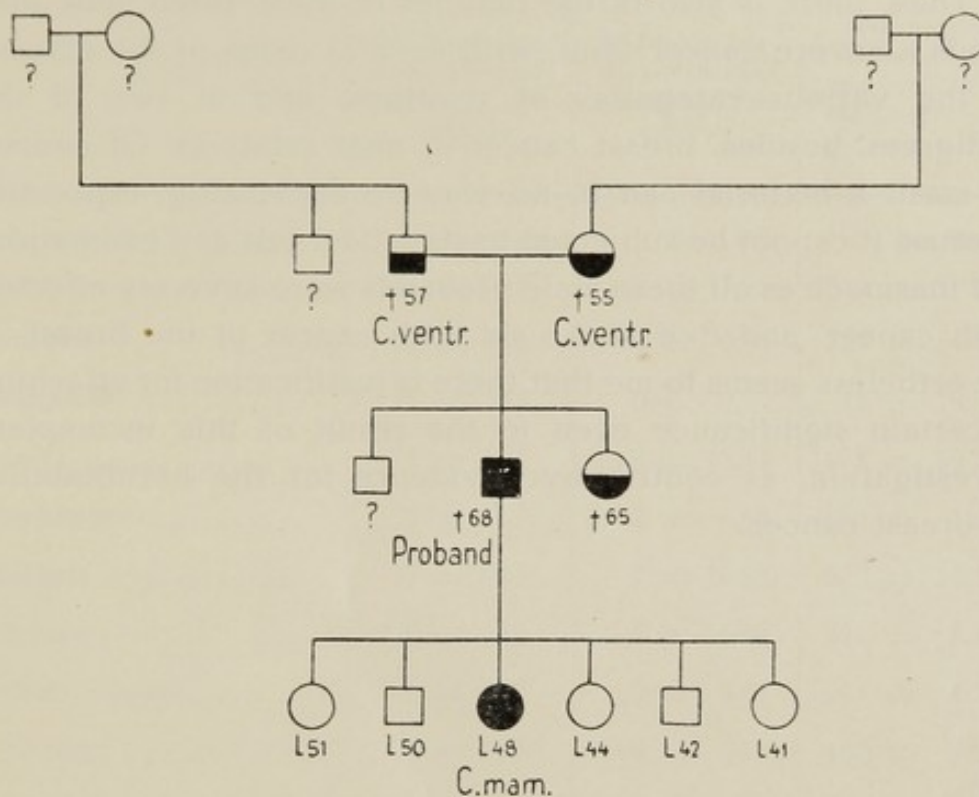


*Proband* (Radium Center, no. 16533). □ Born in Copenhagen July 12th, 1861. Manufacturer. Married. Formerly well, except for a nephrolithiasis, for which he underwent an operation in 1928. No previous mammary affection. He had not noticed the swelling in the right breast until a few days before he was admitted to the Radium Center. Histologic diagnosis of the specimen from the operation: Solid carcinoma.

*Third sister.* ○ Born 1866. Died in Copenhagen Sep. 7th, 1927, of cerebral tumor and had previously been operated on for cancer of the breast. The diagnosis verified by death certificate.

*Fifth sister.* ○ Born Aug. 15th, 1869. Died in Copenhagen May 20th, 1940, of cancer of the uterus. The diagnosis verified by death certificate.

*Mother's eldest brother.* □ Born Nov. 27th, 1830. Died Aug. 7th, 1897, of cancer of the kidney. The diagnosis verified by death certificate.



*Proband* (Roentgen Clinic of the Copenhagen Municipal Hospital, no. 2275). □ Born in Roskilde Oct. 15th, 1866. Workingman. Divorced. Father of six children. No preceding trauma or benign tumor. The swelling in the breast noticed a few months before his admission to the Municipal Hospital in 1931. Histologic diagnosis of specimen from the operation: Solid, myxomatous carcinoma.

*Father.* Born 1832. Died in Copenhagen Dec. 4th, 1889, of cancer of the stomach. The diagnosis verified by death certificate.

*Mother.* Born 1840. Died May 14th, 1915, of cancer of the stomach. The diagnosis verified by death certificate.

*Sister.* Born Dec. 13th, 1870. Died in Copenhagen July 23rd, 1936, of cancer of the stomach. The diagnosis verified by death certificate.

*Second daughter.* Born Nov. 14th, 1896. In 1930 treated at the Radium Center for carcinoma of the breast with metastases to the thorax.

Thus, there is also in the families of these three male probands a severe cancer taint, with several cases of the disease in the various categories of relations, and in two of the pedigrees, besides, breast cancer in near relatives. Of course, so small a material can in no way be convincing, especially because it cannot be subjected to statistical test and estimation; but inasmuch as all these male probands were severely affected with cancer, and five of the six with cancer of the breast, it nevertheless seems to me that there is justification for attaching a certain significance even to the result of this incomplete investigation, as contributive evidence for the heriditability of breast cancer.

TABLE XXI

Showing the relative Frequency of Cancer of different Sites in the female Relations of the Probands, as compared with the Control Material and a Material of 5066 female Cases from the Cancer Registry.

SITE	200 female relations in the pedigrees of the probands	43 female relations in the pedigrees of the controls	5066 female cases (living and dead) from the Cancer Registry
	Per Cent	Per Cent	Per Cent
Uterus .....	31 = 15.5	6 = 13.95	814 = 16.07
Ovary .....	12 = 6.0	4 = 9.30	223 = 4.40
Genitals .....	1 = 0.5	0 = 0	44 = 0.87
Breast.....	71 = 35.5	8 = 18.61	975 = 19.25
Esophagus .....	3 = 1.5	2 = 4.65	83 = 1.64
Stomach .....	37 = 18.5	7 = 16.28	679 = 12.40
Intestine .....	6 = 3.0	3 = 6.98	421 = 8.31
Rectum, Anus.....	7 = 3.5	2 = 4.65	243 = 4.80
Abdomen .....	12 = 6.0	0 = —	487 = 9.61
Skin .....	0 = —	2 = 4.65	240 = 4.74
Lip .....	0 = —	0 = —	13 = 0.26
Upper air passages.....	1 = 0.5	0 = —	46 = 0.91
Upper alimentary tract..	3 = 1.5	0 = —	41 = 0.81
Lung.....	0 = —	1 = 2.33	79 = 1.56
Urinary tract.....	2 = 1.0	2 = 4.65	128 = 2.53
Lymphogranuloma.....	0 = —	0 = —	47 = 0.93
Leukosis .....	3 = 1.5	0 = —	88 = 1.74
Nervous system.....	0 = —	1 = 2.33	113 = 2.23
Other organs.....	9 = 4.5	3 = 6.98	179 = 3.53
Sarcoma .....	2 = 1.0	2 = 4.65	123 = 2.43
	200 = 100	43 = 100.01	5066 = 100.02

TABLE XXII

Showing the relative Frequency of Cancer of different Sites in the male Relations of the Probands, as compared with the Control Material and a Material of 3982 male Cases from the Cancer Registry.

SITE	125 male relations in the pedigrees of the probands	38 male relations in the pedigrees of the controls	3982 male cases (living and dead) from the Cancer Registry
	Per Cent	Per Cent	Per Cent
Breast.....	3 = 2.4	1 = 2.63	4 = 0.1
Esophagus .....	9 = 7.2	5 = 13.16	137 = 3.44
Stomach .....	55 = 44.0	12 = 31.58	925 = 23.23
Intestine .....	10 = 8.0	3 = 7.89	321 = 8.06
Rectum, Anus.....	10 = 8.0	4 = 10.53	390 = 9.80
Abdomen .....	11 = 8.8	4 = 10.53	289 = 7.26
Skin .....	0 = —	0 = —	306 = 7.68
Lip .....	0 = —	0 = —	116 = 2.91
Upper air passages .....	3 = 2.4	0 = —	79 = 1.98
Upper alimentary tract..	1 = 0.8	1 = 2.63	42 = 1.07
Lung.....	4 = 3.2	1 = 2.63	239 = 6.00
Genitals.....	2 = 1.6	1 = 2.63	326 = 8.19
Urinary tract .....	7 = 5.6	3 = 7.89	182 = 4.57
Lymphogranuloma .....	0 = —	0 = —	71 = 1.78
Leukosis .....	2 = 1.6	1 = 2.63	115 = 2.89
Nervous system.....	2 = 1.6	0 = —	136 = 3.42
Other organs.....	5 = 4.0	1 = 2.63	165 = 4.41
Sarcoma .....	1 = 0.8	1 = 2.63	139 = 3.49
	125 = 100	38 = 99.99	3982 = 100.03

*Chapter VIII*

COMPARISON OF THE OBSERVED  
FREQUENCIES OF CANCER IN CORRES-  
PONDING CATEGORIES OF RELATIONS  
IN THE PROBAND- AND CONTROL  
MATERIALS

As the problem is presented, a comparative estimation of the cancer incidence in the corresponding categories of relations naturally falls into three parts: (1) comparison of the incidences of breast cancer, (2) of the incidences of endogenous cancer as a whole, (3) of the incidence of uterine and ovarian cancer. That it has been necessary to introduce a new concept: endogenous cancer as a whole, is because, as already said, the cases of cancer found in the pedigrees of the probands do not include all the forms of the disease.

The appended Tables XXI and XXII show the percentages of observed cancers of different sites, for women and men separately, in the proband material, and, for comparison with this, the corresponding observations both from the control material and from the material of 5066 women and 3982 men from the Cancer Registry, which in the following will be used for estimation of the cancer risk. It will be seen that there are no cases of skin- or lip cancer in the families of the probands, while the incidence of cancer of other sites is more or less the same in the three materials, except as regards the breast, where the deviation is considerable, and some minor deviations in the other groups. As experience seems to show that the development of such tumors as lip- and skin cancer is chiefly

conditioned by exogenous factors, whereas the development of breast cancer depends on endogenous, hereditary factors, the other forms of tumor must be supposed to be grouped between these two extremes, since the development of cancer of different sites is determined firstly by a hereditary disposition, secondly by endogenous and exogenous factors of more or less unknown nature and action.

As I in this investigation have worked with probands whose cancer is chiefly of endogenous, hereditary character, it is natural that the endogenous forms of the disease should be those oftenest occurring in the pedigrees, and that the exogenous are not represented. Consequently, the cases of cancer of different sites found among the relatives of the probands cannot be spoken of as "cancer of all sites"; therefore, I have chosen the term: endogenous cancer as a whole, as collective expression for the cancers of various sites occurring in the families carrying the taint.

In the following is given a survey of the relative frequency of cancer in corresponding categories of relations, in the same order as in the foregoing. The results are given in tabular form, and the observed figures on which the calculations are based are those given in Tables I and II.

1. THE RELATIVE FREQUENCY OF BREAST CANCER  
IN CORRESPONDING CATEGORIES  
OF RELATIONS

The P-value calculated by the Method described p. 47.

TABLE XXIII

	P	Remarks
Mother .....	0.00012	Significant increase
Sister .....	0.0016	" "
Mother's sister .....	< 0.00001	" "
Father's sister .....	0.00596	" "
Mother's mother .....	0.06950	No increase
Father's mother .....	0.3275	"



The Table shows that while there is no increase in the frequency of breast cancer in the comparatively small, "thinned-out" groups of grandmothers, the increase in the other categories of relatives is statistically significant.

2. COMPARISON OF THE FREQUENCY  
OF ENDOGENOUS CANCER AS A WHOLE IN CORRES-  
PONDING CATEGORIES OF RELATIONS WITH  
THE  $\chi^2$  TEST

TABLE XXIV

	$\chi^2$	f	P	Remarks
Mother .....	21.489	1	< 0.001	Significant increase
Father .....	8.802	1	0.01 > P > 0.001	" "
Sister .....	16.539	1	< 0.001	" "
Brother .....	6.573	1	0.02 > P > 0.01	Increase
Mothers' mother ..	11.820	1	< 0.001	Significant increase
" father ..	3.379	1	0.1 > P > 0.05	No increase
Fathers' mother ..	3.895	1	0.05 > P > 0.02	Increase
" father ..	1.540	1	0.3 > P > 0.2	No increase
Mothers' sister ...	38.451	1	< 0.001	Significant increase
" brother ..	14.484	1	< 0.001	" "
Father's sister ..	21.992	1	< 0.001	" "
" brother ..			< 0.001	" "

The result may be summed up as follows. In all the categories of near relations there is an absolute, unmistakable excess incidence of endogenous cancer as a whole. In the "thinned-out" grandmother groups there is in the mothers' mothers a positive, in the fathers' mothers a probable excess incidence; in the grandfather groups the excess seems doubtful.

3. THE RELATIVE FREQUENCY OF UTERINE  
AND OVARIAN CANCER IN CORRESPONDING  
CATEGORIES OF RELATIONS

With regard to cancer of these two sites, which I have considered together because the number of observed cases in

TABLE XXV

	P	Remarks
Mother .....	0.0159	Increase
Sister .....	0.0374	Doubtful
Mother's sister .....	0.0470	"
Father's sister .....	0.0189	"
Mother's mother .....	0.263	No increase
Father's mother .....	0.492	"

each category of relations was so small, the result of the investigation is doubtful, and therefore does not warrant any conclusions with regard to possible excess incidence among the relatives of the probands.

## Chapter IX

### ESTIMATION OF THE CANCER RISK

Since it must be considered as probable that hereditary factors play an important part in the development of breast cancer, it lies near to search for a hereditary behavior according to Mendelian principles. This involves an attempt to calculate the frequency of carriers of the taint; but a satisfactory calculation of this is closely bound up with the fact that the disease manifests itself at different age-periods. In order to make a fairly approximate correction for the numerical error on the frequency of carriers which may result from this, I have used a larger material for comparison. For breast cancer this consists of the same 1565 female breast cancer patients from the Cancer Registry who also served as controls in the foregoing investigations, and in whose cases the diagnosis had been verified by histologic examination. They are divided into age groups according to their age at the time of first admission to hospital. Also for cancer as a whole, i.e. cancer of all sites, I have used a material from the Cancer Registry, consisting of all the 3982 male 5066 female cases, living and dead, reported from hospitals at admission, or by death certificate alone, in the course of 1942, and summed up by Jan. 1st, 1943.

In this material from the Cancer Registry it has been impossible to determine the exact age at first admission to hospital of the cases notified by death certificate at death (i.e. about 39 per cent), because the length of survival for each of the different forms of the disease is not known; but as it for most

of them is comparatively short, the figures have been used as found; that is to say that in some cases the age at the time of death has been reckoned as age at the first manifestation of the disease. It will be possible, however, to eliminate this element of uncertainty when the registration of cancer in Denmark, by the Cancer Registry, shall have been continued for still a number of years. The institution will then be able to follow each registered cancer patient from the onset of the disease until death, and to determine the yearly mortality rate for cancer of each site, so that the conditions for genetic cancer research will be more favorable than to-day.

TABLE XXVI

Age	0	30	35	40	45	50	55	60	65	70	75	80
3982 men	149	70	89	129	232	268	374	550	594	618	479	430
5066 women	142	118	233	270	408	440	585	593	627	614	528	508

The distribution by age of the 3982 men and 5066 women is shown in Table XXVI and graphically represented in Fig. 5.

Table XXVII illustrates by an example how the correction may be made by means of this material for comparison.

Table I (p. 40) shows among 381 sisters 13 cases of breast cancer, i.e. an apparent cancer risk of  $\frac{13}{381} = 3.41$  per cent. If we now, as first approximation, assume that these 381 individuals derive from an aggregate in which the incidence of breast cancer is fairly stationary, the age distribution in this aggregate can be calculated by finding the number of individuals under observation at the beginning of each of the age periods considered, and from this again the calculated total number of individuals under observation in the middle of each age period; this figure being approximately the mean of the number of individuals at the beginning and the end of each interval. (Number of individuals under observation at the middle of each age period).

For comparison, Table XXVII gives the distribution, according to age at the first manifestation of the disease, of the

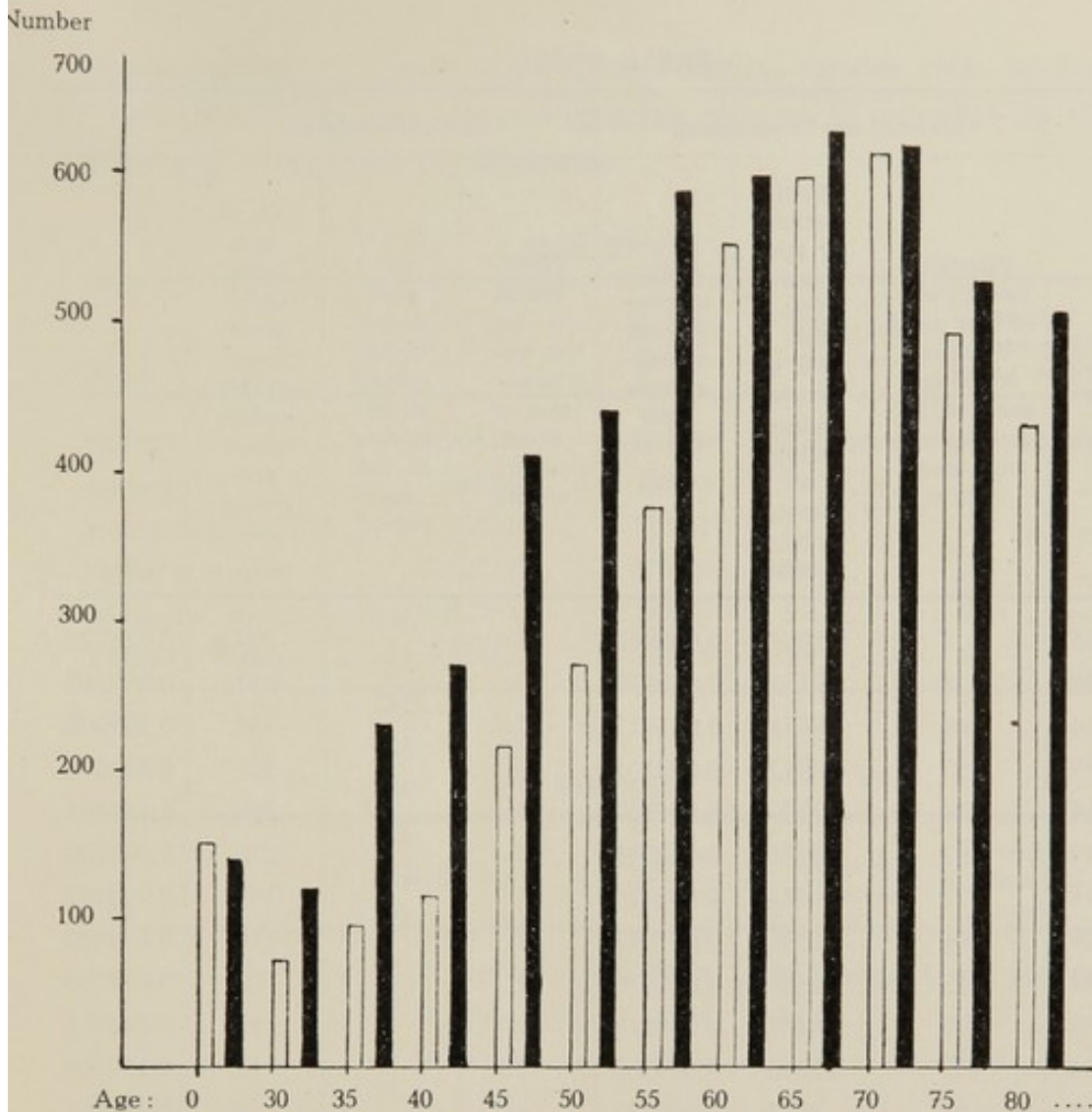


Fig. 5.—The distribution by age of the Cancer Registry's material of ■ 5066 women and □ 3982 men, with cancer of all sites notified from hospitals or by death certificate in 1942.

1565 women with breast cancer, and the distribution by age, on Nov. 5th, 1940, of the female population between the ages of 20 and 80 in Greater Copenhagen (the municipality of Copenhagen and the boroughs of Frederiksberg and Gentofte). If we place the figures in these two columns in relation to each other, we get the relative frequency of cancer carriers, with  $p_i$  in each age class, and this frequency is a function both of the cancer-carrier frequency and the degree of manifestation.

If these frequencies are found unchanged also in the observed material, the expected number of affected individuals

TABLE XXVII

Age-group	Material for Comparison			Observed Material			$l_i \times p_i$
	Distribution by age at first manifestation of the disease, of 1565 women with breast cancer	Distribution by age, on Nov. 5th, 1940, of female population of Greater Copenhagen	Relative frequency of individuals with cancer $p_i$	Distribution by age at examination or death, of 381 sisters	No. of persons under observation at beginning of the age-period	No. of persons under observation at the middle of the age-period $l_i$	
20—25	3	45067	0.000067	25	381	369	0.024723
25—29	8	47155	0.000170	9	356	352	0.059840
30—34	69	45638	0.001512	27	347	334	0.505008
35—39	87	40942	0.002135	35	320	303	0.643875
40—44	175	37822	0.004627	52	285	259	1.198393
45—49	262	32536	0.008053	46	233	210	1.691130
50—54	172	29075	0.005916	51	187	162	0.958392
55—59	204	25686	0.007942	53	136	110	0.873620
60—64	223	22367	0.009970	41	83	63	0.628110
65—69	171	16477	0.010378	19	42	33	0.342474
70—74	115	12250	0.009388	13	23	17	0.159596
75—79	48	7925	0.006057	4	10	8	0.048456
80	28	5705	0.004908	6	6	3	0.014724

$$\sum p_i = 0.071113$$

$$\sum l_i p_i = 7.148341$$

in the observation material can be calculated as  $\sum l_i p_i$ . As we by approximation must have the cancer risk in the material used for comparison,  $P_s$ , equal to  $\sum p_i$ , we must, in order to eliminate the effect of the manifestation's dependence on age,

reckon with an aggregate of  $\frac{\sum l_i p_i}{\sum p_i} = \frac{7.148341}{0.071113} = 100.52$ , corres-

ponding to 13 found cases of breast cancer instead of the stated 381. We then find the cancer risk for all ages together to be

$\frac{13}{100.52} = 12.93$  per cent. In the same manner are calculated the

figures given in Table XXVIII for breast-cancer risk, and in Table XXIX for risk of endogenous cancer in general in the different categories of relations.

TABLE XXVIII

	$\sum l_i p_i$	$\frac{\sum l_i p_i}{\sum p_i}$	Observed breast cancer	Correction of observed breast cancer
Mother .....	8.966381	126.09	10.2 percent	15.9 percent
Sisters .....	7.148341	100.52	3.4 " "	12.9 " "
Mother's mother ..	8.762024	123.21	2.2 " "	3.3 " "
Father's mother ...	7.527281	105.80	2.6 " "	3.8 " "
Mother's sister ..	13.322033	187.30	5.4 " "	9.1 " "
Father's sister ...	9.355873	131.56	5.4 " "	9.1 " "

TABLE XXIX

	$\sum l_i p_i$	$\frac{\sum l_i p_i}{\sum p_i}$	Observed cancer	Correction of observed cancer
Mother .....	28.594946	84.96	27.5 percent	64.7 percent
Father .....	31.509245	66.62	20.1 " "	60.0 " "
Sisters .....	16.783148	49.86	7.9 " "	60.2 " "
Brothers .....	12.641712	26.73	4.2 " "	59.9 " "
Mother's mother ..	29.245041	86.89	12.6 " "	26.5 " "
" father ...	30.044827	63.52	10.1 " "	26.8 " "
Father's mother ..	25.064341	74.47	7.0 " "	14.8 " "
" father ...	27.815213	58.81	8.1 " "	22.1 " "
Mother's sister ..	42.426283	126.05	16.1 " "	40.5 " "
" brother ..	31.353041	66.29	10.1 " "	36.2 " "
Father's sister ...	29.193254	86.73	13.4 " "	34.6 " "
" brother ..	34.767541	73.50	6.4 " "	20.4 " "

## Chapter X

### DISCUSSION AND CONCLUSIONS

The results of the genetic, clinical study of breast cancer related in the foregoing chapters lead to the belief that inherited disposition plays the chief part in the development of cancer. The probands were non-selected and represent the different social strata of the population; therefore, it is unlikely that extraneous factors such as infection, conditions of environment, housing or alimentation should have any material influence on the occurrence of cancer of the breast. The results of the investigations may be summarised as follows.

1.—The demonstration of an indubitable increase in the frequency of breast cancer among the female relations of the probands, and a very marked incidence, as expected, among the small material of males, makes it overwhelmingly probable that the development of cancer of the breast is due to hereditary predisposition.

2.—The demonstration of an indubitable increase in the frequency of endogenous cancer as a whole in the families of the probands, both in the male and female groups of relatives, makes it probable that the hereditary disposition to cancer of the breast is closely associated with a disposition to other forms of endogenous cancer.

If we try to form an estimate of the hereditary behavior of cancer, such an estimate must be based on the calculated figures for the risk of getting the disease, which may be taken as a combined expression for the frequency of the hereditary disposition and the degree of its manifestation. Before any idea



can be formed of a hereditary behavior according to the Mendelian principles it must be considered whether cancer of the breast is a genetic entity independent of other forms, or whether the endogenous cancers as a whole constitute a genetic entity; that is if there exists a general "cancer gene", which determines endogenous cancer, and the localisation of the tumors is controlled either by one, possibly several, genes for localisation, or by endogenous, extrachromosomal factors or exogenous factors.

What result, then, would we expect from the investigations, if breast cancer were a genetic entity?—We would expect that only the frequency of this specific tumor would show increase in the families of the probands, and that there would be no increase in cancers of other sites, either in the male or the female groups of relatives. But the investigation has shown that at the same time as there was an increase in the frequency of breast cancer among the female relatives there was also, both among the females and the males, an indubitable increase of endogenous cancer in general; and this strongly indicates that the hereditary disposition to cancer of the breast is not an entity, but is the same as a general hereditary disposition to endogenously determined cancer.

How, then, can it be explained that endogenous cancers of widely different localisation and nature are conditioned by the same hereditary disposition?—Theoretically, there are, as said, several possibilities. It may be imagined that the localisation of the tumor depends not only on a general cancer gene, but, besides, on one or several genes for localisation, endogenous extrachromosomal or exogenous factors. The experimental experiences have not given any grounds, however, for supposing that the various localisation of the tumors should be due to such special genes. On the contrary, the results of researches in recent years have in steadily increasing degree lent strength to the view that the development of tumors is in a great measure dependent on non-hereditary factors, endogenous or exogenous, and that the manifestation of breast cancer, especially, is influenced by hormonal action. The observed

increase in the frequency of breast cancer may thus be readily explained by the assumption of the influence of such an endogenous, chromosomal factor on a general disposition to cancer. This only holds true, however, provided that breast cancer does not constitute the all-overwhelming part of the endogenous cancers in general among the female relations of the probands, as compared with the control material.

In the schematic survey, on p. 69, of the observed cases of cancer among the relations of the probands, it is seen that among 200 female relatives with cancer, breast cancer was represented with 71 cases (= 35.5 per cent). The corresponding figures for the female relatives of the controls can be calculated from Table XXI (p. 69), and show among 43 women with cancer 8 cases of breast cancer (= 18.6 per cent). The difference, for breast cancer is thus  $35.5 - 18.6$  per cent = 16.9 per cent; the standard error of the difference 6.82 per cent; 3 times the standard error of the difference 20.46 per cent. Thus, the relative frequency of breast cancer, in the proband material, as compared with the control material, does not exceed 3 times the standard error of the difference.

When we consider the calculated figures for cancer risk in the category of relatives where this risk is greatest, we find that the breast-cancer risk for the mothers, which is 15.86 per cent, constitutes 24.4 per cent of the figure for endogenous cancer risk as a whole, which is 64.74 per cent. The standard error of these figures cannot be calculated, because the cancer risk figures have been calculated by methods of approximation; but on an estimate the circumstance that the figure for breast-cancer risk constitutes 25 per cent of the figure for the morbidity risk from endogenous cancer in general gives no ground for abandoning the view that a common hereditary disposition under the influence of endogenous extra-chromosomal or exogenous action may find expression in various forms of tumor.

If we presume, then, that the development of all endogenous malignant tumors is due to one, common hereditary disposition, an attempt to form an estimate of the hereditary behavior, such

an estimate must be based on the said figures for morbidity risk from endogenous cancer as a whole, though with the reservation necessary in regard to figures resulting from the application of rather gross methods of approximation.

For comparison with such empiric figures for potential inheritance, we have tables which show the expected morbidity incidence, with respectively recessive and dominant inheritance, among different categories of relatives under varying conditions of morbidity incidence among the population in general, (see Kemp<sup>56</sup>: *Arvelighedslære*, p. 113). If we compare the figures for morbidity risk in the present material with these tables, we see that the possibility of recessive inheritance may be excluded, both because the incidence found has been much higher than might be expected, and because the figure for morbidity in the brother- and sister group with recessive inheritance should be expected to be much higher than in the father- and mother groups. Moreover, the proportion of consanguineous unions was not higher among the parents of the probands than among the population in general, such unions occurring only in two of the pedigrees. On the other hand, the figures for morbidity risk—about 60 per cent—found both in the brother- and sister group and in the father- and mother groups point strongly in the direction of dominance.

A comparison of the figures for morbidity risk in the various categories of relations,—parents, brothers and sisters, grandparent, uncles and aunts,—whith those expected according to the calculations, we find that with a morbidity rate of between 1 and 10 per cent among the population in general they correspond more or less to the expected figures for a disease with dominant inheritance. If we take the control material as expression for the population as a whole, we find that there among 1502 adult females occurred 43 cases of cancer (= 2.86 per cent), among 1380 males 38 cases (= 2.75 per cent). When we correct these figures with regard to the age distribution and calculate the figures for the morbidity risk, we get the following figures for the latter: for females 8.5 per cent, for males 10.8 per cent.

The conclusion to be drawn from these investigations must then be that there exists a latent hereditary predisposition to cancer, and that the manifestation of the tumors occurs as the result of this latent tendency becoming activated through the influence of endogenous extrachromosomal or exogenous factors of more or less unknown nature. The hereditary tendency, which must be considered to be non-specific, in so far as it can result in the development at any rate of endogenous tumors in general, is transmitted dominantly and exists in between 1 and 10 per cent of the population.

My material does not warrant any further conclusions respecting the causation of cancer in man, and a fully satisfactory explanation of the fact that the tumors can show so great a variation in the hereditarily cancerous families cannot be expected until a series of genetic studies based on various forms of tumor shall have been completed and their results can be compared and correlated with those here presented.

My conclusion raises the question if the knowledge of cancer being a heritable disease, and the establishment of figures for the genetic prognosis, can be of any practical significance for the fight against the disease. The German authors Britz<sup>17</sup> and Wachtel<sup>104</sup> have suggested that marriage between persons of highly cancerous families should be advised against in order to get as few homozygotic carriers of the taint as possible. The idea may be excellent, but would no doubt be impossible to carry out, since probably only few persons intending to marry would be willing to follow such a directive in the choice of consort. But at least the knowledge of cancer being hereditarily determined may perhaps create a greater interest in family registration of the cancer cases. This would make members of cancer families interested in informing their physician of the fact, so that they would be under a certain observation. The physician would then be on the lookout for any initial symptoms in such potential carriers of the taint, and this might lead to an early diagnosis of the tumors. The importance of this result is surely beyond any question.

## SUMMARY

### *Introduction*

The author's study is a genetic and clinical investigation of 200 probands with cancer of the breast, with the object of estimating the hereditary behavior of the disease.

### *Chapter I*

Experimental cancer research has shown that a malignant tumor may arise by mutation, and that the character is inherited according to simple Mendelian principles. Also the experiments on animals point to inherited predisposition as an essential condition for the development of the tumors. The results of genetic research on the causes of cancer in man have given grounds for believing that cancer of certain sites, among them the breast, are, partially at least, hereditarily determined, whereas skin- and lip cancers are probably not due to hereditary disposition. Most studies hitherto suffer, however, from demonstrable shortcomings, which invalidate the evidence.

### *Chapter II*

The author's material consists of 200 probands, 197 women and 3 men, with cancer of the breast, the diagnosis being in all cases established by histologic examination. The case histories have been gone through, and all facts of possible etiologic significance have been noted. The investigation of the families of the probands comprises the following categories of relations: parents, brothers and sisters, grandparents, and

brothers and sisters of the parents. Information has been obtained about 3130 relatives, while 171 could not be traced. According to the information obtained, 347 relatives had cancer, and the diagnoses were afterwards verified and confirmed for 95 per cent of the cases. The control material consists of 200 sound individuals in the same age classes as the probands. The investigation and verification of the data concerning them has been of the same extent as with regard to the relations of the former.

### *Chapter III*

The study of the case histories of the probands gives no grounds for supposing that exogenous factors play any important rôle for the development of breast cancer. Tables are given, showing the number of cancer cases found in each category of relations, and their distribution according to site of the tumors. The proband material and the control material are for the sake of readier comparison tabulated side by side. They cannot be directly compared, however, because it is more difficult to obtain sure information about cancer cases among the more distant relatives of the controls than among those of the probands.

### *Chapter IV*

The statistical methods used are described; first the  $\chi^2$  test and the "exact method" used for evaluation of the distributions of frequency, next the method used for calculation of the mortality risk.

### *Chapter V*

Contrary to expectation, the curve of the age distribution at the first manifestation of the disease in the 200 probands was found to be two-peaked, with maxima in the age periods 45-49 and 60-64. That this distribution was not fortuitous is shown by comparison with a larger material, of 1565 women with breast cancer, from the Danish Cancer Registry. In order to

explain this unexpected distribution, a clinical, statistical analysis is made of the 200 probands, by which it is found that most of the probands with a demonstrable taint are found among the young age classes, whereas the second rise is due to non-tainted probands.

### *Chapter VI*

The age distributions in corresponding categories of relations in the proband- and control materials are compared by means of the  $\chi^2$  test and found to agree, which makes it possible to compare the frequencies of cancer.

### *Chapter VII*

Apart from the material, 3 males with breast cancer were examined and their pedigrees investigated. In all three cases the familial cancer taint was very pronounced, in two of them near relatives of the patient had cancer of the breast. Considered in conjunction with the three male cases in the proband material, in which the familial taint was also pronounced, this marked familial incidence of the same form of tumor carries a certain weight as proof of the heritability of breast cancer.

### *Chapter VIII*

The relative frequency of cancer in the corresponding categories of relatives of the probands and the controls is examined by application of the  $\chi^2$  test and the exact method. The author discusses the fact that various forms of cancer, for example lip- and skin cancer, are not represented in the families of the probands, and he comprises the forms occurring in these under the collective term endogenous cancer as a whole. He finds an indubitable excess incidence of breast cancer among the female relations of the probands, with exception of the grandmothers, and likewise an indubitable excess incidence of endogenous cancer as a whole in all the categories of relatives, both male and female, but no sure uterine and

ovarian cancer. He sees in these results a clear indication of hereditary predisposition being the chief factor in the development of cancer.

### *Chapter IX*

The conclusions come to in the foregoing chapter lead the author to examine if the hereditary behavior of breast cancer follows Mendelian principles. The examination of this question involves a calculation of the morbidity risk, because the observed frequencies of cancer must be corrected in view of the fact that the disease manifests itself at varying age periods. In order to make correction for the numerical error that may result from this, he uses for comparison 1565 female breast cancer from the Danish Cancer Registry and another, from the same source, of 5066 female and 3982 male cases of all forms of cancer. An example of the calculations is given, and in tables are shown the calculated figures for mortality risk in the different categories of relations. For "endogenous" cancer as a whole, these are as follows:

	Per Cent		Per Cent
Mothers .....	64.7	Paternal grandmothers	14.8
Fathers .....	60.0	"    grandfathers .	22.1
Sisters .....	60.2	Maternal aunts .....	40.5
Brothers .....	59.9	"    uncles .....	36.2
Maternal grandmothers	26.5	Paternal aunts .....	34.6
"    grandfathers .	26.8	"    uncles .....	20.4

### *Chapter X*

From the result of the comparison of the frequency of cancer in the proband- and control materials, the author concludes that breast cancer is probably hereditary, and that the tendency to this particular form of the disease is bound up with an inherited predisposition to endogenous cancer in general. He discusses the question of cancer of the breast constitutes a genetic entity; and he believes that the development of the



endogenous cancers is probably due to a general hereditary predisposition and the localisation of the tumor determined by endogenous, extrachromosomal or exogenous factors. He therefore bases his view of the hereditary behavior of the breast cancer on the calculated figures for the morbidity risk from endogenous cancer as a whole, and for several reasons excludes the possibility of recessive inheritance.

The figures for the morbidity risk agree approximately with the expectation for diseases with dominant inheritance at an incidence of between 1 and 10 per cent among the population in general. Those for the control material are calculated to 8.5 per cent for females, 10.8 per cent for males.

Finally, he discusses the possibility of prophylactic measures as a help in the fight against cancer, by advice against marriage between individuals of families in which the cancer taint is markedly pronounced. He concludes that such prophylaxis is impracticable, but believes that an increased interest in the registration of cases of cancer may perhaps result in earlier diagnosis and treatment of the tumors.

## DANISH SUMMARY

### *Indledning*

Hensigten med Arbejdet er at belyse cancer mammaes Aarsagsforhold gennem en genetisk-klinisk Undersøgelse af 200 Probander med cancer mammae og at søge at danne sig et Skøn over Arvegangen.

### *Kapitel I*

Den eksperimentelle Svulstforskning har ført Bevis for, at en malign Tumor kan opstaa ved Mutation, og at Egenskaben nedarves efter simple Mendelregler. Dyreforsøgene tyder iøvrigt i Retning af, at arvelige Anlæg er en væsentlig Betingelse for Udviklingen af Svulsterne.

Den humane, arvebiologiske Forskning af Kræftens Aarsagsforhold har givet Grund til at mene, at visse Svulstformer, deriblandt cancer mammae, i hvert Fald delvis er arveligt betinget, medens cancer cutis og cancer labii formentlig ikke skyldes arvelige Anlæg. Der kan dog i alle hidtidige Arbejder paavises Mangler, som udelukker en sikker Bevisførelse.

### *Kapitel II*

Materialet bestaar af 200 Probander, 197 Kvinder og 3 Mænd, med cancer mammae, og Diagnosen er sikret ved histologisk Undersøgelse. Probandernes Sygehistorier er gennemgaaet, og Forhold, som kan tænkes at være af æthiologisk Betydning, er noteret.

Undersøgelsen af Probandernes Slægt omfatter Slægtningegrupperne: Forældre, Søskende, Bedsteforældre og Forældres Søskende.

Oplysninger foreligger om 3130 Slægtninge, medens 171 ikke kunde efterspores. 347 Slægtninge var efter Oplysningerne cancersyge, og Diagnoserne er senere verificerede og bekræftet i 95 % af Tilfældene.

Kontrolmaterialet omfatter 200 sunde Individuer i samme Aldersklasser som Probanderne. Slægtsundersøgelse og Verificering i samme Omfang som i Materialet.

### *Kapitel III*

En Gennemgang af Probandernes Sygehistorier giver ingen Grund til at antage, at exogene Faktorer har væsentlig Betydning for Udviklingen af cancer mammae. I Tabeller er opstillet de fundne Cancertilfælde, Slægtningegruppe for Slægtningegruppe, og en Fordeling efter Localisationen af Svulsterne. Materialet og Kontrolmaterialet er for Sammenligningens Skyld opstillet sideordnet.

### *Kapitel IV*

De anvendte statistiske Metoder omtales, først  $\chi^2$  Prøven og „den eksakte Metode“, der er anvendt ved Vurdering af Hyppighedsfordelingerne, dernæst den til Beregningen af Sygdomsrisikoen anvendte Metode.

### *Kapitel V*

Aldersfordelingskurven efter Alder ved Sygdomserkendelse for de 200 Probander viser sig mod Forventning at være totoppet med Maxima i 45—49 og 60—64 Aars Klasserne. At denne Fordeling ikke beror paa en Tilfældighed, er vist ved en Sammenligning med et større Materiale fra Cancerregisteret paa 1565 Kvinder med cancer mammae. Ved  $\chi^2$  Prøven findes reel Overensstemmelse.

For at give en Forklaring paa denne Aldersfordeling er der foretaget en klinisk-statistisk Analyse af de 200 Probander,

hvorved man finder, at Sandsynligheden taler for, at den sekundære Stigning i 60 til 70 Aars Alderen beror paa en Op-hobning af Probander, som er ubelastede.

### *Kapitel VI*

Ved  $\chi^2$  Prøven sammenlignes og vurderes Aldersfordelin-gerne i tilsvarende Slægtningegrupper i Proband og Kontrol-materialet og findes overensstemmende, hvorfor en Sammen-ligning af de observerede Cancerhyppigheder i de paagæl-dende Grupper er mulig.

### *Kapitel VII*

Udenfor Materialet er der undersøgt 3 Mænd med cancer mammae. Der fandtes hos dem alle svær familiær Belastning med cancer og hos 2 af dem Tilfælde af cancer mammae hos nære Slægtninge. Sammenholdt med Materialets 3 Mænd, hos hvem man havde fundet lignende Forhold, kan denne svære Belastning med den homologe Tumorform tillægges en vis Vægt i Bevisførelsen for cancer mammaes Arvelighed.

### *Kapitel VIII*

Cancerhyppighederne i tilsvarende Slægtningegrupper sam-menlignes ved  $\chi^2$  Prøven og „den exacte Metode“. Man diskutere det Forhold, at ikke alle Former af cancer forekommer i Probandernes Slægter, idet cancer cutis og cancer labii ikke er repræsenteret, og indfører som et sammenfattende Begreb for de i Probandernes Slægter forekommende Former af cancer Betegnelsen: Endogen Totalcancer.

For cancer mammae findes en sikker Forøgelse af Hyppig-heden blandt Probandernes kvindelige Slægtninge, bortset fra Bedstemødrene.

For endogen Totalcancer findes, bortset fra Bedstefædrene, en sikker Forøgelse af Hyppigheden i alle, baade mandlige og kvindelige Slægtningegrupper. For cancer uteri og cancer ovarii findes ingen sikre Tegn paa Overbelastning. Disse Re-

sultater peger utvetydigt paa, at Aarsagen til Kræft for en overvejende Del maa søges i arvelige Anlæg.

### Kapitel IX

Før et Skøn over Arvegangen er mulig, maa der foretages en Beregning af Sygdomsrisikoen, idet de observerede Hyppigheder af cancer maa korrigeres med Henblik paa det Forhold, at Svulsterne manifesteres paa forskellige Alderstrin.

Til denne Korrektion er for cancer mammae anvendt et Sammenligningsmateriale fra Cancerregisteret paa 1565 Kvinder med cancer mammae og for Totalcancer ligeledes et Materiale fra Cancerregisteret paa 5066 Kvinder og 3982 Mænd, levende og døde, med alle Former af cancer. Et Exempel paa Beregningerne gennemgaas og i Tabeller opstilles de beregnede Sygdomsrisikotal for de forskellige Slægtningsgrupper.

For endogen Totalcancer fremkom følgende Tal for Sygdomsrisikoen:

Mødre .....	64.7 %	Farmødre .....	14,8 %
Fædre .....	60,0 %	Farfædre .....	22,1 %
Søstre .....	60.2 %	Mostre .....	40,5 %
Brødre .....	59.9 %	Morbrødre .....	36,2 %
Mormødre .....	26,5 %	Fastre .....	34,6 %
Morfædre .....	26.8 %	Farbrødre .....	20,4 %

### Kapitel X

Resultatet af Sammenligningen mellem Cancerhyppighederne i Proband- og Kontrolmaterialet resumeres, og det fremgaar heraf, at Sandsynligheden taler for, at cancer mammae er arvelig, samt at Anlægget for cancer mammae staar i Sammenhæng med et arveligt Anlæg for endogen Totalcancer.

Spørgsmaalet om cancer mammae udgør en genetisk Enhed diskuteres.

Det maa anses for sandsynligt, at de endogene cancere udvikles som Følge af et alment Arveanlæg, og at Localisationen

af Svulsterne bestemmes af endogene, extrachromosomale Faktorer eller exogene Faktorer.

Som Følge heraf lægges de for endogen Totalcancer beregnede Sygdomsrisikotal til Grund for et Skøn over Arvegangen.

Recessiv Arvegang kan af flere Aarsager udelukkes.

Sygdomsrisikotalene svarer nogenlunde til de forventede Tal for en Sygdom med dominant Arvegang ved en Sygdomshyppighed i Befolkningen paa mellem 1 og 10 %.

Kontrolmaterialets Sygdomsrisikotal beregnes for Kvinder til 8,5 % og for Mænd til 10,8 %.

Til Slut omtales Muligheden af profylaktiske Forholdsregler som Led i Kræftbekæmpelsen ved gennem Ægteskabsvejledning at fraraade Ægteskaber mellem Individider af svært cancerbelastede Slægter. En saadan Profylaxe maa dog anses for at være praktisk uigennemførlig.

En øget Interesse for Slægtsregistrering af Cancertilfælde kan muligvis medvirke til en tidligere Diagnose og Behandling af Svulsterne.

CASE HISTORIES  
AND  
PEDIGREE CHARTS

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This section contains the case histories of the probands and their affected relations, together with pedigree charts comprising the categories of the latter which have been the object of investigation. The case history of each proband includes an anamnesis, especially with regard to such facts as catamenia, number of childbirths, duration and course of nursings; traumas, their nature and the interval elapsed between the accident and the discovery of the tumor; benign mammary tumors; treatment with hormone preparations, the nature and dosage of the latter and the interval elapsed between the treatment and the discovery of the mammary tumor; the interval elapsed between the discovery of the tumor and the institution of treatment. The data respecting operation and histologic diagnosis are derived from the hospital records.

After the case history of the proband follows the data with regard to the affected relations, including year and date of birth, occupation, domicile, year and date of death, diagnosis of the case and the manner in which it has been verified. In the cases where it has not been possible to get the diagnosis verified by death certificate, inquiry to hospital or to the treating physician, a brief description of the disease is given.

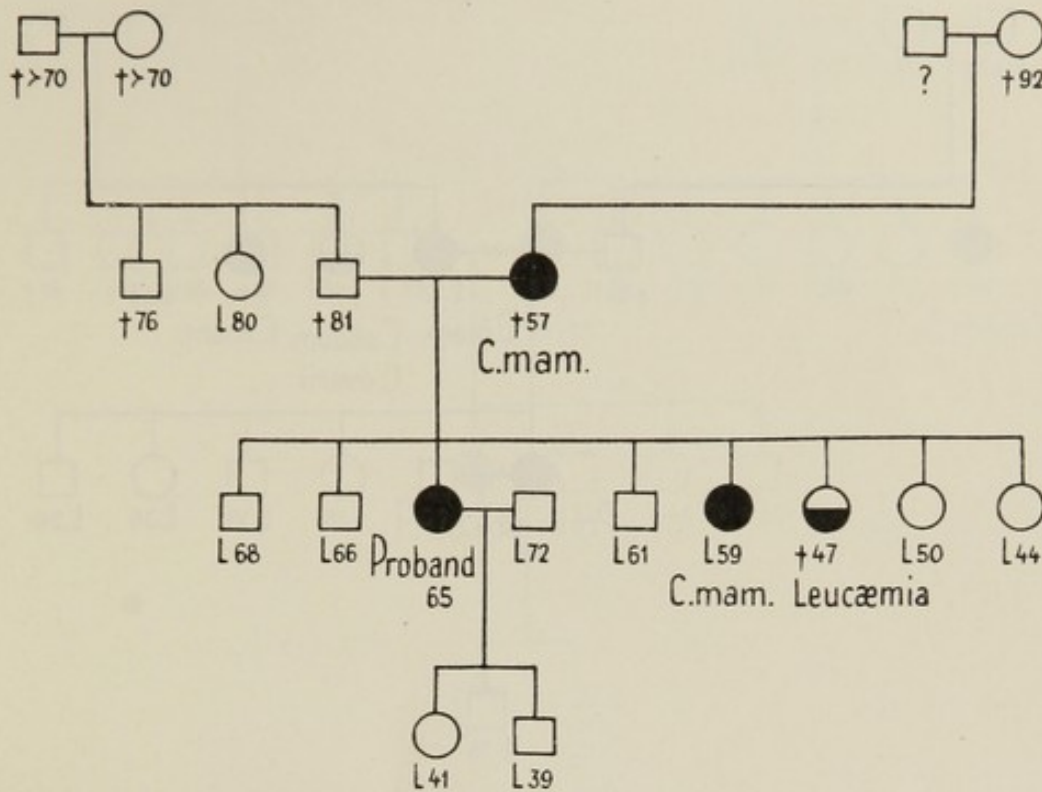
The two hundred family histories are arranged in the following order, according to the category of relations in which cancer was present.

#### I.—CANCER FAMILIES (NOS. 1-154)

A. <i>Breast-cancer families:</i>	No. of Pedigree
a. Mother affected .....	1- 21
b. Father       " .....	22

c. Sisters affected .....	23- 34
d. Mother's mother affected .....	35- 38
e. Father's mother " .....	39- 41
f. Parent's sisters " .....	42- 61
 B. <i>Families with uterine and (or) ovarian cancer.</i>	
a. Mother affected .....	62- 72
b. Sisters " .....	73- 78
c. Mother's mother affected .....	79- 81
d. Father's " " .....	82
e. Parent's sisters " .....	83- 89
 C. <i>Families with cancer in other sites.</i>	
a. Both parents affected .....	90- 92
b. Mother affected .....	93-104
c. Father " .....	105-124
d. Brothers and (or) sisters affected .....	125-133
e. Grandparents affected .....	134-146
f. Brothers and (or) sisters of father and (or) mother affected .....	147-154
 D. <i>Non-cancer families</i> .....	
	155-200

When there are cases of cancer in more than one category of relations, the family is listed under the first of the above-named groups.



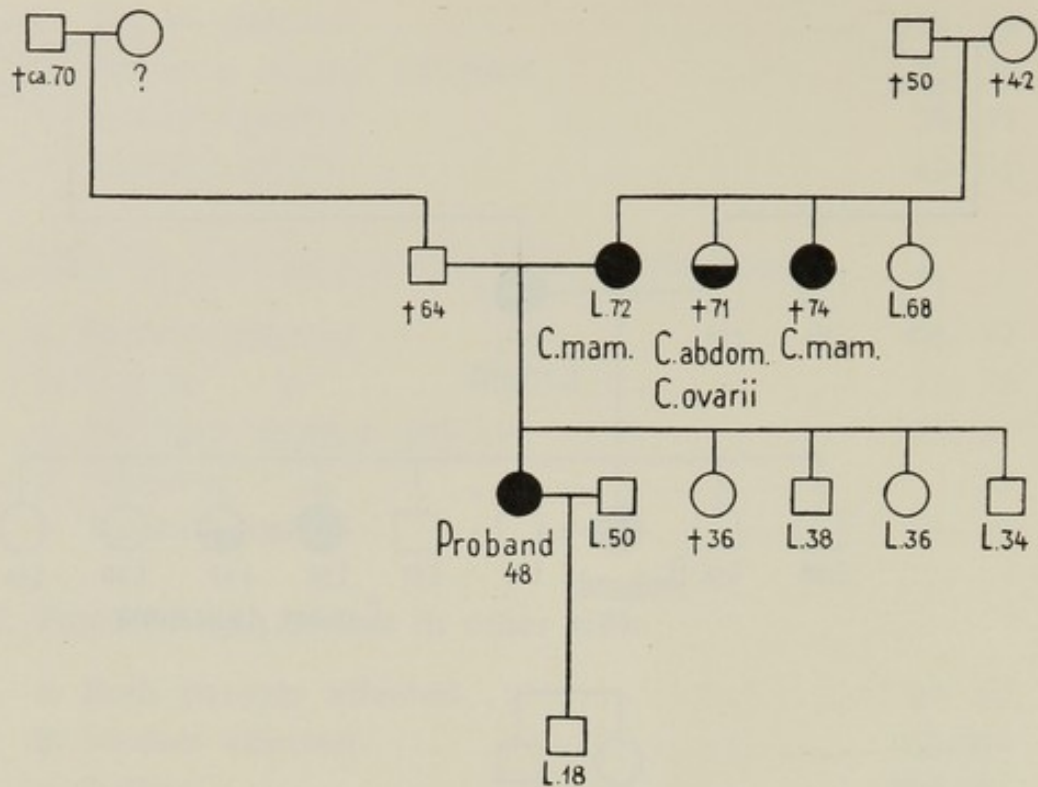
Pedigree 1.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 928/42). —○, born i Sweden Jan. 29th, 1877. ∞ workingman. For many years sufferer from chronic rheumatic polyarthritis. Menstruation from fourteenth to forty-eighth year, regular. Two childbirths. Nursed over a year on each occasion. Tumor in left breast noticed a week before admission. April 10th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Sweden in 1851; died May 25th, 1909, in Ehkorva, Sweden, of cancer of the breast. Came to operation so late that radical operation was out of the question. Died of metastases to lung and pleura.

ELDEST SISTER.—Born Jan. 6th, 1883, ∞ farmer in Ehkorva, Sweden. Operated on at Veksjö Hospital April, 1942, for cancer of left breast with metastases to axillary nodes. Histologic diagnosis: simple carcinoma.

SECOND SISTER.—Born in Ehkorva Sep. 29th, 1892. Housemaid; single. Died in Helsingborg Hospital April, 1935, of leukemia. The diagnosis verified by the hospital.



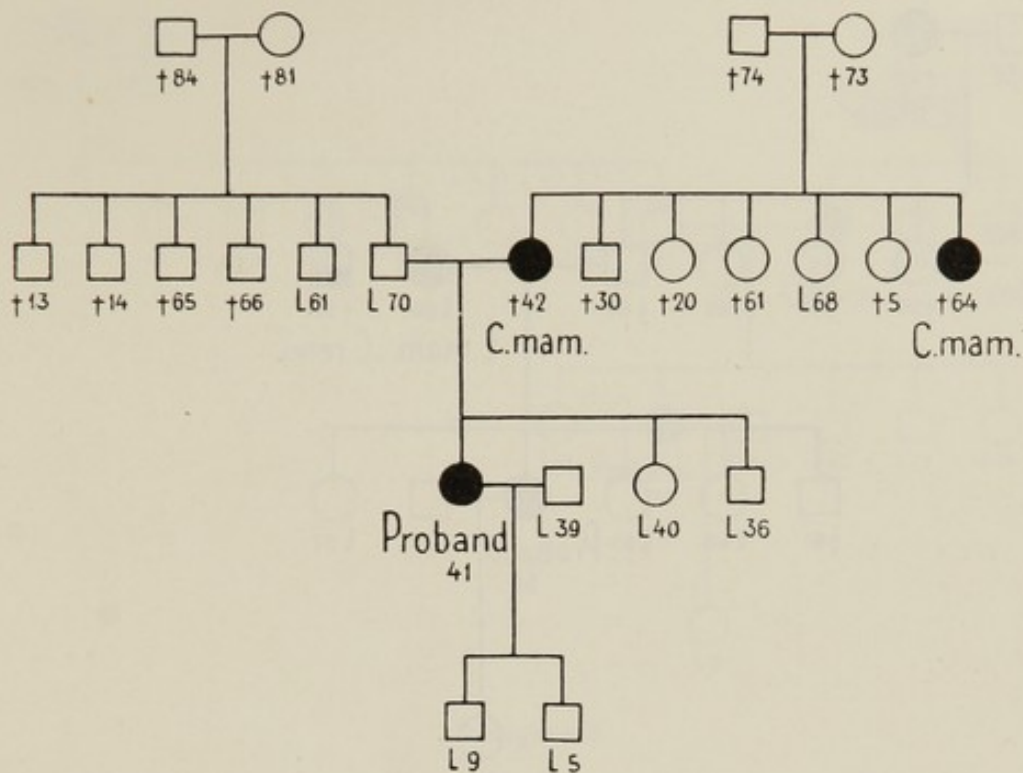
Pedigree 2.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 461/39).—  
 ○, born in Landskrona, Sweden, Apr. 18th, 1891. Seamstress; divorced. Her son and a brother hemophiliacs; also herself some tendency to long bleeding, even after slight, insignificant wounds. Menstruation from nineteenth year, regular. One childbirth. Nursed for nine months. In September 1936 admitted to the State Hospital, service V, for cancer of the right breast. Ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma. In 1939 treated in same hospital for local recurrence.

MOTHER.—Born in Sweden July 12th, 1870. ∞ old age pensioner in Copenhagen. Treated at the Radium Center in Copenhagen (J. 27319) for cancer of the right breast. Refused surgical intervention; hence no histologic diagnosis; but the clinical diagnosis certain, and she was treated with roentgen.

MOTHER'S ELDEST SISTER.—Born in Sweden Dec. 23rd, 1862. Widow, domicile Landskrona. Died in hospital there Oct. 13th, 1942, of cancer of the ovary and abdomen. The diagnosis verified by the hospital.

MOTHER'S SECOND SISTER.—Born in Sweden Sep. 3rd, 1868. ∞ dock laborer in Landskrona. Died 1942. In 1906 operation for cancer, with ablation of right breast. In 1940 local recurrence and symptoms of metastases to the lung. Protracted roentgen treatment without improvement. Diagnosis: breast cancer; metastases.

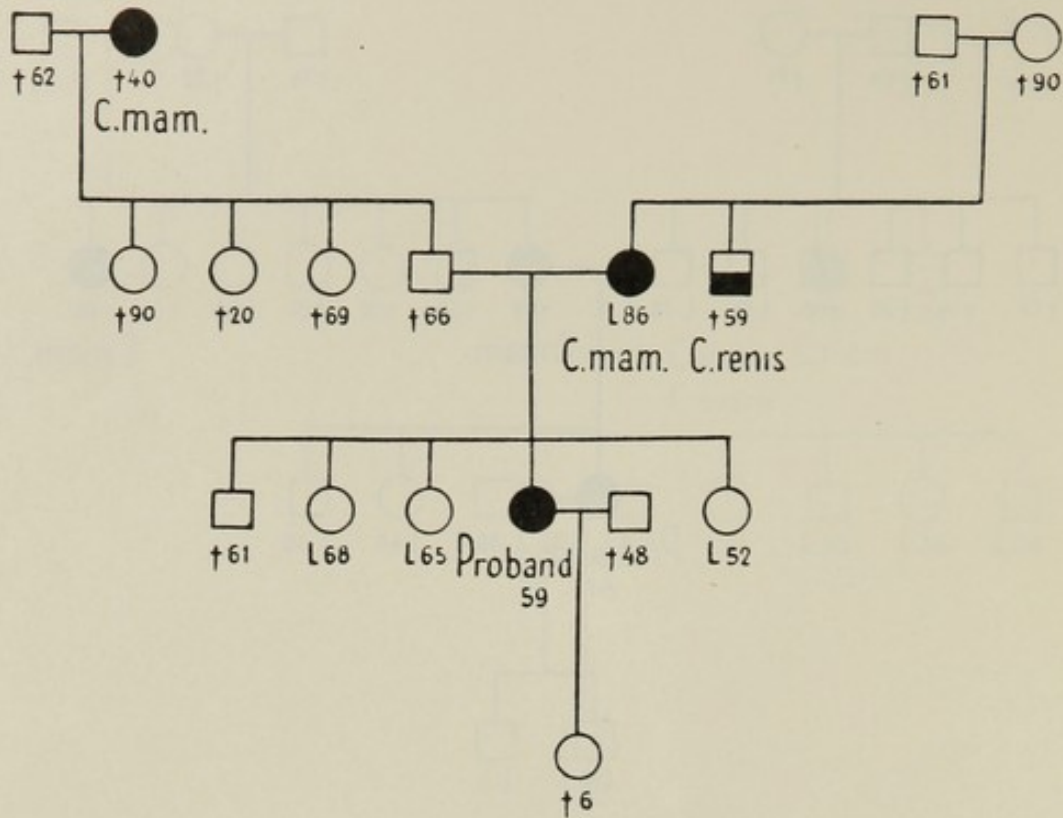


Pedigree 3.

PROBAND (State Hospital, Copenhagen, radiol. service; no. 254/42).—  
 ○, born i Brande May 11th, 1900. ∞ post-office clerk. Formerly well. Menstruation since fourteenth year, regular. Two childbirths. Nursed only a few weeks on each occasion, owing to hypogalactia. Tumor in left breast noticed six months before admission. April 23rd, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Fjerritslev Feb. 22nd, 1876. ∞ provision dealer. Died in Saxild Feb. 3rd, 1919, of heart disease and Basedow's disease. In the two years before she died, a tumor developed in her left breast, but the heart disease forbade surgical intervention and the tumor ended by extending, ulcerating, over the entire surface of the breast. Diagnosis: cancer of the breast.

MOTHER'S SISTER.—Born in Fjerritslev Aug. 22nd, 1878. Storekeeper's widow. Died in Aalborg in 1944. In 1924 operated on at the Carmelite Clinic, Aalborg, for cancer of the breast.



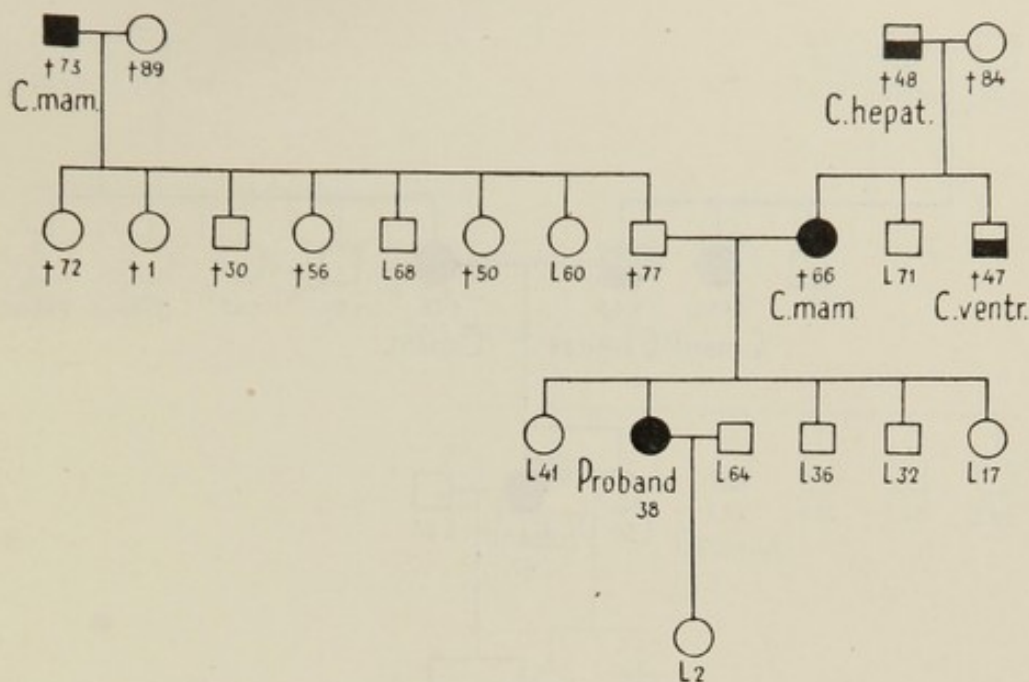
Pedigree 4.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 346/42).—  
 ○, born in Skodsborg March 18th, 1883. Furrier's widow. Formerly well. Menstruation from fourteenth to forty-second year, regular. Menopause normal. One childbirth. Nursed only five weeks, owing to hypogalactia. Tumor of the right breast noticed three months before admission. March 13th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus adenocarcinoma.

MOTHER.—Born in Skodsborg Oct. 13th, 1856. Clothmaker's widow. In August 1920 operated on at St. Joseph's Hospital, Copenhagen, for cancer of the breast. The diagnosis verified by the hospital. Histologic diagnosis: adenocarcinoma.

MOTHER'S BROTHER.—Born in Holte Jan. 22nd, 1853. Waiter. Died in Copenhagen Oct. 30th, 1912, of renal cancer. The diagnosis verified by death certificate.

FATHER'S MOTHER.—Born in Skodsborg 1814. ∞ boilermaker. Died in 1854 of cancer of the breast. As she refused surgical intervention, the tumor eventually developed into a bleeding and ulcerating process involving the entire breast. Diagnosis: cancer of right breast.



Pedigree 5.

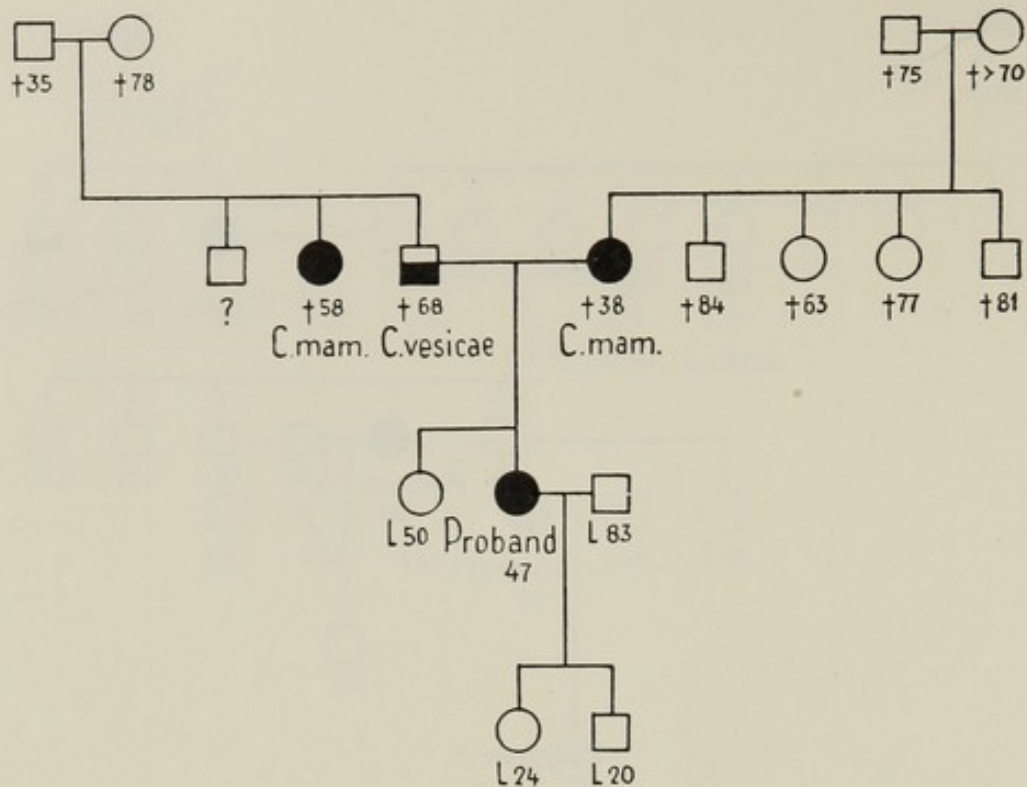
PROBAND (State Hospital, Copenhagen; radiol. service, no. 431/41).—  
 ○, born in Ishøj Dec. 7th, 1902. ∞ typographer. Menstruation since twelfth  
 year, regular. One childbirth, but nursed only a month, owing to hypo-  
 galactia. Tumor in left breast noticed eight days before admission. July 21st,  
 1941, ablation of breast, with evacuation of the axilla. Histologic diagnosis:  
 milk-duct carcinoma.

MOTHER.—Born in Taastrup Aug. 23rd, 1873. ∞ farmer. Died of breast  
 cancer June 24th, 1940. Metastases. Cachexia. Operated on at the State  
 Hospital, Copenhagen, service C, in 1935. The diagnosis verified by death  
 certificate.

MOTHER'S FATHER.—Born in Taastrup Sep. 3rd, 1835. Waggoner. Died  
 of cancer of the liver Sep. 20th, 1883. The diagnosis verified by transcription  
 from Thorslunde church register.

MOTHER'S YOUNGEST BROTHER.—Born in Taastrup 1875. Railway-  
 porter. Died in Næstved Hospital Jan. 4th, 1923, of stomach cancer. The  
 diagnosis verified by the County Hospital, Næstved.

FATHER'S FATHER.—Born in Hadsund 1822. Carpenter. Died in Visborg  
 parish Febr. 12th, 1895, of cancer of the right breast. The disease had been  
 present for fully a year and eventually developed into an ulcerating, sup-  
 purating, fetid tumor larger than a fist. The patient refused hospitalisation.  
 Diagnosis: cancer of the breast.



Pedigree 6.

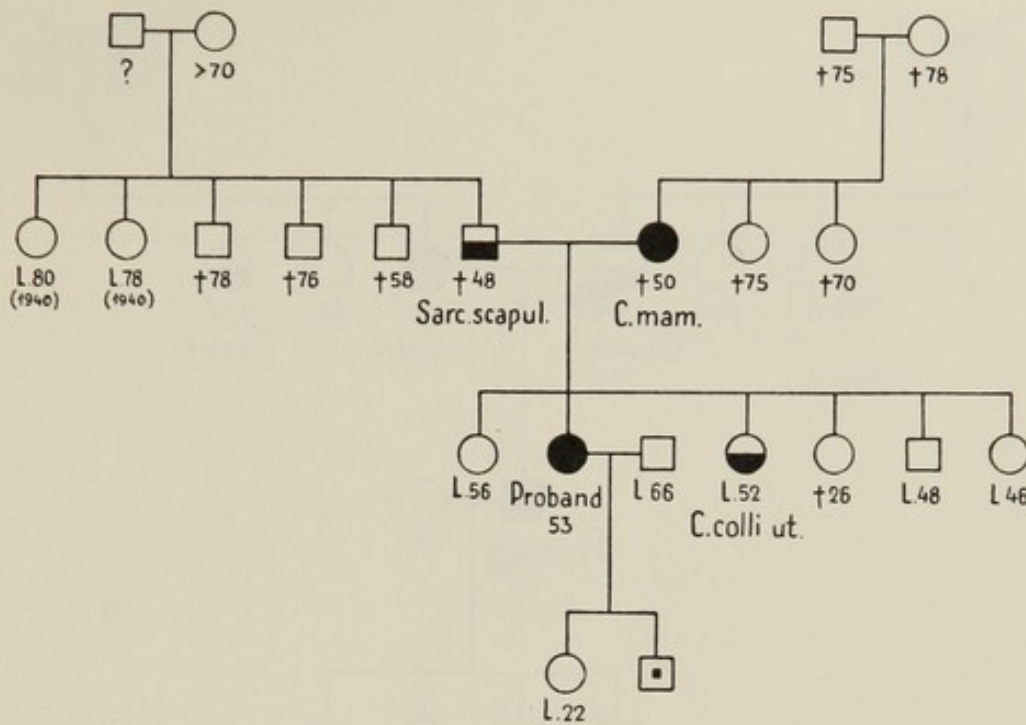
PROBAND (Radium Center, Copenhagen; no. 32048).—○, born in Copenhagen Aug. 22nd, 1896. ∞ organ builder. Formerly well. Menstruation since thirteenth year, regular. Two childbirths. Nursed both times for about a year. Tumor in right breast noticed about six months before admission, but physician not consulted until it began to ulcerate. Biopsy. Histologic diagnosis: papilliferous adenocarcinoma.

MOTHER.—Born in Sweden March 18th, 1863. ∞ foreman. Died in Copenhagen March 30th, 1901, of cancer of the breast. The diagnosis verified by death certificate.

FATHER.—Born in Sweden June 3rd, 1864. Foreman; married. Died in Copenhagen April 15th, 1932, of cancer of the bladder. The diagnosis verified by death certificate.

FATHER'S SISTER.—Born in Sweden March 3rd, 1862. Died in Landskrona Hospital in 1922, of embolus of pulmonary artery following operation for cancer of the breast. Inquiry to hospital not answered, but two relatives of the proband both state that the physicians there had declared to them that the disease was cancer. Diagnosis: cancer of the breast.





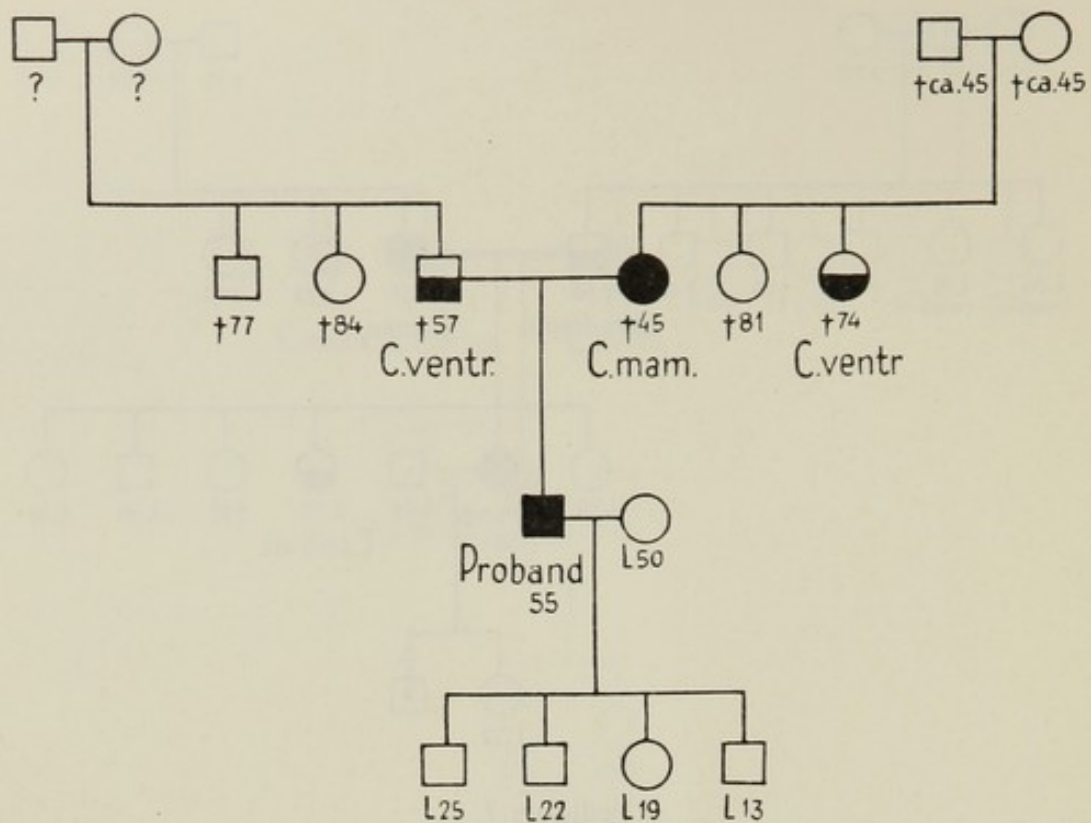
Pedigree 7.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 656).—  
 ○, born in Copenhagen Dec. 15th, 1889. ∞ pensioner. Menstruation from  
 thirteenth to forty-ninth year, regular. Three childbirths, one of the children  
 still-born. Nursed only her first child, for two months, owing to hypo-  
 galactia. In 1915 operated on at the Bispebjerg Hospital for fibroadenoma  
 of right breast. Six months before the time when she noticed any swelling,  
 she had fallen from a ladder and hurt the same breast, which remained tender  
 for some days, but there was no extravasation. Four months before admis-  
 sion she had noticed that her right breast was larger and firmer than the  
 left, and the nipple retracted. Shortly afterwards, a slight ulceration  
 developed. Trephine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Salling May 16th, 1869. Baker's widow. In 1918  
 operated on for mammary cancer, with ablation of right breast. Died in  
 Copenhagen Apr. 18th, 1919, of metastases to the lung. Death certificate:  
 cancer of lung and pleura, with cancer of the breast.

FATHER.—Born in Aarhus June 10th, 1866. Baker. Died 1914 in the  
 Municipal Hospital, Copenhagen (journal no. 101/14), of sarcoma of the  
 scapula.

SISTER.—Born in Copenhagen May 23rd, 1891. ∞ secretary. At time of  
 present writing under treatment at the Radium Center, Copenhagen (Journal  
 no. 19111), for uterine cancer.



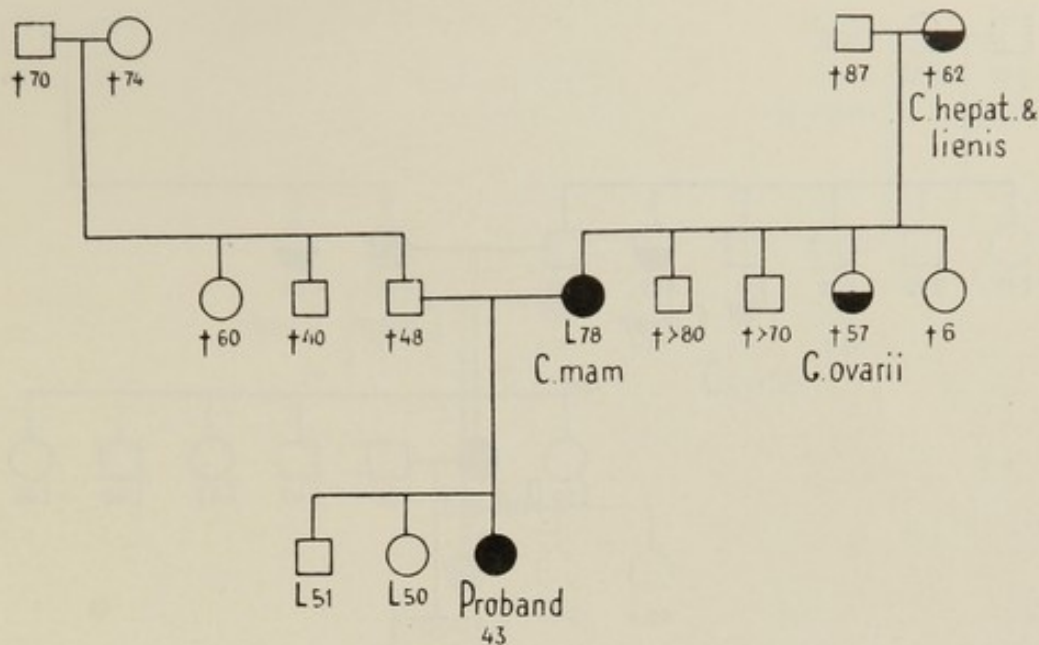
Pedigree 8.

PROBAND (Radium Center, Copenhagen; no. 28950).—□, born in Tigersted May 14th, 1887. Farmer; married; four children. The tumor in left breast noticed over six months before admission. Oct. 3rd, 1942, ablation of the breast and evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born 1850 in Nakskov. ∞ Farmer. Died in Brandstrup (Lolland) 1895, of cancer of the breast. Had been operated on thrice at the hospital in Rødby, the first time with ablation of the breast, the two other times with extirpation of recurrences.

FATHER.—Born 1839 in Maribo. Farmer in Brandstrup. Died 1896, of cancer of the stomach. The treating physician stated that the death was due to a malignant tumor in the stomach, with dissemination in the abdominal organs.

MOTHER'S YOUNGEST SISTER.—Born 1868 in Nakskov. ∞ Farmer. Died in Højfjeld Jullinge July 8th, 1942, of cancer of the stomach. The diagnosis verified by death certificate.



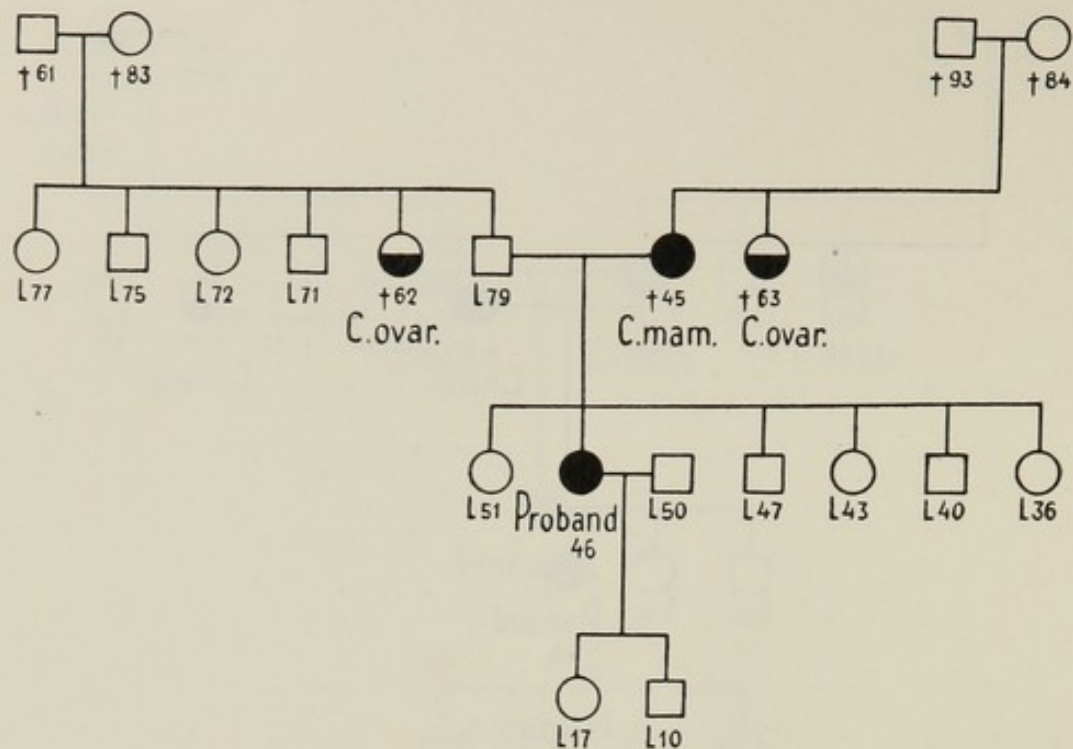
Pedigree 9.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 80/41).—  
 ○, born in Copenhagen Oct. 25th, 1898. Office assistant; single. Menstruation from fifteenth to thirty-eighth year, regular. Menopause normal. Never pregnant. Tumor in left breast noticed three months before admission. Jan. 20th, 1941, ablation of left breast, with evacuation of the axilla. Histologic diagnosis: Carcinoma, partly adenomatous.

MOTHER.—Born in Nykøbing (Falster) Apr. 27th, 1864. ∞ confidential clerk. In 1940 operated on at the State Hospital, Copenhagen, service D, for cancer of left breast. Histologic diagnosis: solid carcinoma.

MOTHER'S MOTHER.—Born 1832. ∞ storekeeper. Died 1884 in Copenhagen, of cancer of the liver and spleen. The diagnosis verified by death certificate.

MOTHER'S NEXT YOUNGEST SISTER.—Born 1869. ∞ chief of police. Died May 1st, 1926, in the Sundby Hospital, surg. service, of cancer of the ovary. The diagnosis confirmed by the hospital. Histologic diagnosis: adenocarcinoma.



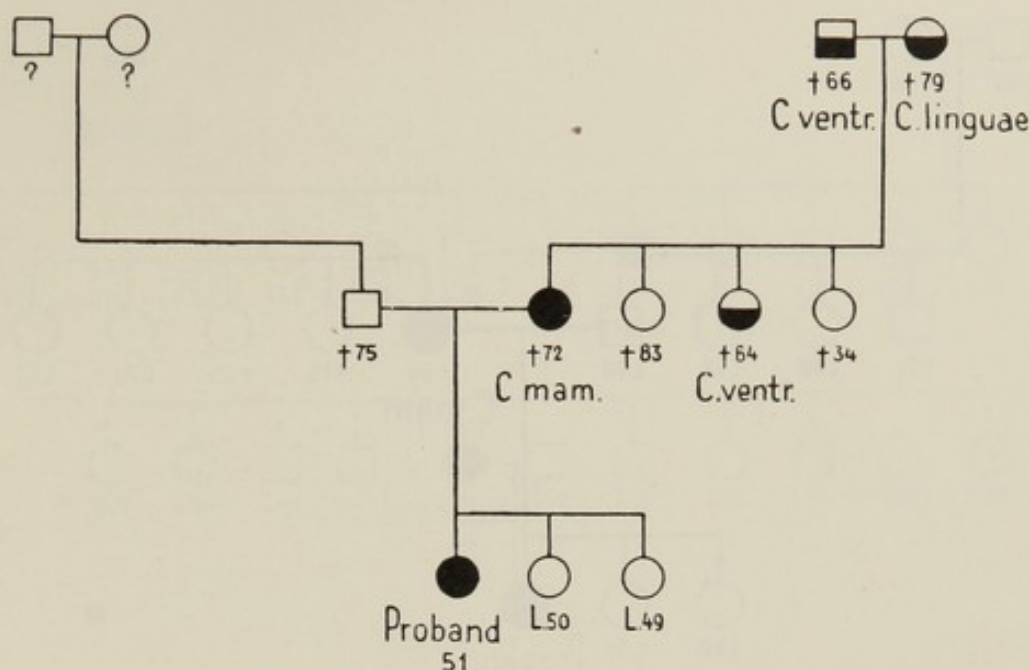
Pedigree 10.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 146/40).—  
 ○, born in Gothenburg, Sweden, Dec. 20th, 1893. ∞ communal workingman.  
 Formerly well. Menstruation since fourteenth year, regular. Two childbirths.  
 Nursed only a couple of months; both times owing to hypogalactia. Tumor  
 in left breast noticed a week before admission. June 17th, 1940, ablation  
 of the breast, with evacuation of the axilla. Histologic diagnosis: solid  
 scirrhous carcinoma.

MOTHER.—Born in Gothenburg June 21st, 1870. ∞ bricklayer. Died  
 Aug. 6th, 1915, in Malmö, Sweden, of cancer of the breast. In May 1915  
 treated at the Malmö Hospital. As the case was inoperable, roentgen and  
 radium were applied. The histologic diagnosis of the malignancy of the  
 tumor established by the Carolinian Institute, Stockholm.

MOTHER'S SISTER.—Born 1865 in Gothenburg. ∞ mechanic. Died 1928,  
 of cancer of the ovary. The information obtained from her daughter, to  
 whom the physicians had stated that it was a case of ovarian tumor, in-  
 operable owing to involvement of the peritoneum.

FATHER'S YOUNGEST SISTER.—Born Feb. 28th, 1881, in Svedala, Swe-  
 den. Died in Malmö Feb. 4th, 1943, of cancer of the ovary. Operated on  
 by Dr. Lindquist, Malmö, Nov. 18th, 1942.



Pedigree 11.

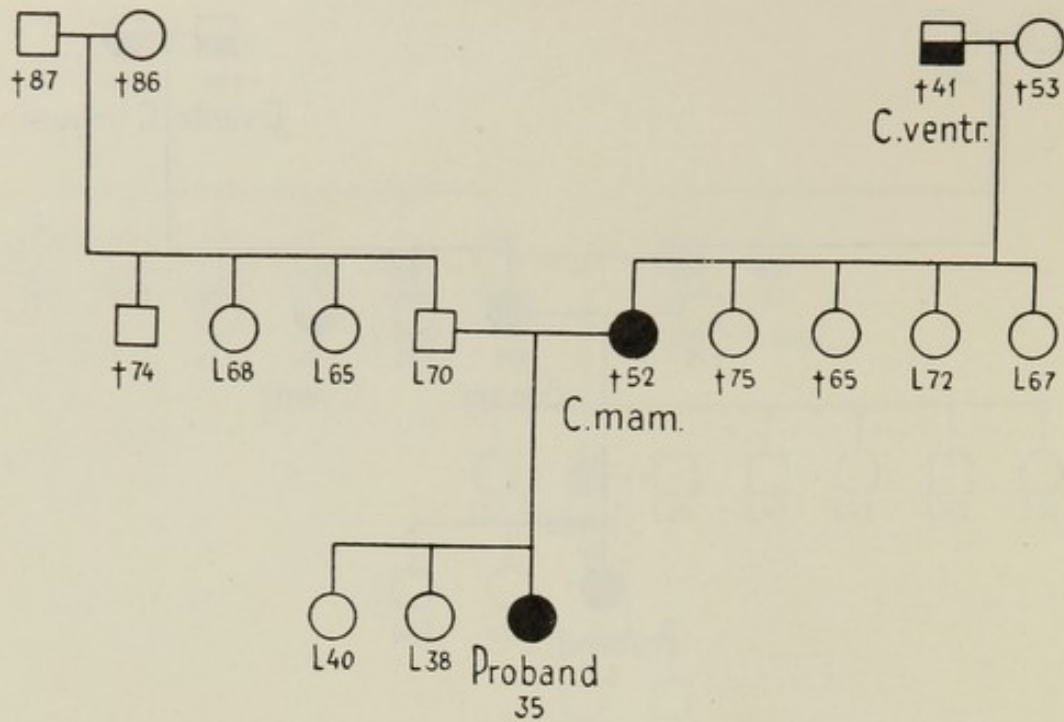
PROBAND (Deaconesses' Hospital, Copenhagen; service B, no. 1409/42). —○, born in Copenhagen Jan. 19th, 1891. Artist painter; single. At eighteen, appendicitis. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Never pregnant. A swelling in the right breast noticed three years before admission to hospital. Consulted physician several times, but was always assured that the tumor was absolutely benign and no cause for worry. Only when there came increasing retraction of the nipple was she referred to a surgical specialist. Aug. 15th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Bloustrød Dec. 2nd, 1859. ∞ masseur. Died in Copenhagen July 23rd, 1932. Two years before she died, a tumor began to develop in her right breast. It gradually increased in size, and the nipple noticeable retracted. In view of her age, the physician consulted thought that surgical intervention should not be attempted. The immediate cause of death was cerebral apoplexy. The diagnosis of breast cancer was verified by inquiry to her physician.

MOTHER'S FATHER.—Born 1834 in Bloustrød. Retired farmer. Died 1900 in Bloustrød, of cancer of the stomach. The disease was of a couple of years' duration, with symptoms of pyloric stenosis, in the last stage icterus. Diagnosis: cancer of the stomach.

MOTHER'S MOTHER.—Born 1835 in Haderslev. ∞ farmer. Died 1915 in Bloustrød, of cancer of the tongue, in the left side of which there was a crateriform ulcer about 3 cm. in diameter. Lymph node metastases in left submaxillary region. Diagnosis: cancer of the tongue.

MOTHER'S SISTER.—Born in Bloustrød Feb. 2nd, 1857. ∞ restaurant-keeper. Died in St. Joseph's Hospital, Copenhagen, May 17th, 1921, of cancer of the stomach. The diagnosis verified by the hospital (Journal no. 75/1921).

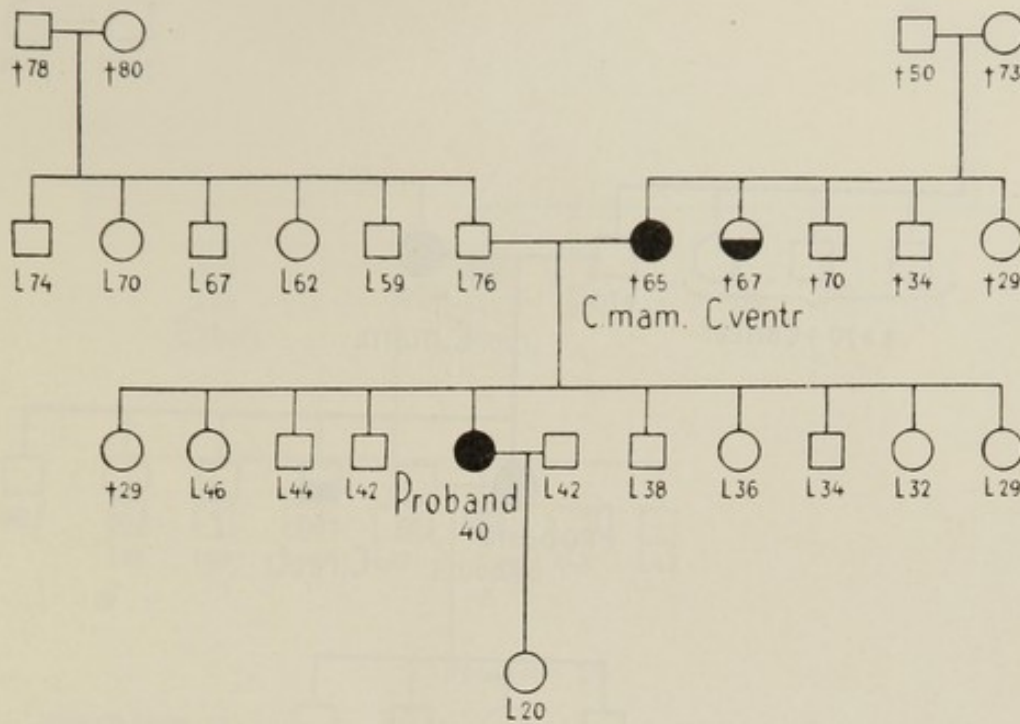


Pedigree 12.

PROBAND (Municipal Hospital, Copenhagen, service 1).—○, born in Vester Aaby May 29th, 1907. Telephone assistant; single. Formerly well. Menstruation since eighteenth year, regular. Never pregnant. Tumor in right breast noticed two weeks before admission. Jan. 16th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Svendborg Jan. 15th, 1872. ∞ commercial agent. Died in Gentofte Apr. 7th, 1924, of breast cancer. The diagnosis verified by death certificate.

MOTHER'S FATHER.—Born 1836. Livery-stable owner in Svendborg. Died there June 22nd, 1877, of cancer of the stomach. The diagnosis verified by death certificate.

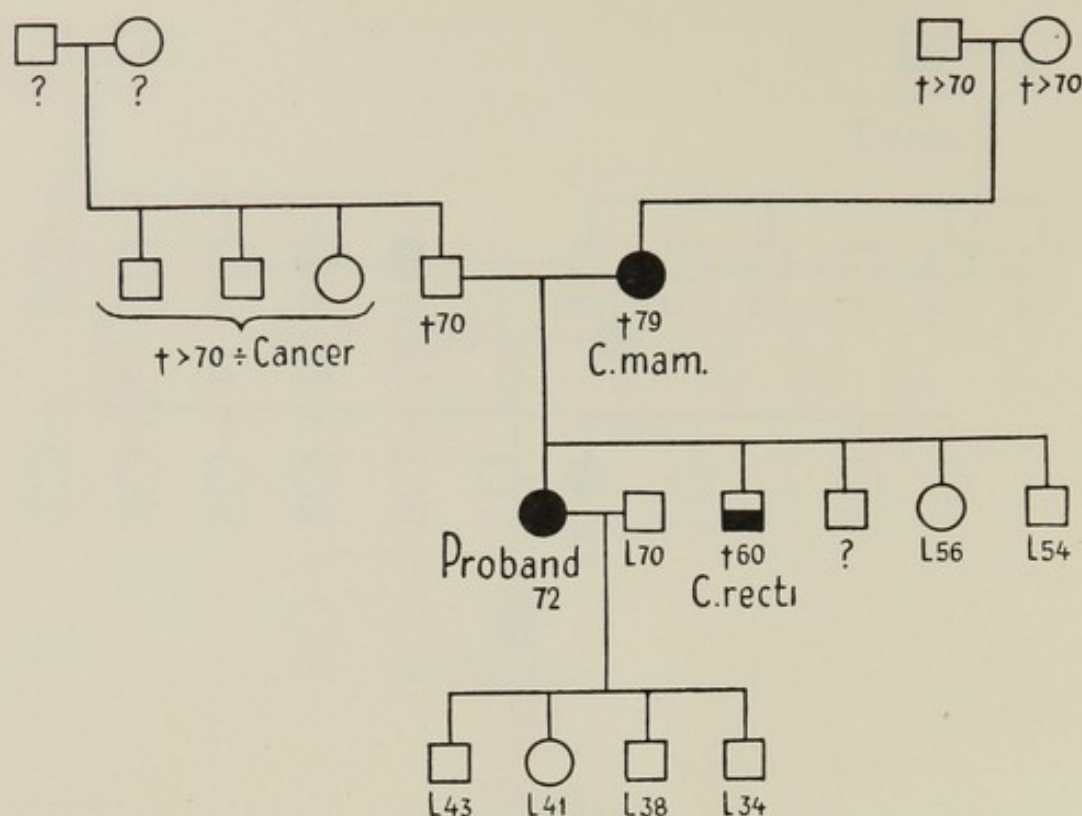


Pedigree 13.

PROBAND (Radium Center, Copenhagen; no. 29934).—○, born in Nykøbing (Falster) June 6th, 1902. ∞ cigarmaker. Formerly well. Menstruation since fourteenth year, regular. One childbirth. Nursed only three months, owing to her work. Thinks that in her occupation with packing of tobacco boxes she has often been exposed to slight injuries of the breast. In 1935 treated at the St. Lukas Hospital, Copenhagen, for ruptured ectopic pregnancy. Tumor in the right breast discovered about six months before admission to hospital. Feb. 1st, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born 1873 in Nykøbing (Falster). ∞ bridge-watchman. Died in Nykøbing Sep. 7th, 1938, of cancer of the breast. The diagnosis verified by death certificate.

MOTHER'S ELDEST SISTER.—Born 1869 in Nykøbing (Falster). ∞ pattern maker. Died in Nykøbing Sep. 8th, 1936, of cancer of the stomach. The diagnosis verified by death certificate.



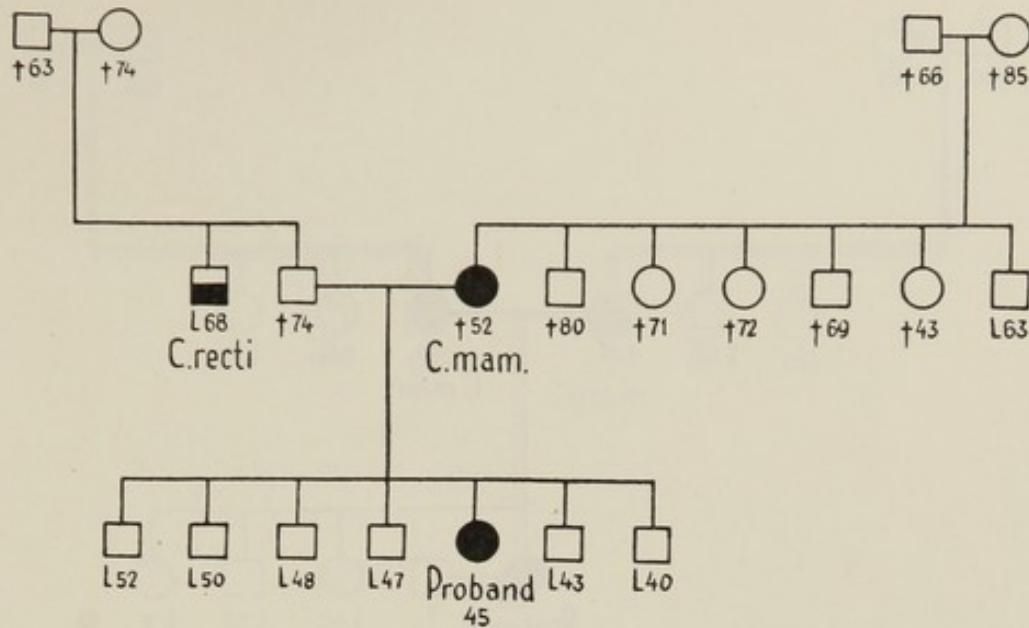
Pedigree 14.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1151/42).—  
 ○, born in Copenhagen Apr. 30th, 1870. ∞ collector. Formerly well.  
 Menstruation from fourteenth to fifty-second year, regular. Four childbirths.  
 Nursed about a year after each. Tumor of left breast noticed eight days  
 before admission. Apr. 30th, 1942, ablation of the left breast, with evacuation  
 of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Svinninge March 15th, 1851. ∞ coachman. Died in  
 Copenhagen Nov. 30th, 1930, of cancer of both breasts. The diagnosis verified  
 by death certificate.

ELDEST BROTHER.—Born 1882 in Copenhagen. Commercial agent. Died  
 in Lyngby in September, 1942, of cancer of the rectum. The diagnosis verified  
 by the Radium Center, Copenhagen, where he had been an out-door patient  
 (Journal no. 26805).



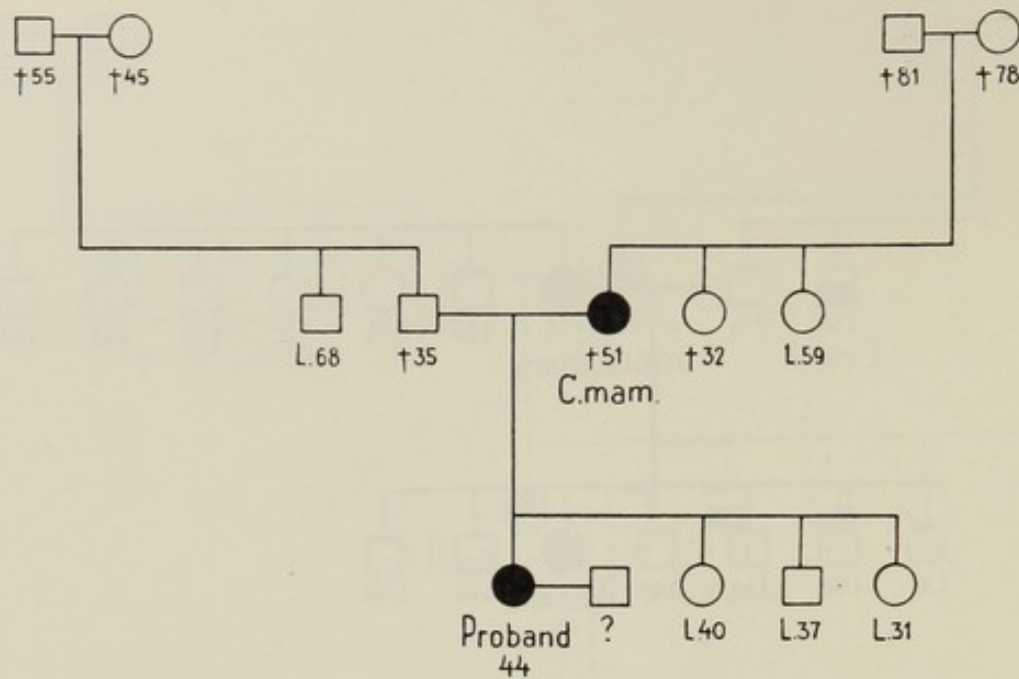


Pedigree 15.

PROBAND (Radium Center, Copenhagen; no. 28024).—○, born in Rødvig March 19th, 1897. Cashier; single. In 1937 treated for Basedow's disease at the Frederiksberg Hospital, otherwise formerly well. Menstruation since seventeenth year, regular. Never pregnant. Tumor of left breast observed three months before admission. Sep. 25th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus carcinoma.

MOTHER.—Born in Sierslev Aug. 7th, 1868. ∞ fisher. Died in Rødvig Apr. 16th, 1920, of breast cancer. The diagnosis verified by death certificate.

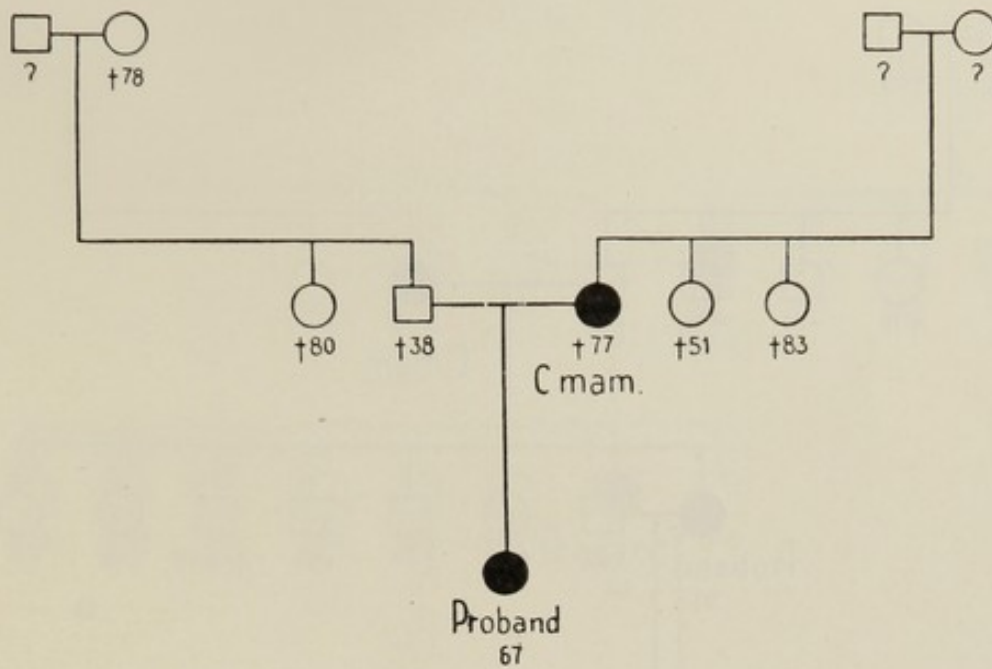
FATHER'S BROTHER.—Born 1874 in Rødvig. Fisher. In 1943 treated at the State Hospital, service D, Copenhagen, for cancer of the rectum (Journal no. 1163/43). Histologic diagnosis: carcinoma of the rectum.



Pedigree 16.

PROBAND (Radium Center, Copenhagen; no. 29877).—○, born in Copenhagen Jan. 19th, 1899. Housemaid; divorced. Menstruation since fourteenth year, regular. Never pregnant. Tumor of right breast noticed a year before admission. Trepine biopsy. Histologic diagnosis: adenocarcinoma.

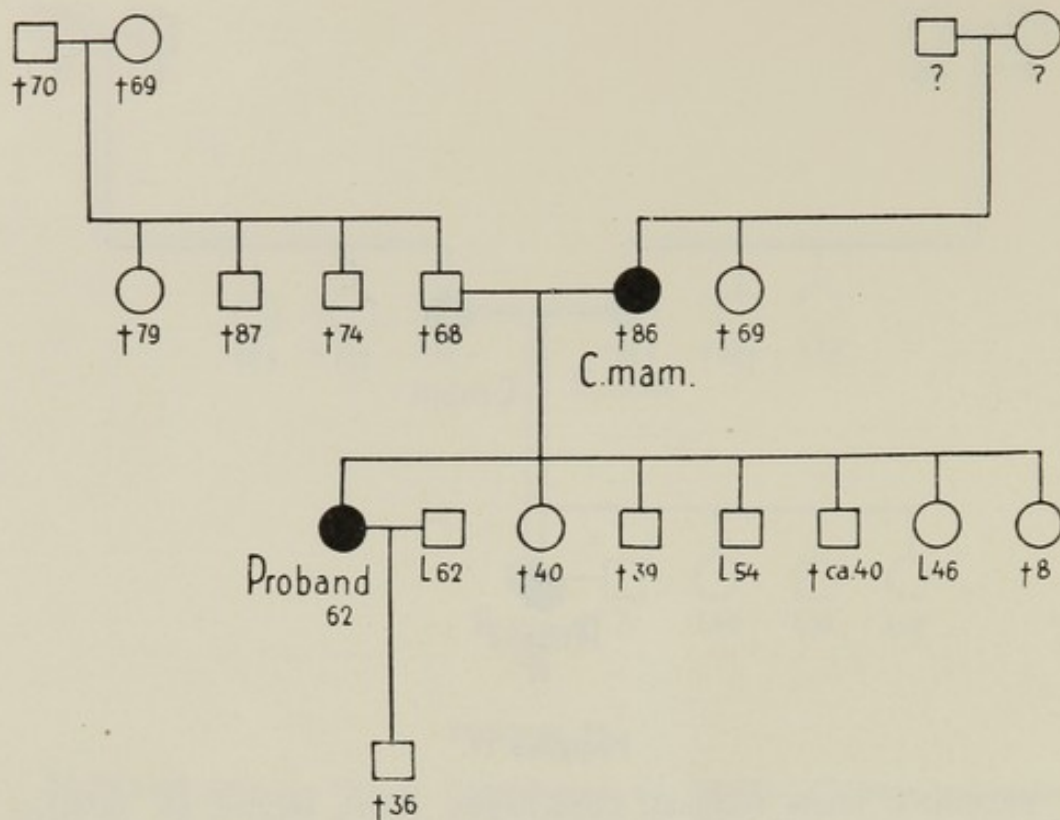
MOTHER.—Born on Læsø Aug. 13th, 1872. Workingman's widow. In 1922 operated on at the Sundby Hospital, for cancer of the breast; the following year signs of metastases to the spinal column. Died in the Municipal Hospital, Copenhagen, May 28th, 1924. The diagnosis verified from the hospital's death register. Diagnosis: breast cancer, with metastases to spinal column.



Pedigree 17.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 10/41).—  
 ○, born in Ruds Vedby May 6th, 1874. Seamstress; single. Menstruation from  
 thirteenth to fifty-second year, regular. Menopause normal. Never pregnant.  
 Tumor in left breast noticed two months before admission. Dec. 21st, 1940,  
 ablation of the breast, with evacuation of the axilla. Histologic diagnosis:  
 adenocarcinoma.

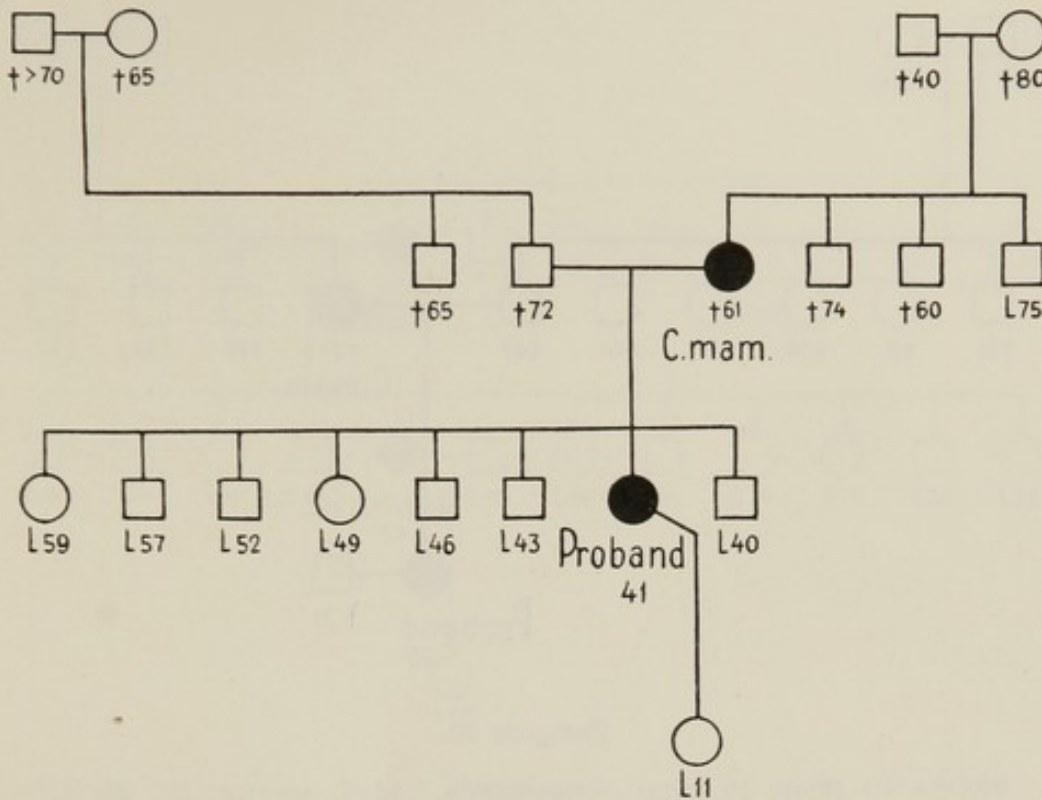
MOTHER.—Born in Bæring Sep. 18th, 1834. ∞ master brewer. In 1890  
 treated at the State Hospital, Copenhagen, for cancer of right breast;  
 operated on and the breast removed. Died in Copenhagen Feb. 4th, 1911.



Pedigree 18.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 1161/42).—  
 ○, born in Aalsgaarde Feb. 18th, 1880. ∞ provision dealer. Formerly well.  
 Menstruation from fourteenth to forty-fifth year, regular. Menopause normal.  
 One childbirth. Nursed six months. Tumor in left breast noticed a year before  
 admission. Feb. 2nd, 1942, ablation of the breast, with evacuation of the  
 axilla. Histologic diagnosis: solid carcinoma.

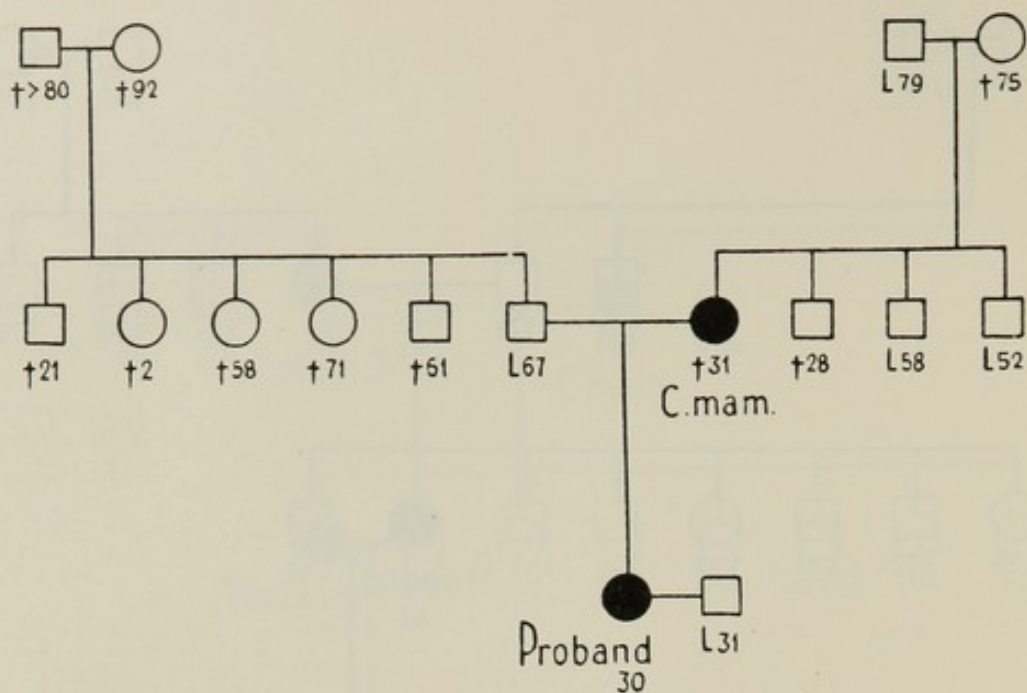
MOTHER.—Born Dec. 16th, 1856. Fisherman's widow. In the summer 1942  
 treated for cancer of the breast at the Radium Center in Copenhagen,  
 (journal no. 27448). Died in December, same year.



Pedigree 19.

PROBAND (State Hospital 1, Copenhagen; radiol. service, no. 187/41).—  
 ○, born in Nakskov May 5th, 1899. Factory worker; single. Formerly well.  
 Menstruation since fourteenth year, regular. One childbirth. Did not nurse,  
 owing to hypogalactia. Tumor in left breast noticed a month before admis-  
 sion. March 12th, 1941, ablation of the breast, with evacuation of the axilla.  
 Histologic diagnosis: adenocarcinoma and solid carcinoma.

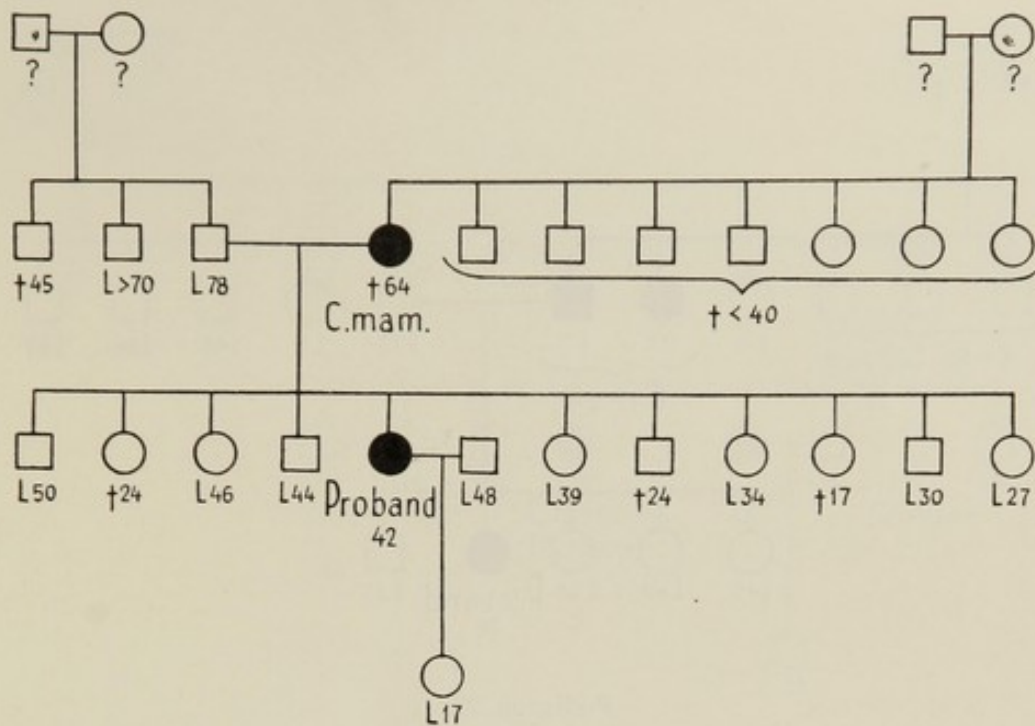
MOTHER.—Born on Langeland Oct. 23rd, 1862. ∞ workingman. Died in  
 Nakskov Oct. 31st, 1923, of cancer of the breast. The diagnosis verified by  
 death certificate.



Pedigree 20.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 466/41).—  
 ○, born in Frederiksberg June 1st, 1910. ∞ nurseryman. Formerly well.  
 Menstruation since fifteenth year, regular. Never pregnant. Three months  
 before admission she had noticed a small lump in her left breast. Sep. 14th,  
 1940, ablation of the breast, with evacuation of the axilla. Histologic diag-  
 nosis: solid carcinoma.

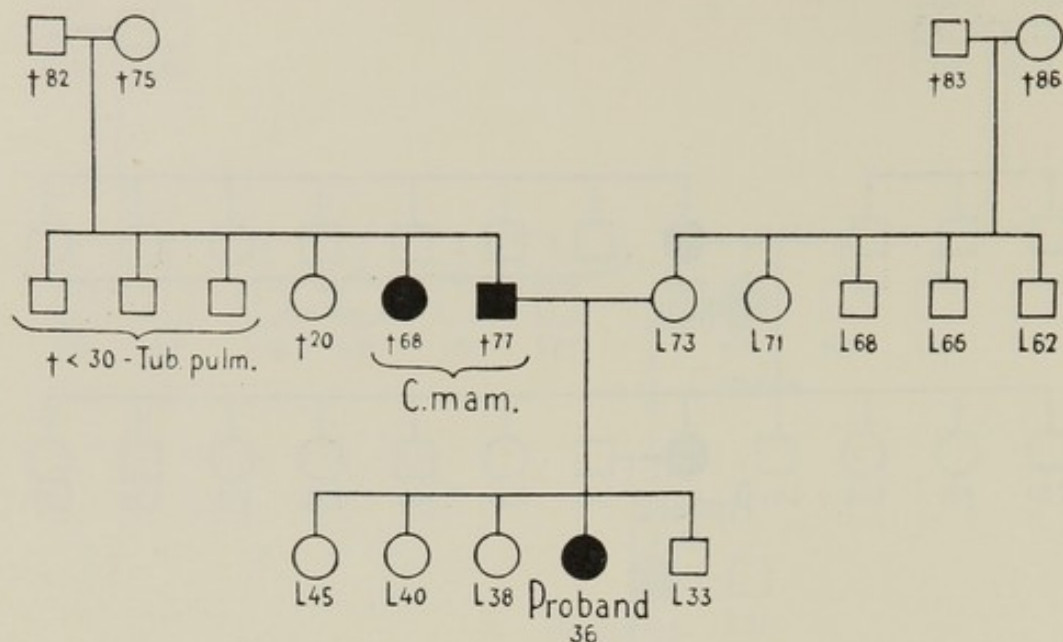
MOTHER.—Born in Copenhagen May 10th, 1886. ∞ workingman. Died  
 in Copenhagen June 11th, 1917, of cancer of the breast. The diagnosis veri-  
 fied by death certificate.



Pedigree 21.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 231/39).—  
 ○, born in Germany Aug. 28th, 1897. ∞ brewery workman. Formerly well.  
 Menstruation since fourteenth year, regular. One childbirth. Nursed seven  
 months. Tumor in left breast noticed two weeks before admission. Apr. 28th,  
 1939, ablation of the breast, with evacuation of the axilla. Histologic diag-  
 nosis: scirrhus carcinoma.

MOTHER.—Born Sep. 7th, 1871. ∞ contractor. Died Sep. 23rd, 1935, in  
 hospital in Barmbach, Germany, of cancer of the liver. Some years before,  
 one of her breasts had been removed, owing to mammary cancer.



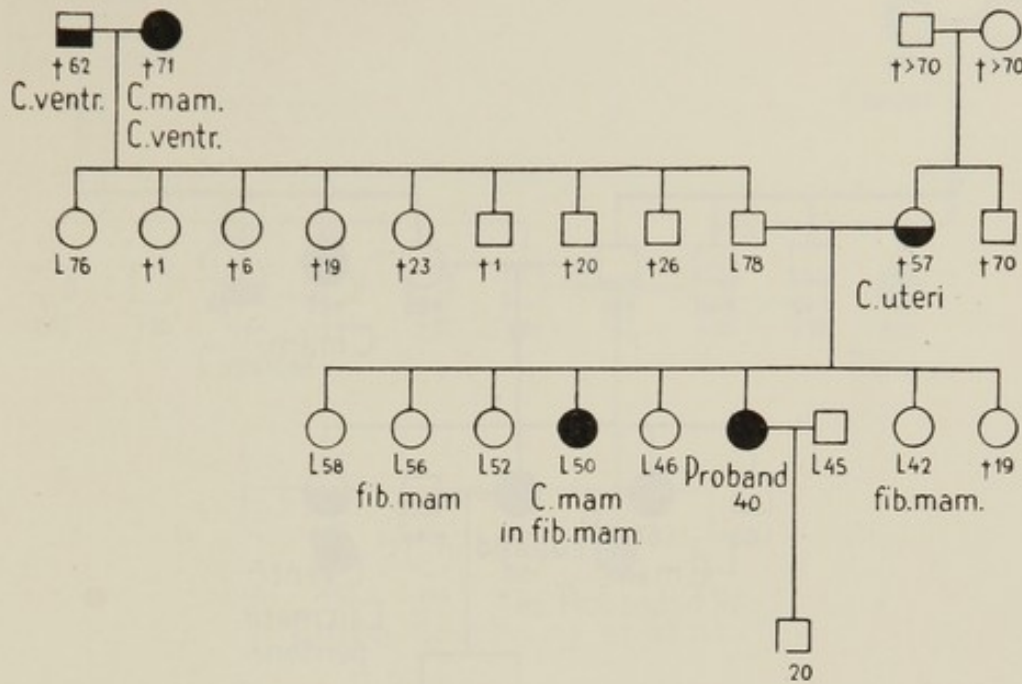
Pedigree 22.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1140/42).—  
 ○, born in Holstebro Sep. 5th, 1906. Hospital nurse; single. Formerly well.  
 Menstruation since fourteenth year, regular. Never pregnant. Tumor in right  
 breast noticed two months before admission. May 8th, 1942, ablation of the  
 breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Vind, near Holstebro, Sept. 29th, 1859. Farm-owner.  
 Died in Vind Dec. 15th, 1936. In 1918, he had been operated on at the  
 Holstebro Hospital and one of his breasts removed. The tumor had slowly  
 developed to the size of an apple, but had not been ulcerating. Inquiry to  
 the hospital has failed to establish its malignancy, because the case record  
 no longer exists. The death certificate was issued by a lay coroner and does  
 not contain any information. The most likely diagnosis is cancer of the  
 breast.

FATHER'S YOUNGEST SISTER.—Born in Vind May 1st, 1857. ∞ farmer.  
 Died in Vinding, near Holstebro, Apr. 8th, 1926, of cancer of the breast. The  
 diagnosis verified by death certificate.





Pedigree 23.

PROBAND (Radium Center, Copenhagen; no. 23422).—○, born in Copenhagen July 16th, 1900. ∞ bookkeeper. In childhood and youth well. Menstruation since fifteenth year, always somewhat irregular. In the last year often slight bleedings during the interval, and always contact-bleeding. Treated by specialist for cervical erosion. In 1930, a fibroadenoma of the right breast was removed at the St. Lucas Hospital. Noticed a small lump in her right breast two months before present admission to hospital. Trepine biopsy from both breasts. Histologic diagnosis: solid carcinoma of right breast, chronic mastitis of the left.

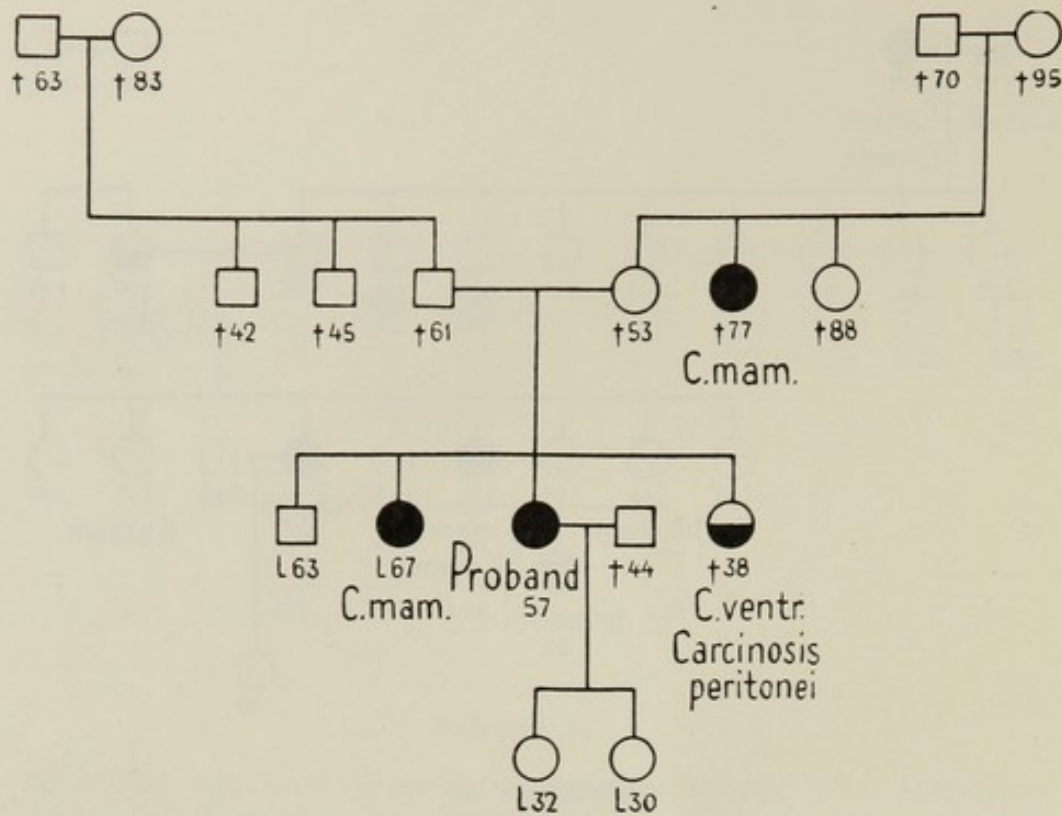
FATHER'S MOTHER.—Born in Svendborg Aug. 2nd, 1840. ∞ shoemaker. Died July 20th, 1911, of cancer of the breast and stomach. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born in Svendborg May 16th, 1838. Shoemaker. Died in Svendborg Nov. 30th, 1900, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER.—Born in Roskilde Apr. 26th, 1868. Divorced. Died in Copenhagen in April, 1925, of cancer of the uterus. The diagnosis verified by the Radium Center (Journal no. 3031/24: inoperable uterine cancer).

MOTHER'S FOURTH OLDEST SISTER.—Born in Copenhagen Feb. 4th, 1893. ∞ lawyer. Died in U.S.A. in 1934, of cancer of the breast. During a visit to Denmark some years before, she had had a small nodule in her right breast removed by surgical operation. Later, the family received information that she in U.S.A. had "had the entire breast removed" owing to recurrence, and that she some years afterwards had died of the disease.

It is interesting to notice that, moreover, two of the proband's sisters have been treated for fibroadenoma of the breast.



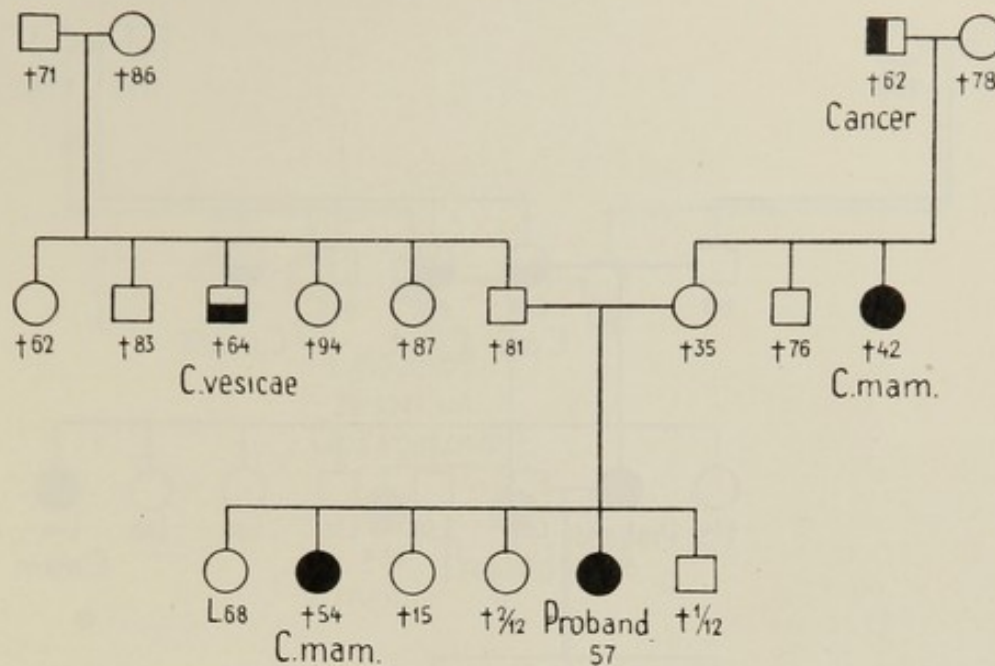
Pedigree 24.

PROBAND (Radium Center, Copenhagen; no. 24421).—○, born in Copenhagen Sep. 10th, 1883. Widow. Clerk. Formerly well. Menstruation from fifteenth to fiftieth year, regular. Menopause normal. Two childbirths. Nursed only respectively one and three months, owing to hypogalactia. Tumor in left breast noticed two months before admission. July 4th, 1941, ablation of the breast, with evacuation of axilla. Histologic diagnosis: solid medullary carcinoma.

MOTHER'S SISTER.—Born in Sweden Jan. 27th, 1847. ∞ mayor. In 1920 operated on for mammary cancer and one breast removed, at the hospital in Varberg, Sweden. Died in Kungsbacka, Sweden, Feb. 10th, 1924, of metastases to the liver. The diagnosis verified by the hospital.

ELDEST SISTER.—Born in Copenhagen Oct. 27th, 1880. ∞ school-teacher. In May, 1941, operated on at St. Maria Hospital, Roskilde, for cancer of the right breast. The diagnosis verified by the hospital. Histologic diagnosis: solid scirrhus carcinoma.

YOUNGEST SISTER.—Born in Copenhagen Apr. 23rd, 1888. ∞ army lieutenant. Died in the State Hospital, Copenhagen, May 5th, 1926, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 25.

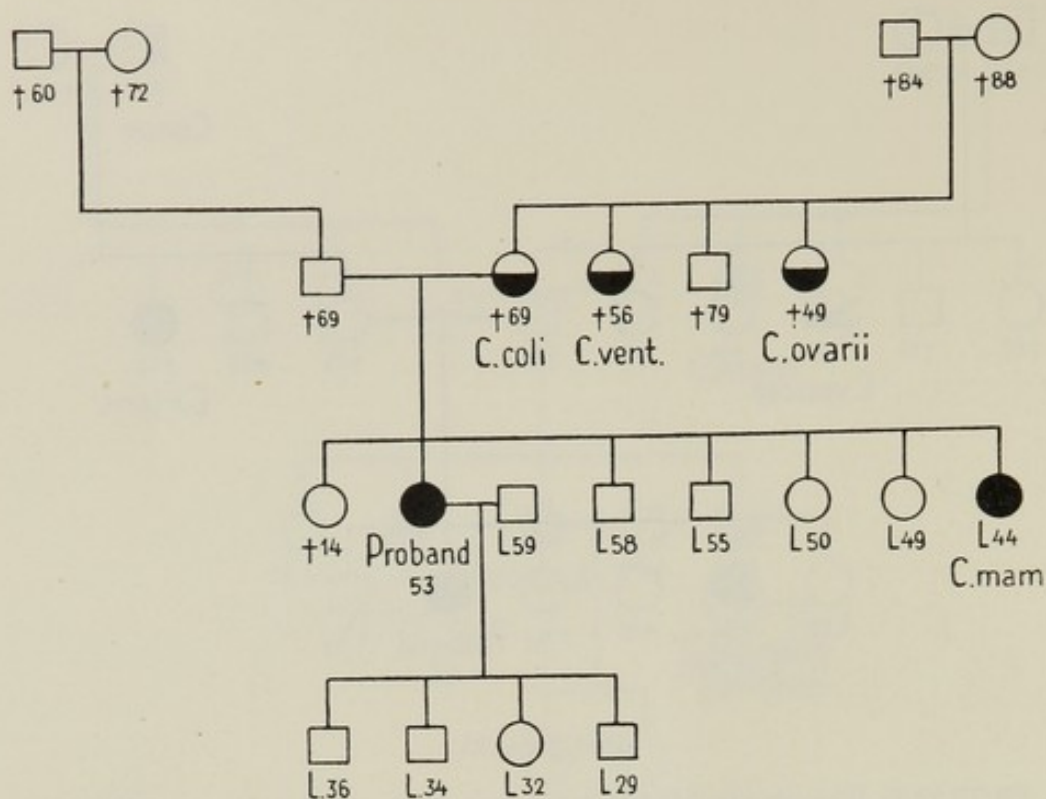
PROBAND (Bispebjerg Hospital; Copenhagen; service D, no. 2067/42).—  
 ○, born in Copenhagen Oct. 2nd, 1885. Teacher, single. Menstruation from  
 fifteenth to fiftieth year, regular. Menopause normal. In 1914, pleurisy. In  
 1936 operated on at the Deaconesses' Hospital, Copenhagen, for ovarian  
 cyst. Never pregnant. Noticed a lump in her right breast three weeks before  
 present admission to hospital. March 27th, 1942, extirpation of tumor in  
 the breast. Histologic diagnosis: colloidal carcinoma.

NEXT OLDEST SISTER.—Born in Rønne Dec. 8th, 1876. ∞ consul. In  
 May, 1929, operated on at the Gentofte County Hospital, for cancer of the  
 breast. Died in Copenhagen Oct. 8th, 1930, of metastases to the lung. The  
 diagnosis verified by death certificate.

FATHER'S NEXT OLDEST BROTHER.—Born in Bodilsker May 20th, 1833.  
 School-teacher. Died in Nykøbing (Falster) Jan. 19th, 1917, of cancer of the  
 bladder. The diagnosis verified by death certificate.

MOTHER'S SISTER.—Born in Holstebro July 24th, 1855. Single. Died in  
 Copenhagen Aug. 17th, 1897, of breast cancer with metastases to the lung.  
 Diagnosis verified by death certificate.

MOTHER'S FATHER.—Born in Aarhus Nov. 8th, 1814. Clergyman. Died  
 in Kirkehyllinge Dec. 21st, 1876, of cancer. Death certificate does not exist,  
 but in the parish register for Kirkehyllinge cancer is given as the cause of  
 death, without statement of localisation.



Pedigree 26.

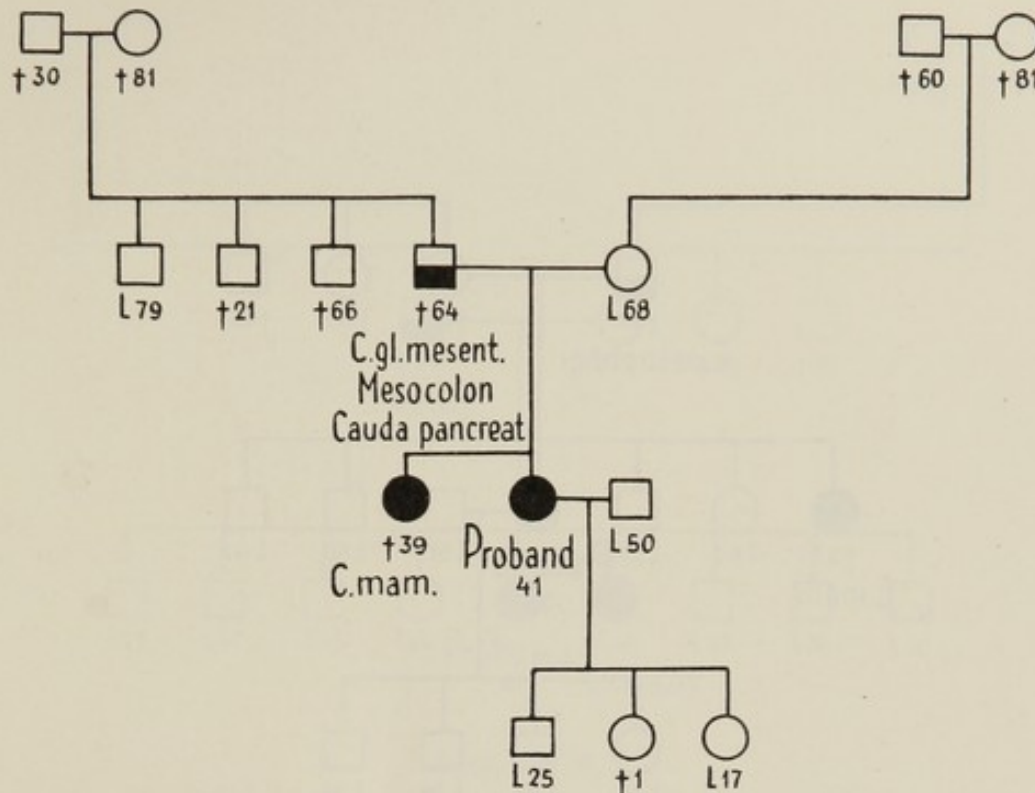
PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Randbøl May 25th, 1882. ∞ pensioner. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Four childbirths. Nursed for about a year each time. Tumor in left breast noticed two months before admission. Aug. 15th, 1935, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid, scirrhus carcinoma.

YOUNGEST SISTER.—Born in Odense Apr. 14th, 1897. ∞ electrician, Hjørring. In Jan. 1941 treated at the Hjørring Hospital, for cancer of the breast, which was ablated. Histologic diagnosis of specimen from operation: solid carcinoma.

MOTHER.—Born in Randbøl Feb. 26th, 1861. ∞ forest-guard. Died in Odense Jan. 3rd, 1931, of cancer of the colon. The diagnosis verified by death certificate.

MOTHER'S ELDEST SISTER.—Born 1850 in Randbøl. ∞ farmer, Starup by Kolding. Died 1906, of cancer of the stomach. The diagnosis verified by inquiry to treating physician.

MOTHER'S YOUNGEST SISTER.—Born 1863 in Randbøl. Midwife, single. Died 1912 in Give Hospital, of ovarian cancer. Attempt to get the diagnosis verified by inquiry to the hospital failed, because the existing records do not go so far back; but it appears that the physician who treated her shall have stated to several members of the family that it was a case of malignant tumor of an ovary.

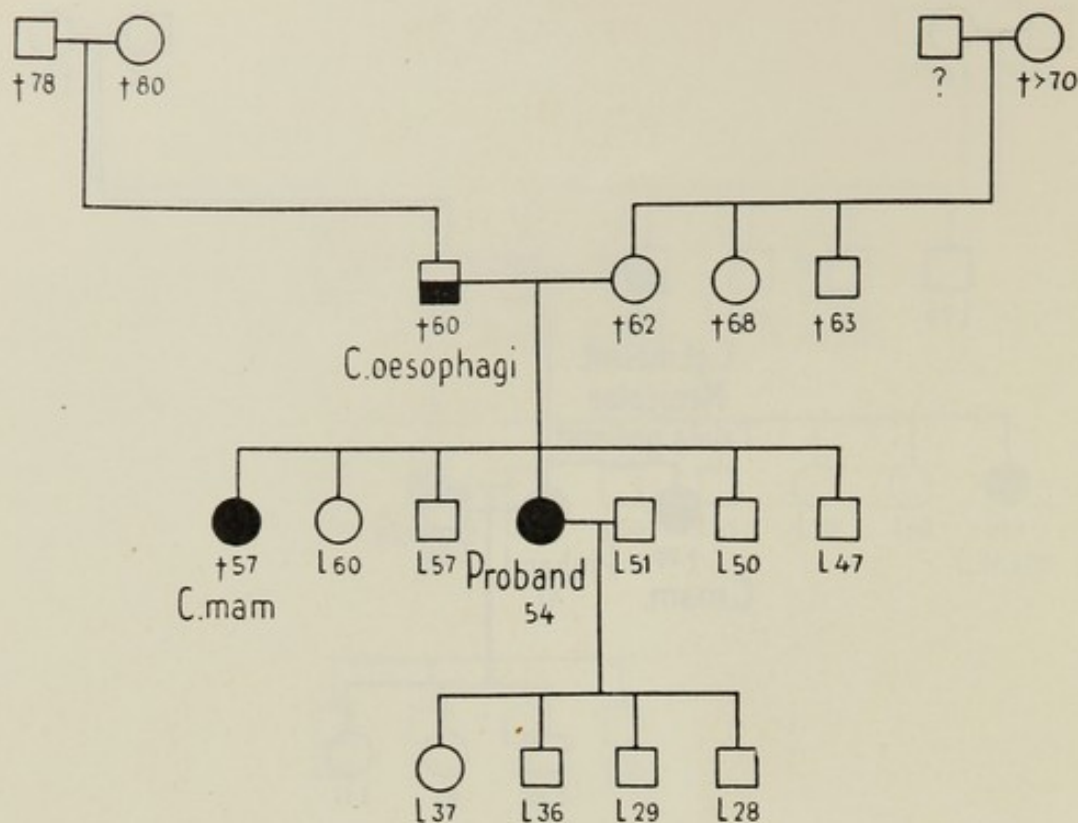


Pedigree 27.

PROBAND (Radium Center, Copenhagen; no. 21068).—○, born in Copenhagen Nov. 22nd, 1897. ∞ tailor. As child and young well. Menstruation since fifteenth year, always irregular. In September, 1941, treated at the Radium Center, with roentgen, for persistent memorrhagia. Since then no bleeding. Since 1941 she has taken 1 mg. of estibilin daily, to lessen her climacteric troubles. In September, 1939, treated at the Radium Center for cancer of the left breast. Two weeks before present admission (1943) she noticed a lump in her right breast. Trepine biopsy. Histologic diagnosis: adenocarcinoma.

FATHER.—Born in Hobro Dec. 8th, 1867. Shoemaker. Died in the Frederiksberg Hospital July 9th, 1932, of carcinoma of mesenteric glands, cancer of pancreas and mesocolon.

SISTER.—Born in Copenhagen Apr. 26th, 1896. ∞ mechanic. Died in Køge march 31st, 1936, of cancer of the breast. Had in 1935 been treated at the Radium center, Copenhagen (Journal no. 12803). Histologic diagnosis: scirrhous carcinoma.

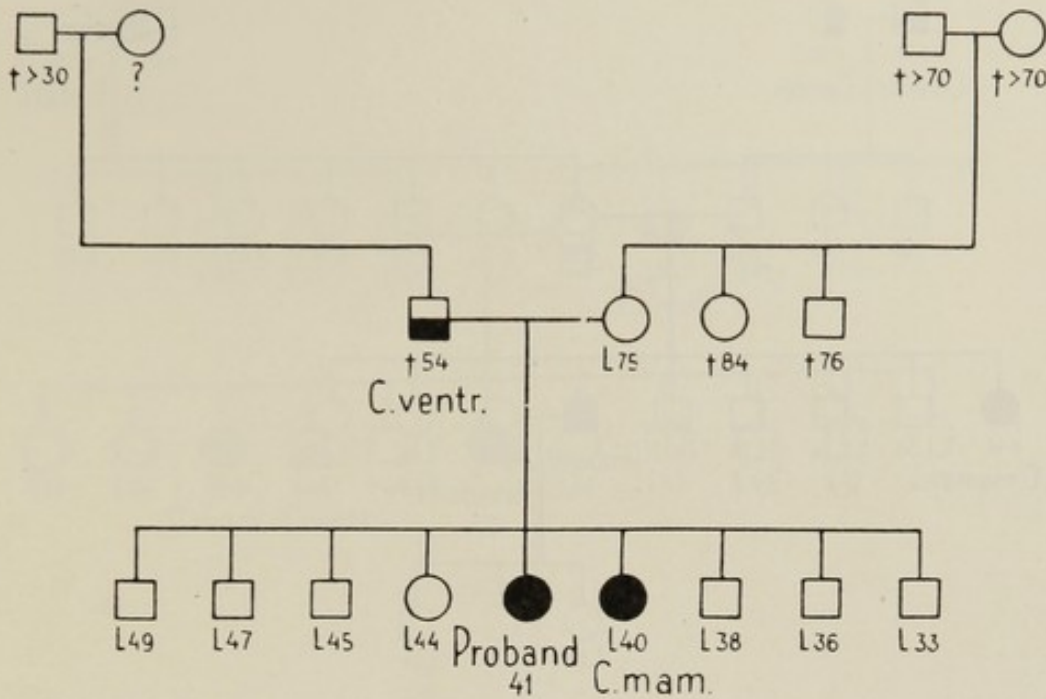


Pedigree 28.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 373/43).—  
 ○, born in Copenhagen June 5th, 1889. ∞ workingman. Formerly well.  
 Menstruation from thirteenth to fifty-third year, regular. Menopause normal.  
 Four childbirths. Nursed all the children for up to a year. Tumor in right  
 breast noticed two months before admission. July 11th, 1943, ablation of the  
 breast, with evacuation of the axilla. Histologic diagnosis: solid, partly  
 adenomatous carcinoma.

FATHER.—Born in Sorterup March 6th, 1853. Workingman. Died Nov.  
 14th, 1913, of cancer of the esophagus. The diagnosis verified by death  
 certificate.

ELDEST SISTER.—Born in Copenhagen Nov. 17th, 1876. ∞ tramway  
 functionary. Died Oct. 1933. In 1932 treated at the Municipal Hospital, Co-  
 penhagen, service 1, for cancer of the right breast. Histologic diagnosis:  
 solid carcinoma.

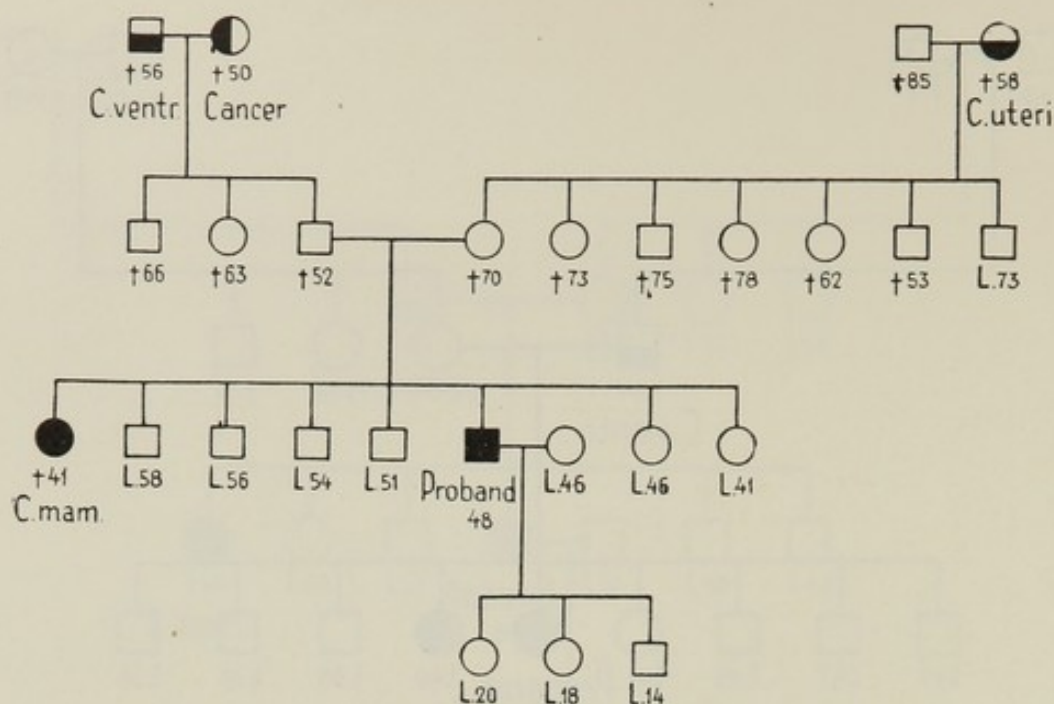


Pedigree 29.

PROBAND (Radium Center, Copenhagen; no. 26640).—○, born in Copenhagen Dec. 12th, 1901. Laboratory assistant, single. Formerly well. Menstruation from eighteenth year, regular. Never pregnant. Tumor in right breast noticed about five months before admission. Trepine biopsy. Histologic diagnosis: adenocarcinoma and solid carcinoma.

FATHER.—Born in Sweden Dec. 31st, 1865. Coachman. Died in the Frederiksberg Hospital, Copenhagen, 1919, of cancer of the stomach. The diagnosis verified by the hospital.

YOUNGEST SISTER.—Born in Copenhagen Feb. 1st, 1902. ∞ house-painter. In 1941 treated at the Radium Center, Copenhagen, for cancer of the breast (Journal no. 24565). Histologic diagnosis: adenocarcinoma.



Pedigree 30.

PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 617/42). —□, born in Slangerup March 24th, 1894. Confidential clerk; married. Formerly well; never mastitis; not aware of any injury to the breast. Noticed in the summer, 1938, that the left nipple was somewhat more retracted than the right, but did not seek medical advice until immediately before his admission to hospital in 1940, when he felt a solid lump below the areola and there at the same time came a slight serosanguinolent secretion from the nipple. March 11th, 1940, excision of the right breast and axillary lymph nodes. Histologic diagnosis: mammary adenocarcinoma. In 1942 treated with roentgen for local recurrence and axillary metastases.

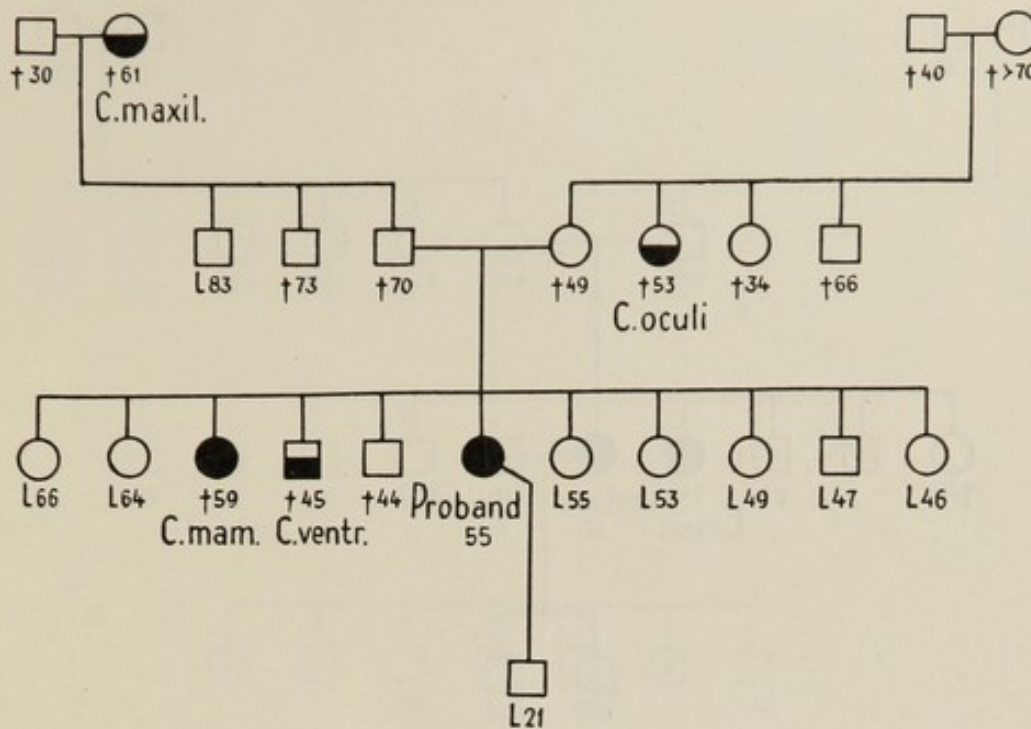
SISTER.—Born in Slangerup Sep. 10th, 1883. ∞ school-teacher. Died May 2nd, 1925, of cancer of the breast with metastases to bones. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born Dec. 26th, 1833. Mill-owner. Died March 22nd, 1888, of cancer of the stomach. The diagnosis verified by extract from parish register (Hjørlande parish).

FATHER'S MOTHER.—Born 1835. ∞ miller in Hjørlande. Died Dec. 22nd, 1885; according to the Hjørlande parish register of cancer, respecting the localisation of which no information has, however, been obtainable.

MOTHER'S MOTHER.—Born 1828. ∞ farmer. Died 1886 in Saltrup, of cancer of the uterus. The treating physician has stated to two of the proband's older relatives that the death was due to uterine cancer with dissemination in the abdominal cavity and the liver.





Pedigree 31.

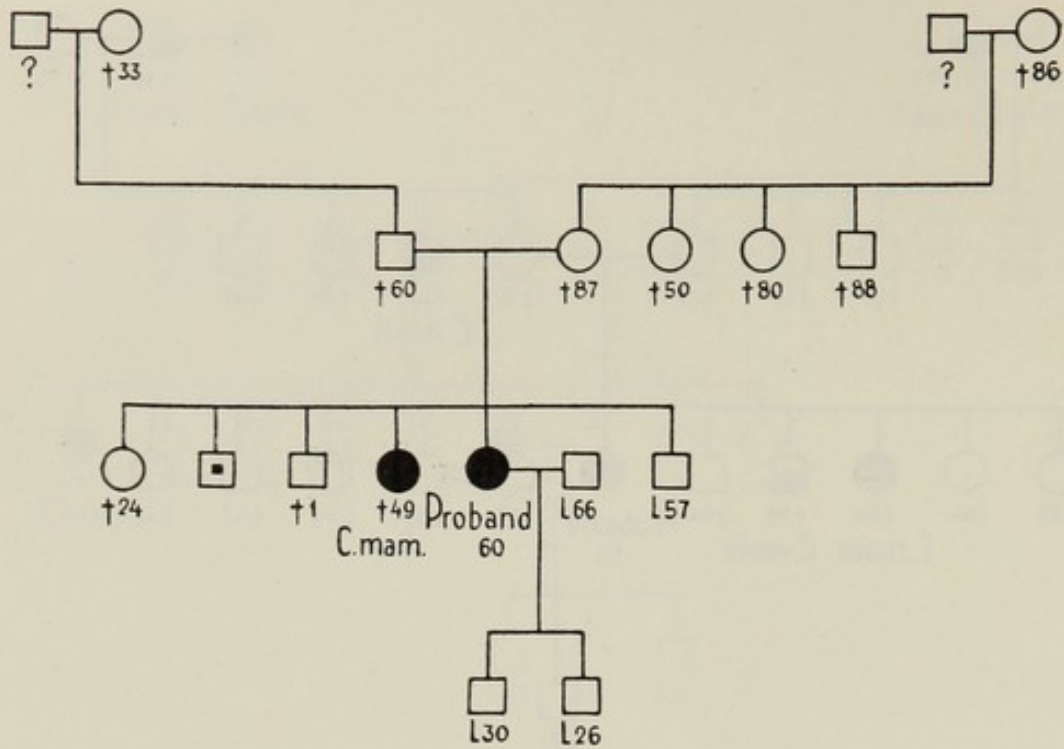
PROBAND (State Hospital, Copenhagen; service D, no. 826/42).—○, born in Kerteminde Sep. 22nd, 1886. Charwoman; single. Formerly well. Menstruation from sixteenth to sixty-fifth year, regular. Menopause normal. One childbirth. Nursed only a couple of months, owing to hypogalactia. Tumor in left breast noticed three days before admission. March 7th, 1942, extirpation of the tumor. Histologic diagnosis: solid carcinoma. March 14th, same year, ablation of the breast, with evacuation of the axilla.

MOTHER'S MOTHER.—Born June 3rd, 1816. ∞ workingman. Died 1877 in Kerteminde, of cancer of the maxilla. There was an ulcerated tumor on the left cheek, extending inwards to the mouth, and greatly enlarged lymph glands in the neck. The author thinks there can be no doubt that the diagnosis must be cancer of the maxilla.

MOTHER'S ELDEST SISTER.—Born in Lumby Oct. 6th, 1850. Housekeeper, single. Died 1913 in Lumby. In 1910 she had had her right eye removed by operation at St. Joseph's Hospital, Odense, and the specialist had informed the family that it was a case of malignant tumor. The physician who treated her at her home stated that death was due to metastases to the liver from the tumor in the eye. Diagnosis: cancer of the eye.

ELDER SISTER.—Born in Kerteminde Jan. 27th, 1880. ∞ electrician. Died in Copenhagen Oct. 29th, 1939, of cancer of the breast with metastases to the lung. The diagnosis verified by death certificate.

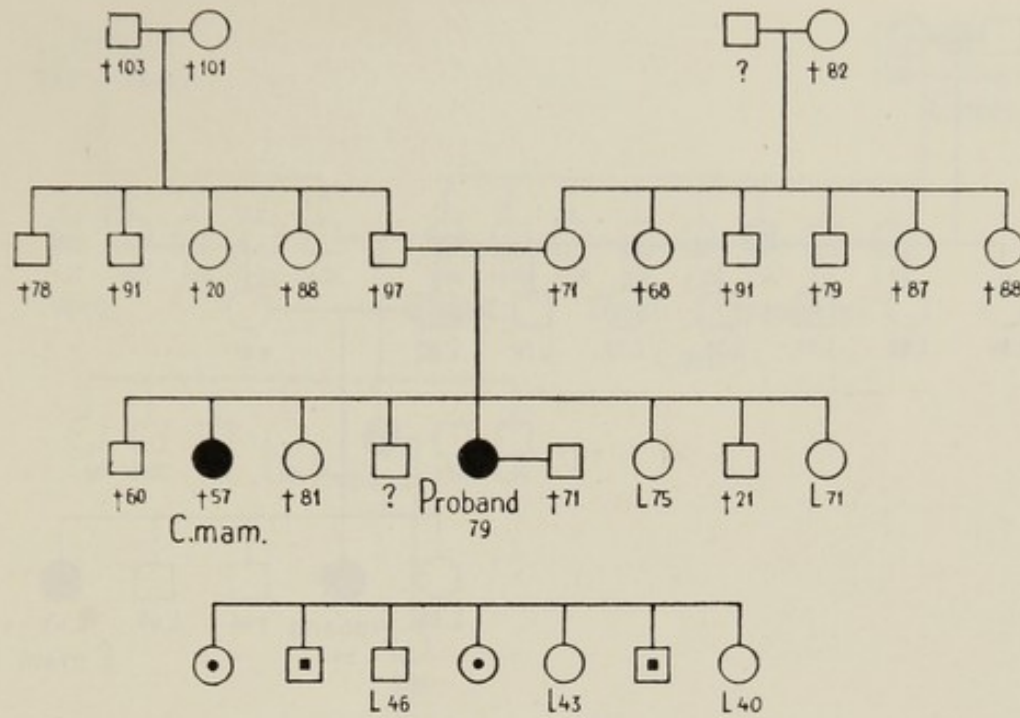
ELDEST BROTHER.—Born in Kerteminde March 16th, 1882. Housepainter. Died in the Municipal Hospital, Copenhagen, Dec. 17th, 1927, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 32.

PROBAND (Bispebjerg Hospital, Copenhagen; service D, no. 1923/42).—  
 ○, born Dec. 10th, 1881. ∞ school inspectress. Formerly well. Menstruation  
 from fourteenth to fifty-third year, regular. Menopause normal. Two child-  
 births. Nursed for about a year each time. The tumor in her right breast  
 noticed eight days before admission. May 16th, 1942, ablation of the breast,  
 with evacuation of the axilla. Histologic diagnosis: scirrhus carcinoma.

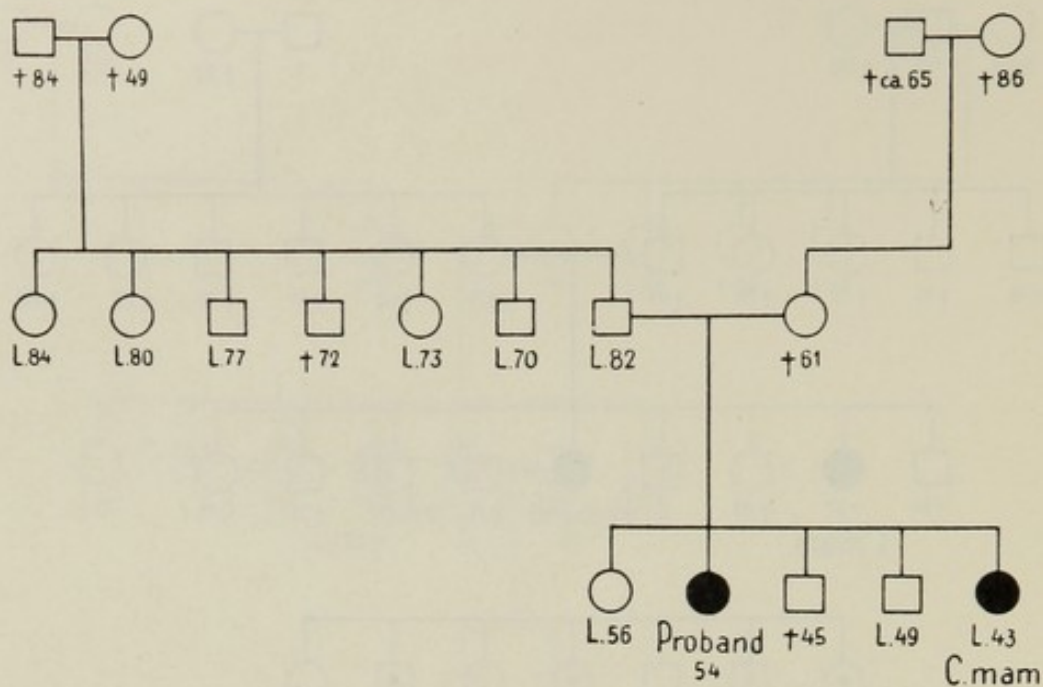
SISTER.—Born in Copenhagen Dec. 21st, 1879. School inspectress, single.  
 Died in Copenhagen Dec. 9th, 1929, of cancer of the breast. Metastases. The  
 diagnosis verified by death certificate.



Pedigree 33.

**PROBAND** (Radium Center, Copenhagen; no. 31347).—○, born in Ystad, Sweden, June 8th, 1864. Widow. Formerly well. Menstruation from fourteenth to forty-sixth year, regular. Menopause normal. Seven childbirths. Nursed all the children at least a year. In 1887, suppurating mastitis in left breast. Treated at the Frederiksberg Hospital, Copenhagen, with incision. Noticed the tumor in the left breast two months before present admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.

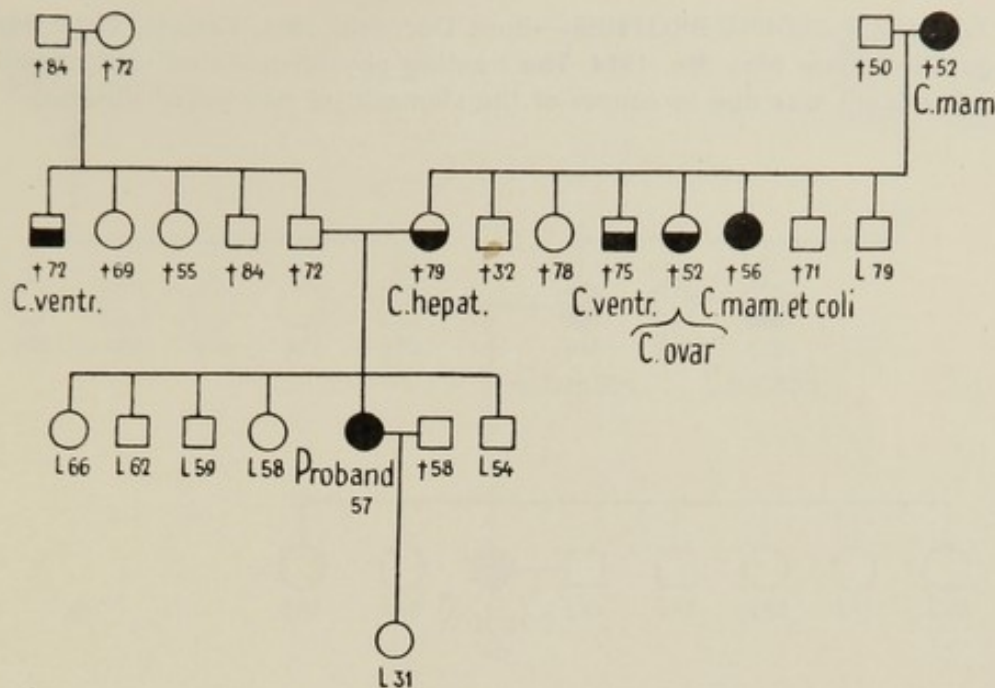
**ELDEST SISTER.**—Born in Ystad 1856. ∞ business manager. In 1911 operated on at hospital in Lund (Sweden), with ablation of left breast. Twice later treated with roentgen for metastases. Died in Malmö 1913.



Pedigree 34.

PROBAND (Radium Center, Copenhagen; no. 29665).—○, born in Copenhagen Feb. 28th, 1889. Seamstress, single. As child and young well. Menstruation from fourteenth to forty-ninth year, regular. Has for three years been taking estibilin (1 tablet à 0.1 mg. twice daily) for climacteric symptoms with hot flushes and headache. In 1913, ablation of left breast at the Bispebjerg Hospital, Copenhagen. Histologic diagnosis: cystic mastitis. Tumor in right breast noticed a week before present admission. Apr. 10th, 1943, ablation of the breast, with evacuation of axilla. Histologic diagnosis: solid medullary carcinoma.

SISTER.—Born in Copenhagen Aug. 28th, 1900. ∞ commercial agent. In 1936 treated at the Radium Center in Copenhagen (Journal no. 14815) for cancer of the right breast; histologic diagnosis medullary carcinoma; and in 1942 for cancer of the left breast.



Pedigree 35.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 370/40).—  
 ○, born in Østre Hæsinge Feb. 26th, 1883. Craneman's widow. Formerly  
 well. Menstruation from fourteenth to fifty-third year, regular. Menopause  
 normal. One childbirth. Nursed six months. A week before admission she  
 noticed a lump in her right breast. July 2nd, 1940, ablation of the breast,  
 with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER'S MOTHER.—Born in Hæsinge June 4th, 1822. ∞ miller. Died  
 in Arreskov Nov. 21st, 1874, of cancer of the breast. The tumor had not  
 been treated, and had in the course of a year developed into an enormous  
 ulcerated lump involving the entire breast and extending to the thorax.  
 Died under increasing cachexia. Diagnosis: cancer of the breast.

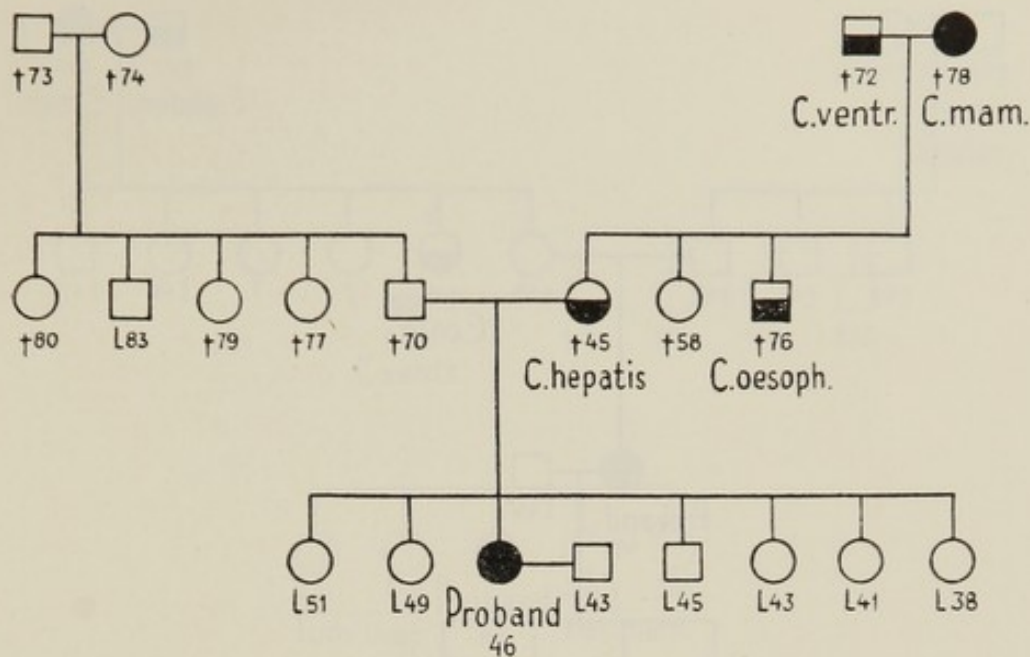
MOTHER.—Born in Hæsinge Nov. 23rd, 1848. ∞ farmer. Died in Hæsinge  
 Apr. 25th, 1928, of cancer of the liver. The diagnosis verified by death  
 certificate.

MOTHER'S NEXT ELDEST BROTHER.—Born in Hæsinge Aug. 11th, 1857.  
 General storekeeper. Died in the Bispebjerg Hospital, Copenhagen, service  
 A, Oct. 20th, 1933, of perforating cancer of the stomach. The diagnosis  
 verified by death certificate.

MOTHER'S NEXT YOUNGEST SISTER.—Born in Hæsinge Oct. 4th, 1858.  
 Died July 11th, 1911, in St. Elisabeth's Hospital, Copenhagen, of cancer of  
 the ovary. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born in Hæsinge May 13th, 1862. In  
 1905 operated on at Dr. Maaloe's clinic, Copenhagen, for cancer of the right  
 breast, which was removed. Readmitted in 1919, for cancer in the colon;  
 laparotomy and colostomy done, but the cancer inoperable. Died in Maaløv  
 Jan. 14th, 1919.

FATHER'S ELDEST BROTHER.—Born Dec. 6th, 1881. Farmer, Øster Hæsinge. Died there May 9th, 1914. The treating physician stated to the family that the death was due to cancer of the stomach, of two years' duration.



Pedigree 36.

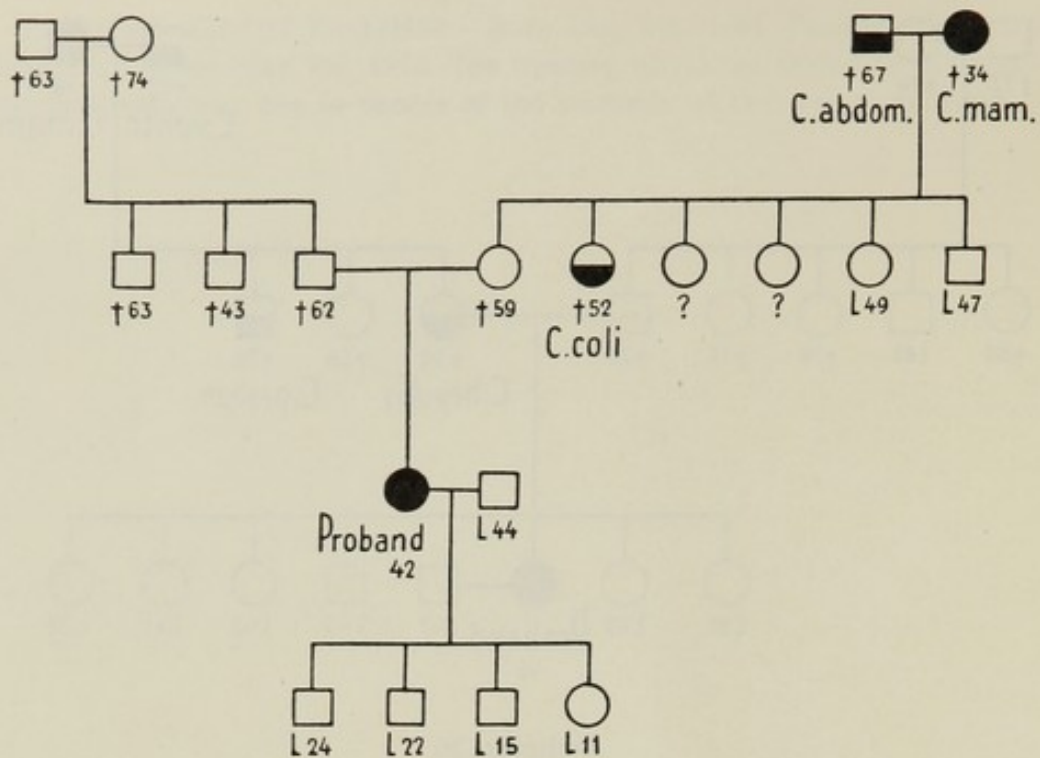
PROBAND (Radium Center, Copenhagen; no. 30551).—○, born in Rønne Aug. 10th, 1896. ∞ seaman. Formerly well. Menstruation since fourteenth year, regular. The bleedings in the last two years somewhat irregular and less copious than before. At the same time some climacteric troubles in the form of headaches, nervousness and periodical heat flashes, for which she has for two years been treated with estibilin tablets. Tumor in left breast noticed about a year before admission. In 1939 operated on for fibroadenoma of right breast. Trepine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER'S MOTHER.—Born 1826 in Knudsker. ∞ stone cutter. Died 1905 in Rønne, of cancer of the breast. The diagnosis verified by death certificate.

MOTHER'S FATHER.—Born 1832 in Knudsker. Stone cutter. Died 1904, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER.—Born in Rønne Jan. 20th, 1868. ∞ blacksmith. Died in Rønne May 21st, 1912, of cancer of the liver. The diagnosis verified by death certificate.

MOTHER'S BROTHER.—Born in Knudsker Feb. 19th, 1857. Stone cutter. Died in Rønne Sep. 2nd, 1933, of cancer of the esophagus. The diagnosis verified by death certificate.



Pedigree 37.

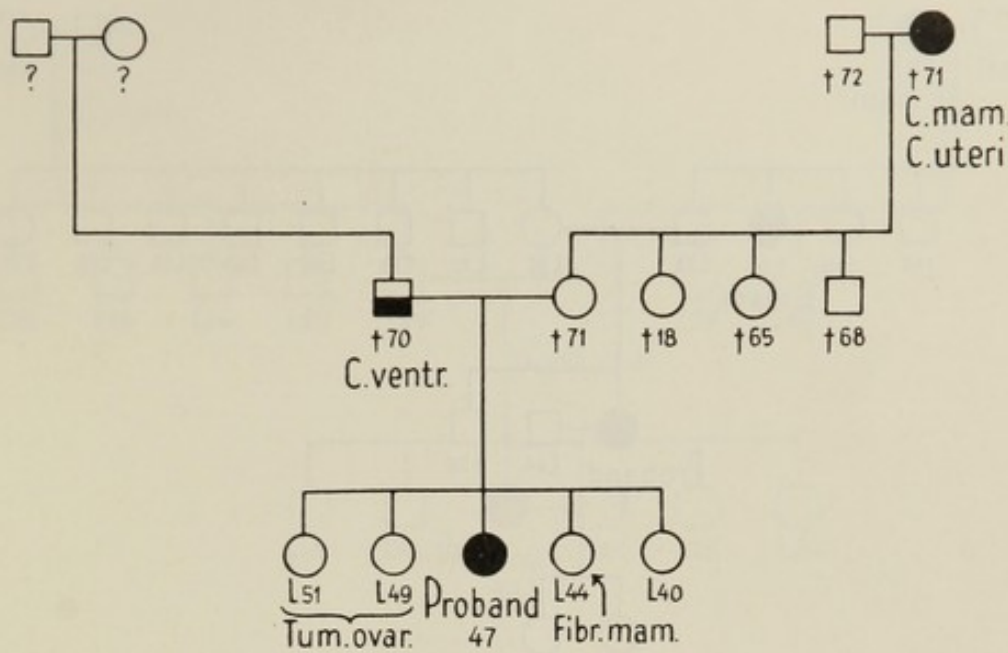
PROBAND (Radium Center, Copenhagen; no. 26271).—○, born in Copenhagen June 9th, 1899. Pianist; divorced. Formerly well. Menstruation since thirteenth year, regular. Four childbirths. Nursed respectively eighteen nine, nine and ten months. The nipple of left breast always been slightly inverted, which made the nursing rather difficult. A year before she noticed the tumor in the left breast, she had fallen with her bicycle, the handle-bar of which struck her in the breast, but there was no extravasation. Consulted her physician a month after she had discovered the tumor. Feb. 21st, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER'S MOTHER.—Born 1855 in Copenhagen. ∞ instrument maker. In 1876 admitted to the Frederiks Hospital, Copenhagen, treated there for cancer of the breast, which was eventually ablated. Died in Copenhagen Febr. 4th, 1889.

MOTHER'S FATHER.—Born 1850 in Sweden. Instrument maker. Died in the Municipal Hospital, Copenhagen, Aug. 8th, 1917, of cancer of the stomach. The diagnosis verified through the death register of the hospital.

MOTHER'S SISTER.—Born 1885 in Copenhagen. ∞ building contractor. Died 1937 in Roskilde, of cancer of the colon. The diagnosis verified by death certificate.



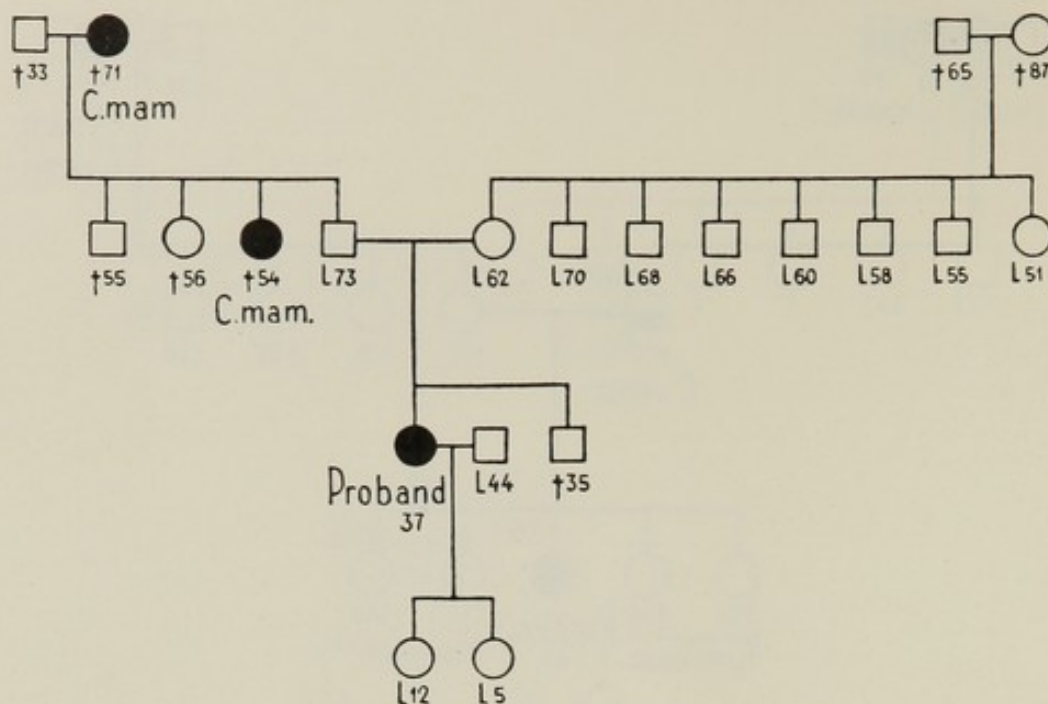


Pedigree 38.

**PROBAND** (State Hospital, Copenhagen; radiol. service).—○, born in Lundtofte Apr. 24th, 1895. Business manageress; unmarried. Formerly well. Menstruation since fifteenth year, regular. Never pregnant. Tumor in the right breast noticed about a month before admission. Feb. 16th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

**MOTHER'S MOTHER.**—Born 1828 in Copenhagen. ∞ work foreman. Died in Lyngby May 5th, 1900, of cancer of the uterus. The diagnosis verified by death certificate.

**FATHER.**—Born in Brede Sep. 1st, 1863. Butcher. Died in Lundtofte Dec. 21st, 1933, of cancer of the stomach, for which he had the year before been treated at St. Joseph's Hospital, Copenhagen. The diagnosis verified by death certificate.

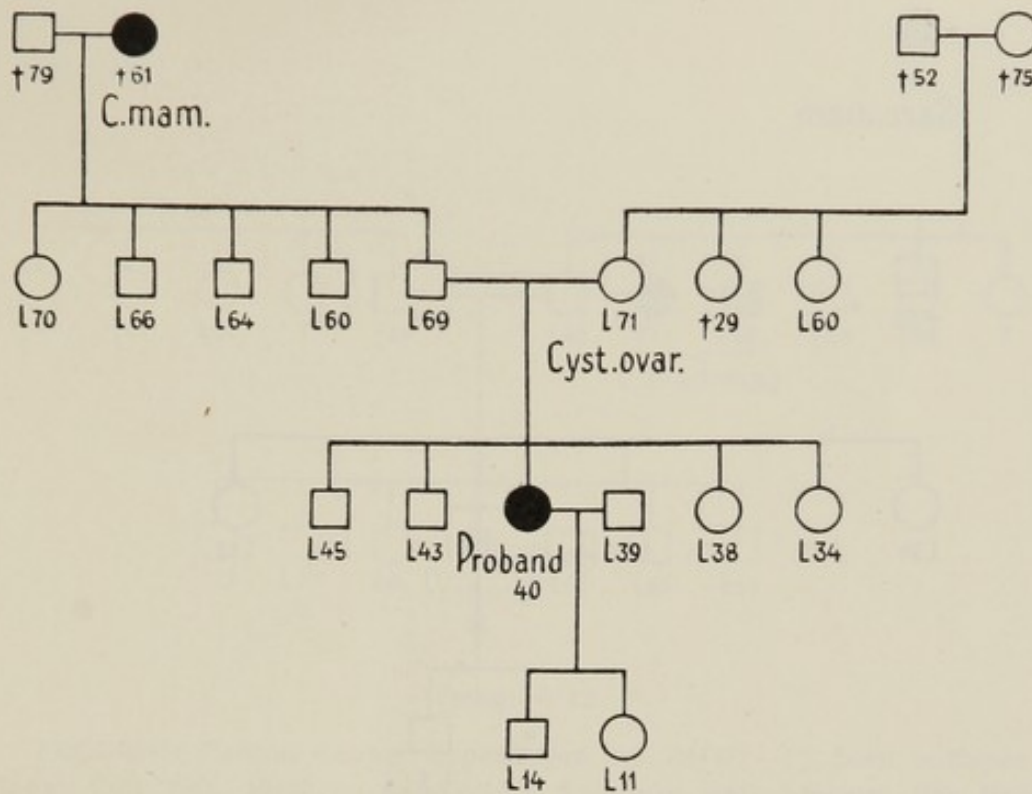


Pedigree 39.

PROBAND (Radium Center, Copenhagen; no. 25443).—○, born in Copenhagen Sep. 2nd, 1904. ∞ fishmonger. Formerly well. Menstruation since fifteenth year, regular. Two childbirths. Nursed about a year each time, but during the last lactation got galactophoritis of right breast. Was treated at home with hot compresses. Noticed a lump in her right breast three weeks before admission. Nov. 3rd, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

FATHER'S MOTHER.—Born in Lejre June 30th, 1832. Porter's widow. Died 1904 in Copenhagen. In 1901 treated at the Municipal Hospital, Copenhagen, for cancer of the breast (Journal no. 53/1901). Histologic diagnosis: carcinoma.

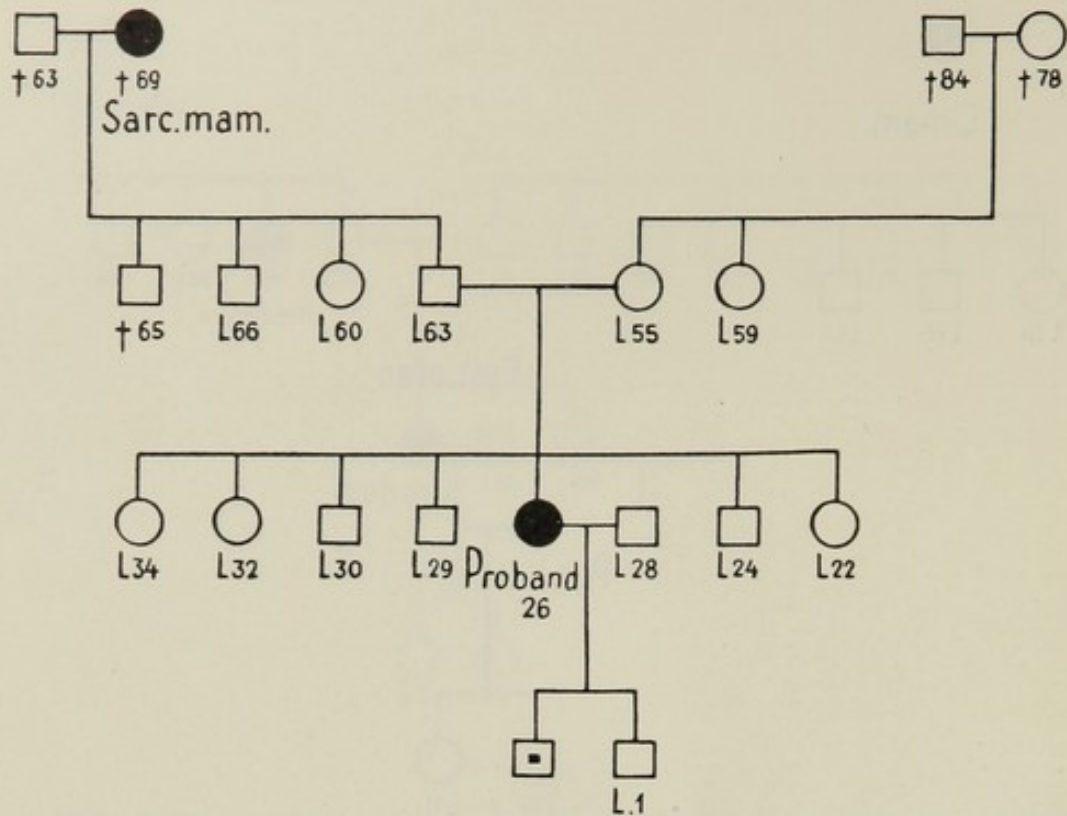
FATHER'S YOUNGEST SISTER.—Born 1868 in Korsør. Dressmaker; single. Died in the St. Johannes Hospital, Copenhagen, June 30th, 1922, of cancer of the breast and thorax. The diagnosis verified by death certificate.



Pedigree 40.

PROBAND (Radium Center, Copenhagen; no. 26679).—○, born in Fredericia May 24th, 1901. ∞ telegraph clerk. Formerly well. Menstruation since fifteenth year, regular. Two childbirths. Nursed about eleven months each time. Noticed a small lump in her right breast three months before admission. April 28th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma; chronic, cystic mastitis.

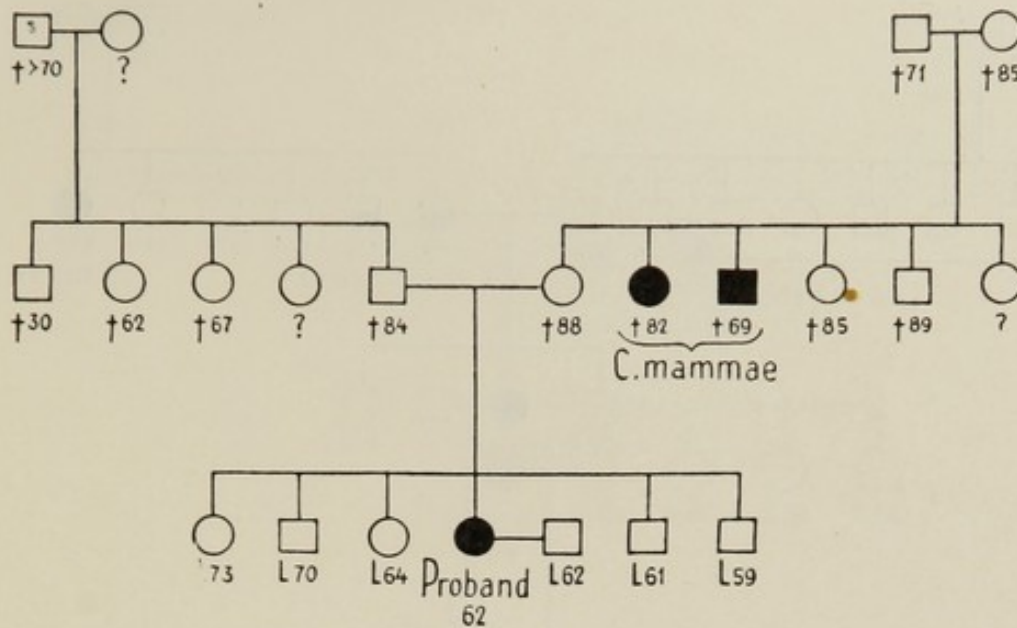
FATHER'S MOTHER.—Born in Holsten Aug. 14th, 1845. ∞ cigar maker. Died 1906. A couple of years before her death operated on for cancer of the breast, by Dr. Guldberg, Horsens, and one of her breasts removed. Cause of death: metastases to the liver.



Pedigree 41.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 758).—  
 ○, born in Ganløse Aug. 28th, 1916. ∞ carpenter. Formerly well. Menses since fourteenth year, regular. Two childbirths; one child stillborn, the other living and well. Nursed only three months, owing to hypogalactia. Tumor in left breast noticed four months before admission. Extirpation of tumor in left breast. Histologic diagnosis: solid carcinoma in mammary fibroadenoma.

FATHER'S MOTHER.—Born in Ganløse Feb. 6th, 1851. ∞ farmer. Died in Ganløse Sep. 29th, 1920, of sarcoma of the breast. The diagnosis verified by death certificate.

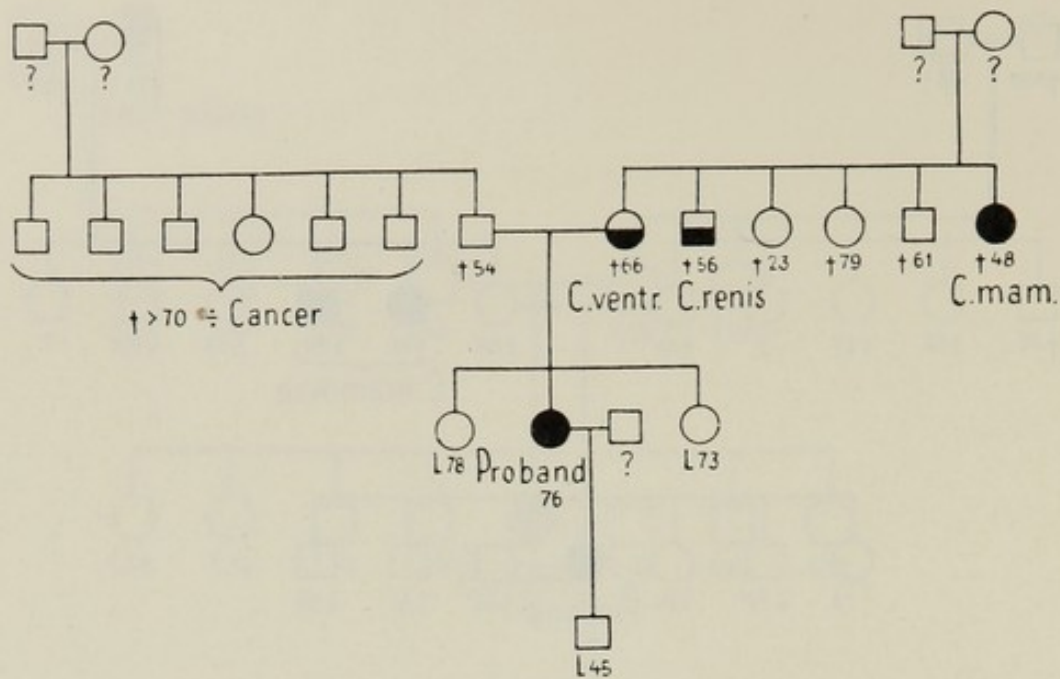


Pedigree 42.

PROBAND (Radium Center, Copenhagen; no. 34437).—○, born in Copenhagen Sep. 16th, 1878. ∞ tobacconist. Formerly well. Menstruation from eighteenth to fiftieth year, regular. Menopause normal. Never pregnant. Tumor in right breast noticed six months before admission. June 21st, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid medullary carcinoma.

MOTHER'S ELDEST SISTER.—Born in Gilleleje July 7th, 1833. ∞ fisherman. In 1885 operated on at the Deaconesses' Hospital, Copenhagen, by Prof. Paulli, for mammary cancer, and one of her breasts removed. Died Aug. 1st, 1915.

MOTHER'S ELDEST BROTHER.—Born in Gilleleje Sep. 8th, 1836. Ship's officer (first mate). Reported to have died in San Francisco, U.S.A., in 1906, of cancer of the breast, which eventually developed into a large ulcer, for which he refused operation.



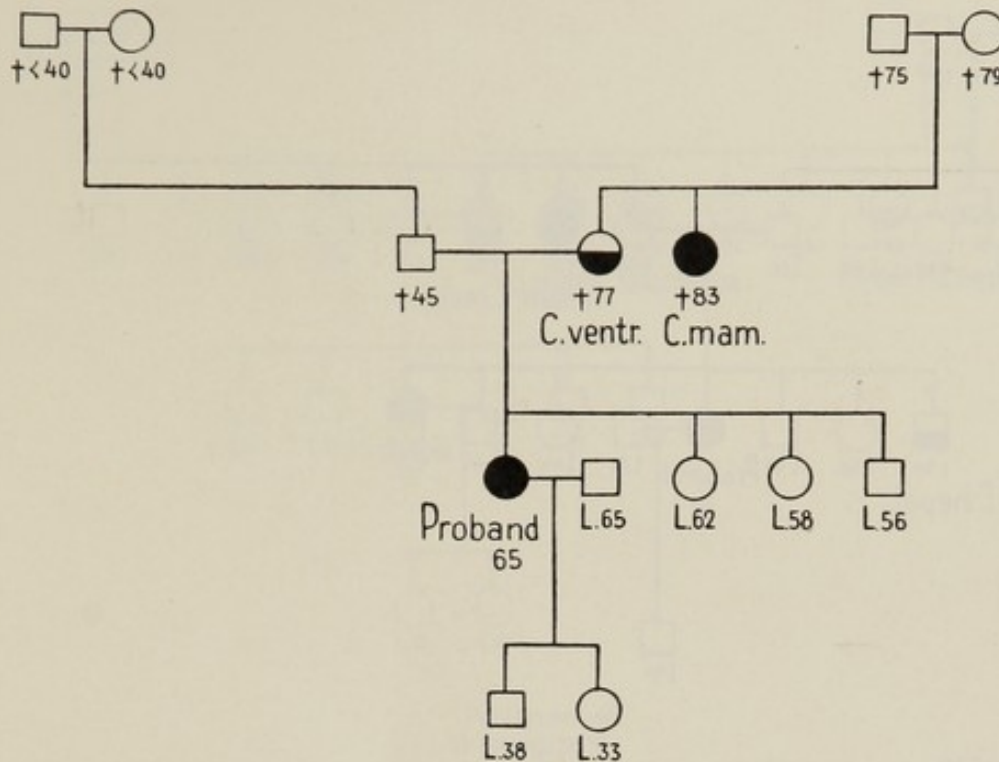
Pedigree 43.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 1310/42). —○, born in Rudkøbing March 2nd, 1866. Music teacher; single. Formerly well. Menstruation from fourteenth to thirty-eighth year. Menopause normal. One childbirth. Did not nurse, owing to hypogalactia. In 1942, cerebral apoplexy, with temporary paralysis of right arm. Tumor in left breast noticed about four years before admission. June 6th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid, partly alveolar carcinoma.

MOTHER.—Born in Copenhagen June 25th, 1836. ∞ typographer. Died in Copenhagen Aug. 23rd, 1902, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born 1825 in Copenhagen. School teacher, single. Died 1873 in Prof. Howitz's clinic, Frederiksberg, Copenhagen. At her admission, the tumor was already large and ulcerated, and the professor informed the family that the affection was so neglected that no hope of cure by operation could be expected.

MOTHER'S ELDEST BROTHER.—Born 1823 in Copenhagen. Office clerk. Died Jan. 9th, 1880, in the Municipal Hospital, Copenhagen, of cancer of the kidney. The diagnosis verified by the death register of the hospital.

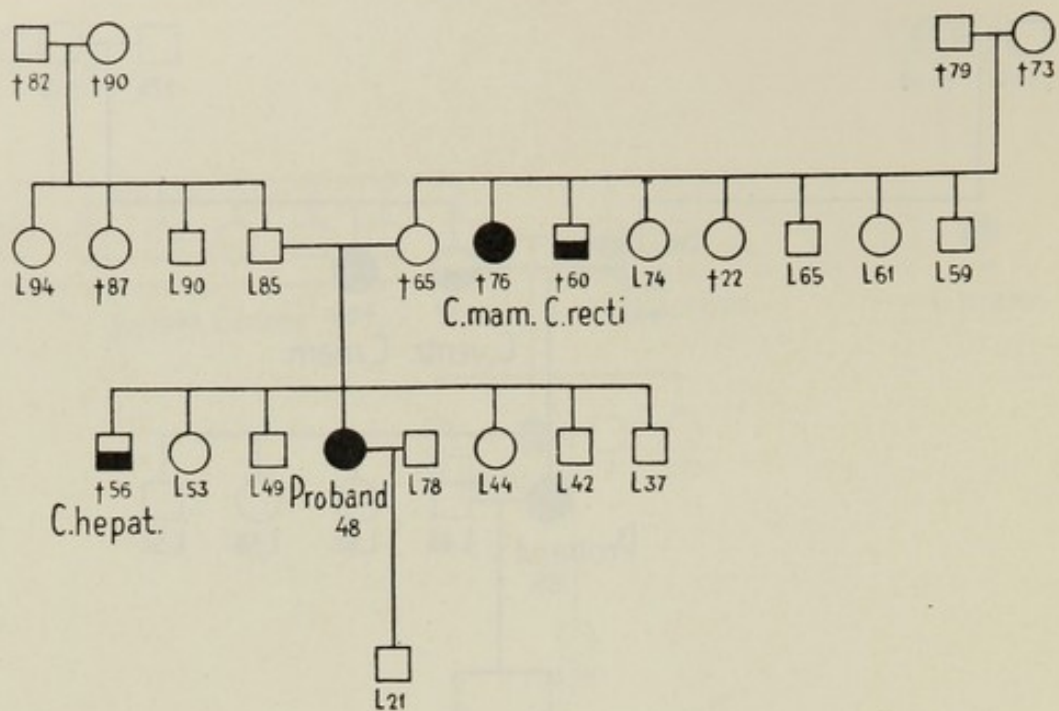


Pedigree 44.

PROBAND (Radium Center, Copenhagen; no. 26779).—○, born in Buttrup Nov. 26th, 1876. ∞ heating engineer. Menstruation from sixteenth to forty-ninth year, regular. Two childbirths. Nursed a year each time. Polyarthritides deformans of many years' duration. Tumor in left breast noticed two weeks before admission. Trepine biopsy. Histologic diagnosis: adenocarcinoma.

MOTHER.—Born in Buttrup Dec. 3rd, 1850. Widow. Died June 18th, 1928, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S SISTER.—Born in Buttrup March 28th, 1851. Factory worker; unmarried. Died in the Nørre Hospital, Copenhagen, Nov. 29th, 1934, of inoperable cancer of the breast. The diagnosis verified by the hospital.



Pedigree 45.

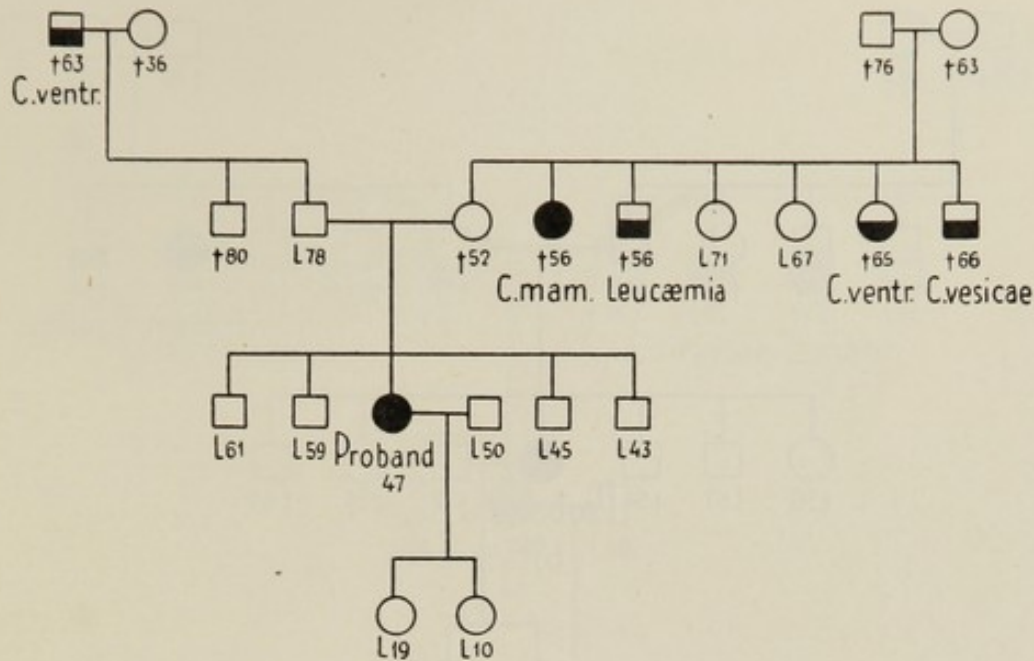
PROBAND (Radium Center, Copenhagen; no. 28299).—○, born in Aalborg Feb. 22nd, 1894. ∞ house-owner. Formerly well. Menstruation since fifteenth year, regular. One childbirth; nursed until the baby died six weeks old. For six months pricking pains in the left breast, but had not herself noticed any tumor there. Oct. 27th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus cancer of the breast.

MOTHER'S ELDEST SISTER.—Born in Smidstrup July 9th, 1861. Died in Smidstrup Apr. 4th, 1938, of cancer of the breast. The diagnosis verified by death certificate.

MOTHER'S ELDEST BROTHER.—Born in Smidstrup Apr. 14th, 1866. Rural mail carrier. Died in Smidstrup June 10th, 1926, of cancer of the rectum. The diagnosis verified by death certificate.

ELDEST BROTHER.—Born in Aalborg Nov. 30th, 1886. Bricklayer. Died May 30th, 1942, of occult cancer and cancer of the liver. The diagnosis verified by death certificate. Shortly before death treated at the Aalborg Municipal Hospital.





Pedigree 46.

PROBAND (Municipal Hospital, Copenhagen; service 5, no. 855/42).—  
 ○, born in Copenhagen Apr. 16th, 1895. ∞ confidential clerk. Formerly well. Menstruation since fifteenth year, regular. Two childbirths. Nursed a little less than a year each time. Six years ago she fell on the stairs and hurt her breast against the bannister. There was some pain, but no swelling or extravasation. A month before admission she noticed a lump, the size of a hazelnut, in her left breast. Pre-operative roentgen treatment was given, and by Nov. 4th, 1941, the tumor had disappeared, wherefore surgical intervention was abandoned; but seven months later there came local recurrence, and on Apr. 30th, 1942, operation was done, and the tumor extirpated. Histologic diagnosis: solid carcinoma.

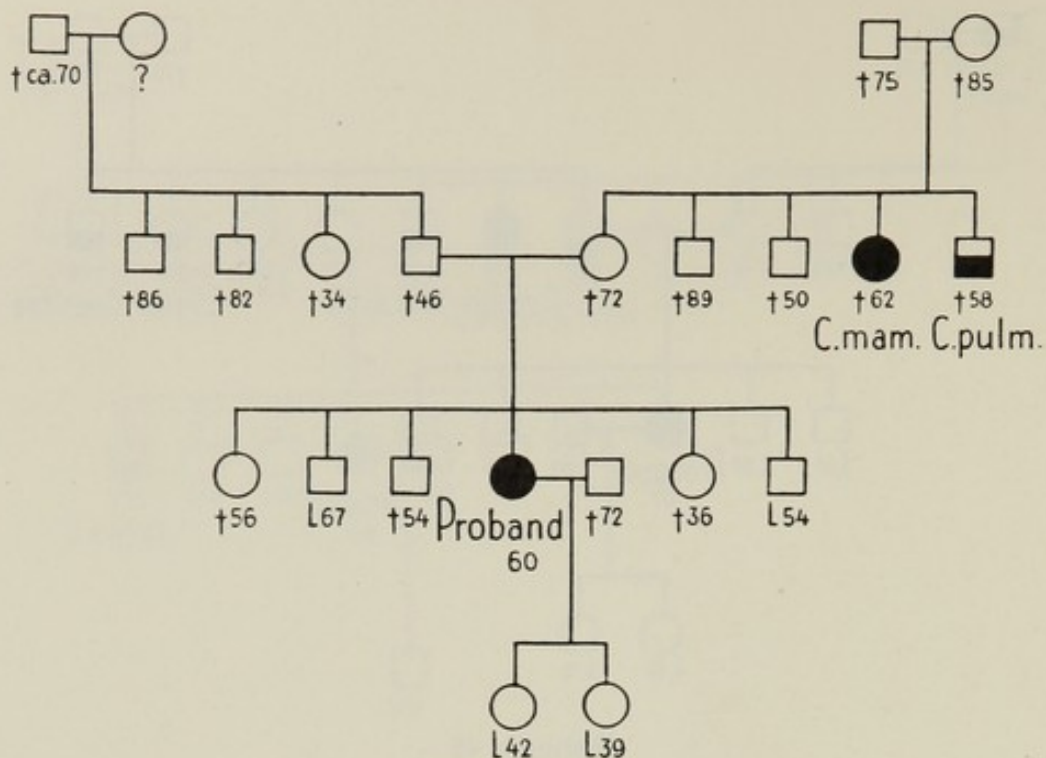
FATHER'S FATHER.—Born Oct. 16th, 1833. Farmer. Died in Copenhagen 1896, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S ELDEST SISTER.—Born in Veflinge July 23rd, 1856. ∞ farmer. Died in Odense Feb. 23rd, 1913, of cancer of the breast, with metastases. The diagnosis verified by death certificate.

MOTHER'S ELDEST BROTHER.—Born in Veflinge Feb. 22nd, 1859. Farmer. Died in Copenhagen Dec. 14th, 1915, of leukemia. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born in Veflinge Oct. 10th, 1868. Single. Died in Copenhagen Aug. 22nd, 1934, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST BROTHER.—Born in Veflinge March 12th, 1870. Died in the Municipal Hospital, Copenhagen, Aug. 29th, 1936, of cancer of the bladder. The diagnosis verified by death certificate.

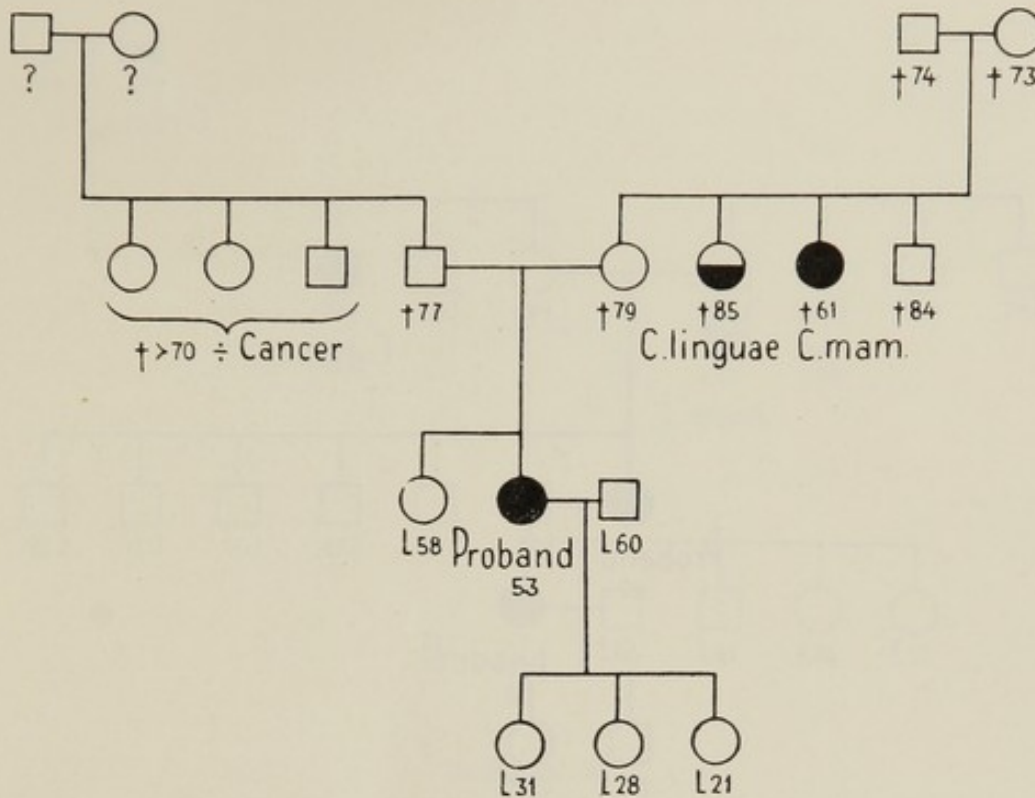


Pedigree 47.

PROBAND (Radium Center, Copenhagen; no. 21573).—○, born in Copenhagen Aug. 28th, 1881. Janitor's widow. As child and young well. Menstruation from seventeenth to forty-ninth year. Menopause normal. Two child-births. Nursed over a year each time. In 1939 treated at the Radium Center, Copenhagen, for cutaneous horn of the neck and papilloma in the skin of the right breast. Noticed a walnut-sized lump in the latter about a year before present admission to hospital. Apr. 8th, 1942, ablation of breast, with evacuation of axilla. Histologic diagnosis: adenocarcinoma, partly scirrhous.

MOTHER'S SISTER.—Born in Copenhagen July 10th, 1859. ∞ butcher. Died in Randers Sep. 4th, 1921, of cancer of the breast. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST BROTHER.—Born in Copenhagen July 17th, 1855. Butcher. Died in the Municipal Hospital, Copenhagen, Aug. 29th, 1913, of cancer of the lung. The diagnosis verified by the postmortem protocol of the hospital.

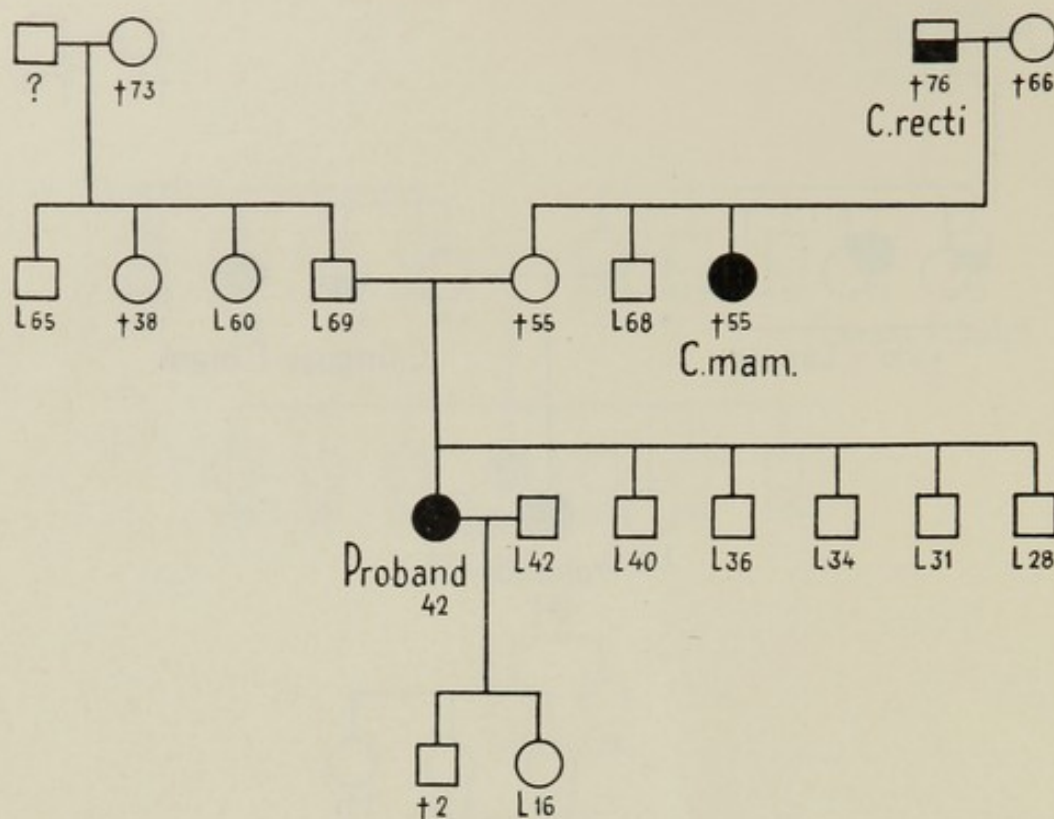


Pedigree 48.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 656/42).—  
 ○, born in Tjæreby Nov. 5th, 1888. ∞ carriage builder. Formerly well.  
 Menstruation from fourteenth to forty-eighth year. Menopause normal. Three  
 childbirths. Nursed only a few months, owing to hypogalactia. Tumor in  
 right breast noticed a few days before admission. Apr. 27th, 1942, ablation  
 of breast, with evacuation of axilla. Histologic diagnosis: adenocarcinoma.

MOTHER'S YOUNGEST SISTER.—Born 1853 in Bøgelunde. In January  
 1911 operated on at St. Joseph's Hospital, Copenhagen, for cancer of  
 the breast. Died April 1914. Diagnosis: cancer of the breast.

MOTHER'S ELDEST SISTER.—Born in Bøgelunde May 20th, 1852. ∞  
 rural small-holder. Died Feb. 5th, 1938, of cancer of the tongue, for which  
 she had been treated at the Radium Center in Copenhagen (journal no.  
 17462). Diagnosis: cancer of the tongue.

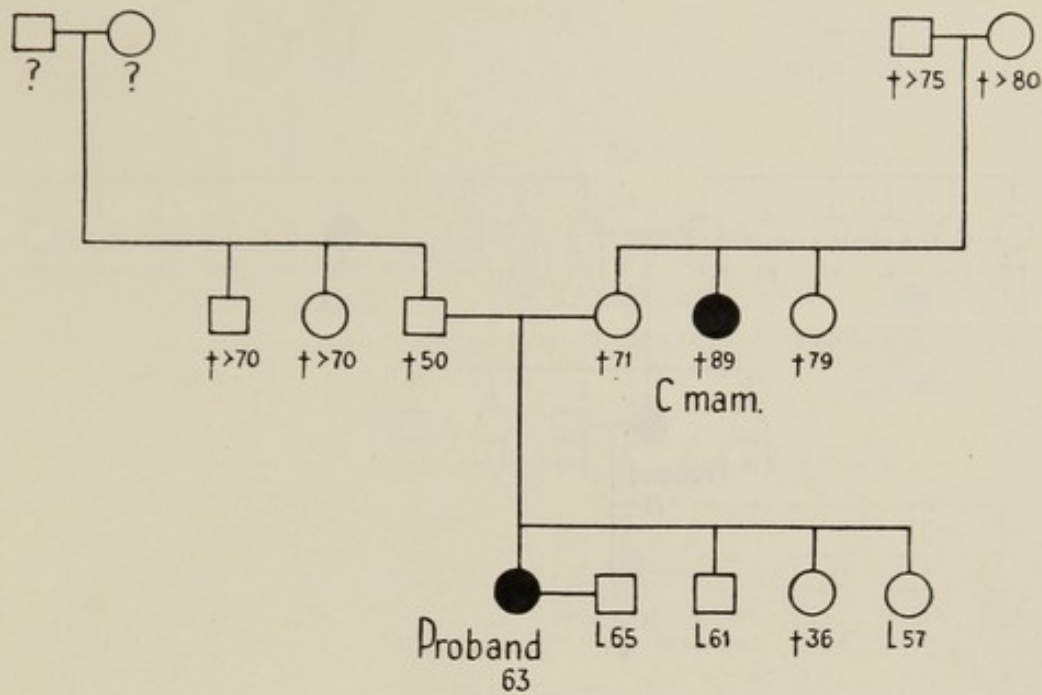


Pedigree 49.

PROBAND (Radium Center, Copenhagen; no. 31830).—○, born in Copenhagen Apr. 5th, 1901. ∞ bookkeeper. Formerly well. Menstruation since eleventh year, regular. Two childbirths. Nursed each time about nine months. Since 1936, she has at times noticed a slight milky secretion from the nipple of the right breast. Tumor not noticed until five days before admission. Oct. 7th, 1943, trephine biopsy. Histologic diagnosis: adenocarcinoma.

MOTHER'S FATHER.—Born 1850 in Aarhus. Cabinetmaker. Died in St. Joseph's Hospital, Odense, March 29th, 1926, of cancer of the rectum. The diagnosis verified by death certificate.

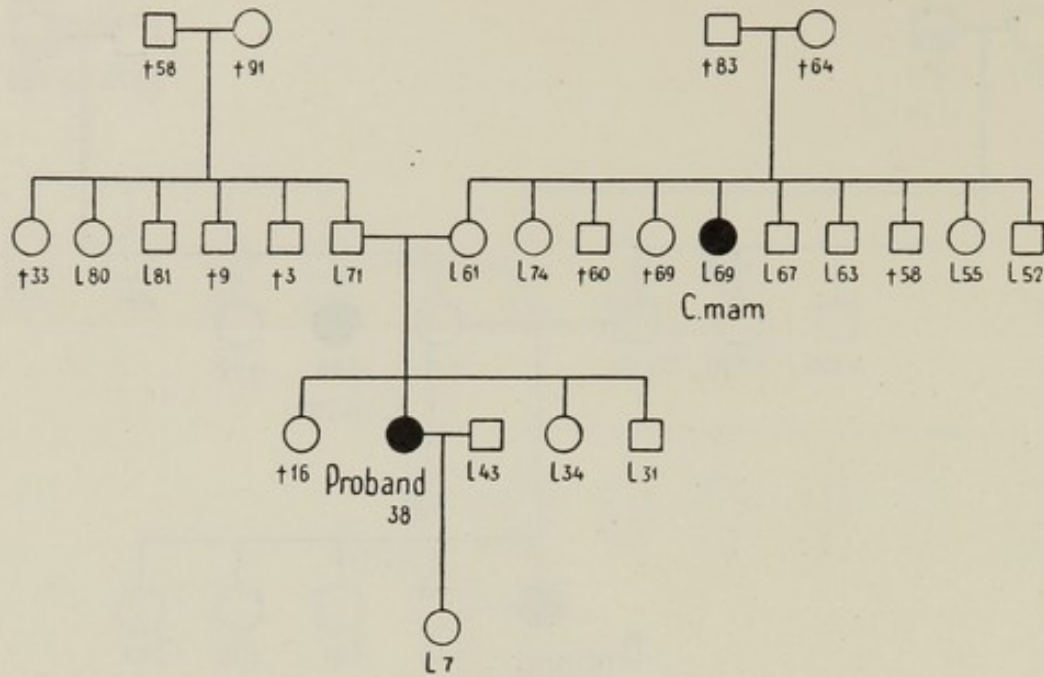
MOTHER'S SISTER.—Born in Aarhus March 22nd, 1882. ∞ coachman. Died Feb. 22nd, 1938, of cancer of the breast, with metastases to organs. The diagnosis verified by death certificate.



Pedigree 50.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1683/42).—  
 ○, born in Frederikshavn Feb. 19th, 1879. ∞ tailor's cutter. Formerly well.  
 Menstruation from fourteenth to fifty-second year. Menopause normal. Never  
 pregnant. Tumor in left breast noticed two weeks before admission. July  
 27th, 1942, ablation of the breast, with evacuation of the axilla. Histologic  
 diagnosis: solid carcinoma.

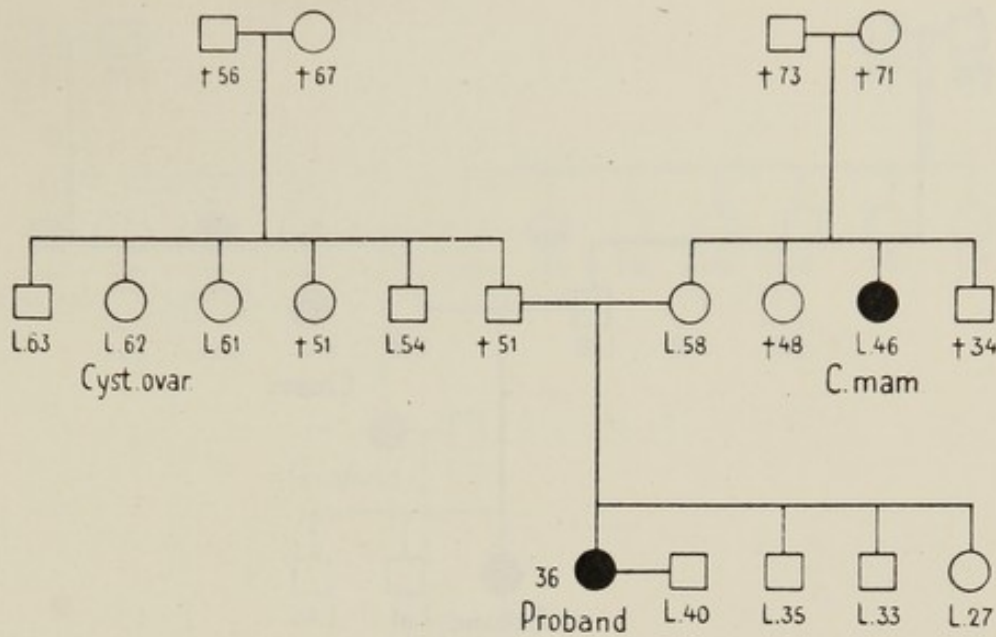
MOTHER'S SISTER.—Born 1850 in Flemløse. ∞ wholesale merchant.  
 Died 1939 in Altona, Germany. In 1919 operated on in Hamburg for mam-  
 mary cancer, and one of her breast removed.



Pedigree 51.

PROBAND (Radium Center, Copenhagen; no. 27458).—○, born in Odense March 7th, 1904. ∞ hospital functionary. Formerly well. Menstruation since fourteenth year, regular. One childbirth. Nursed six months. Came to the hospital for advice three days after she had noticed the lump in her right breast. Trephine biopsy. Histologic diagnosis: adenocarcinoma.

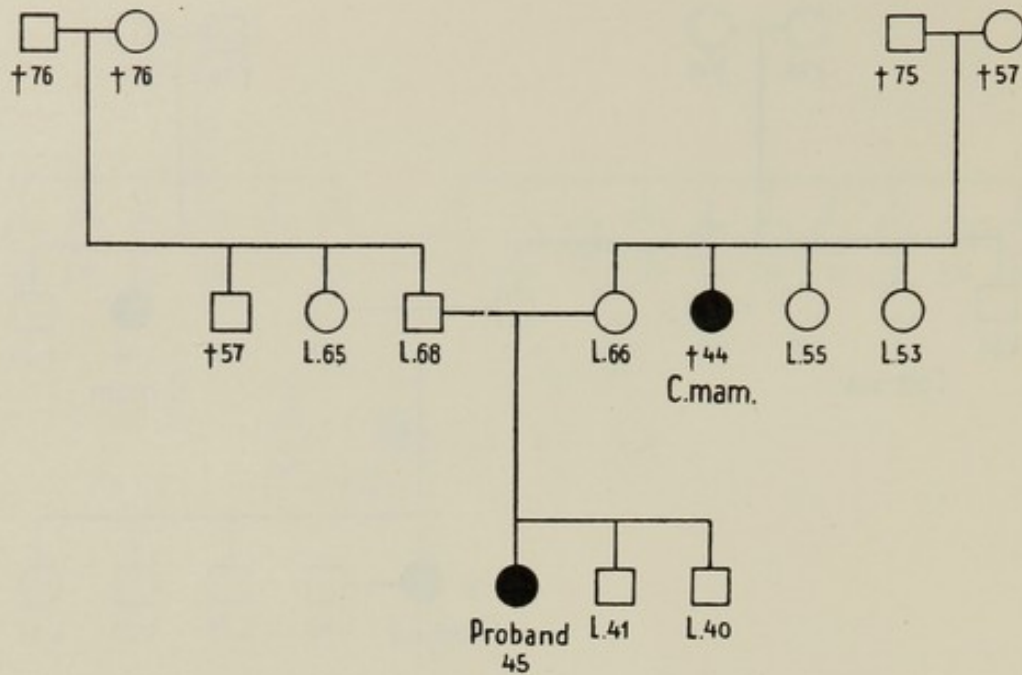
MOTHER'S SISTER.—Born in Kertinge Dec. 29th, 1873. ∞ business manager. In 1918 operated on for mammary carcinoma and one of her breasts removed. The diagnosis verified by the Municipal Hospital, Aarhus.



Pedigree 52.

PROBAND (Radium Center, Copenhagen; no. 26600).—○, born in Maribo Apr. 29th, 1906. ∞ florist. Menstruation since fifteenth year, regular. Never pregnant. A slowly growing tumor in the right breast noticed six weeks before admission. Trephine biopsy. Histologic diagnosis: fibroadenomatosis, incipient cancer. As the tumor rapidly grew, pre-operative roentgen treatment was given, and Aug. 12th, 1942, the breast was ablated, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER'S SISTER.—Born in Kjølmg May 6th, 1897. Housekeeper, single. In November, 1941, treated at the Radium Center, Copenhagen, for mammary cancer, and one of her breasts removed (journal no. 25433). Histologic diagnosis: adenocarcinoma.

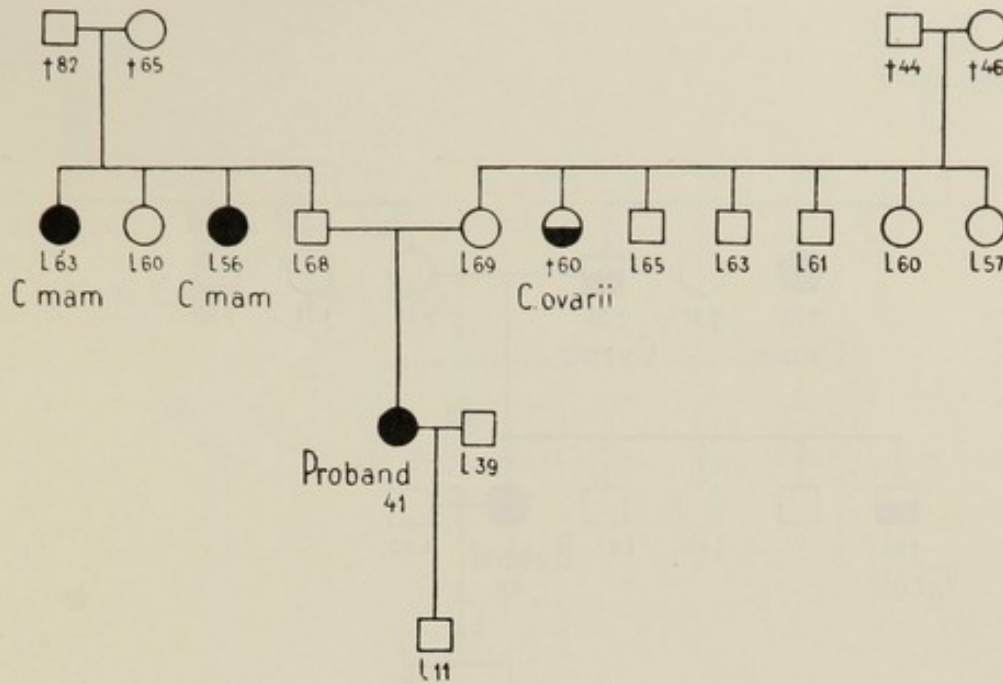


Pedigree 53.

PROBAND (State Hospital, Copenhagen; service D, and radiol. service, no. 122/42).—○, born in Helsingør March 18th, 1897. Hospital nurse, single. Menstruation since fourteenth year, regular. Never pregnant. Noticed a lump in her left breast a few days before admission to service D. May 18th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER'S SISTER.—Born in Taastrup Jan. 22nd, 1882. In 1923 operated on at the Helsingør Hospital, for cancer of the breast. Died in Helsingør Jan. 16th, 1926. Death certificate: cancer of the lung and liver, ex cancer of the breast.





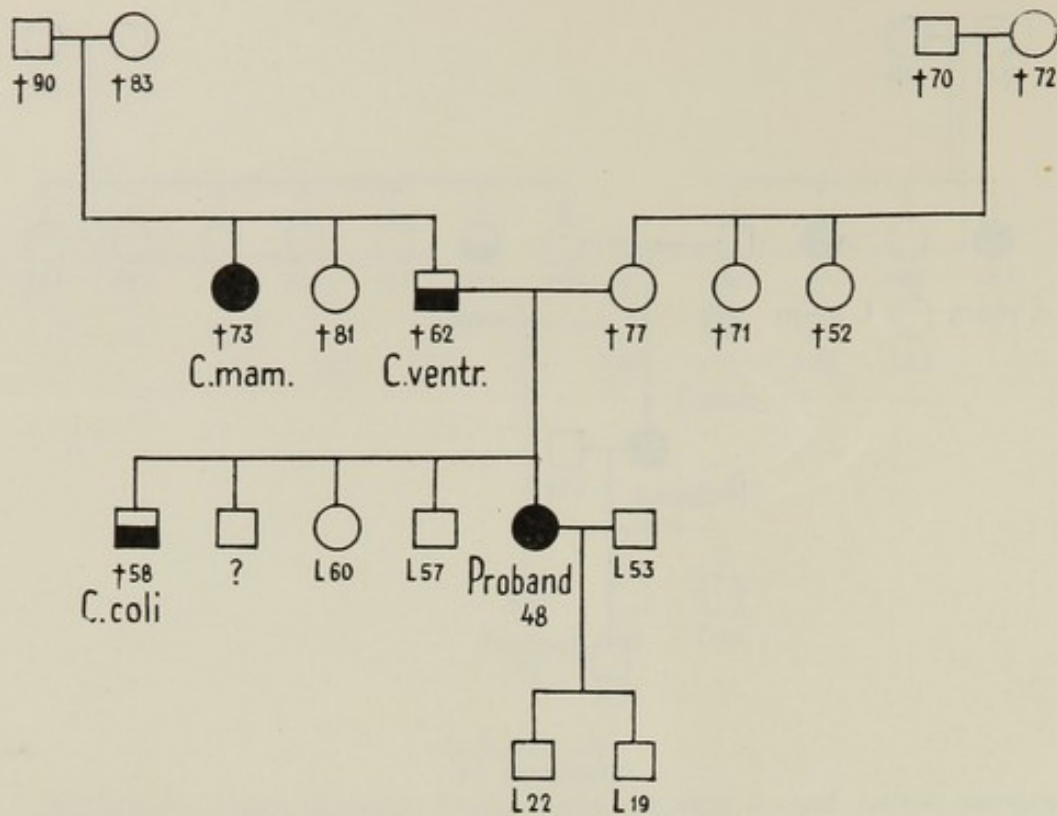
Pedigree 54.

PROBAND (Radium Center, Copenhagen; no. 31829).—○, born in Copenhagen Apr. 24th, 1902. ∞ printer. Formerly well. Menstruation since thirteenth year, regular. One childbirth. Did not nurse, owing to agalactia. Noticed a lump in her right breast Aug. 15th, 1943. On 22nd, same month, operated on, and tumor extirpated. Histologic diagnosis: solid carcinoma.

FATHER'S ELDEST SISTER.—Born 1880. ∞ electrician. In 1940, at the Næstved County Hospital, ablation of right breast. Histologic diagnosis: carcinoma.

FATHER'S YOUNGEST SISTER.—Born Nov. 20th, 1886. ∞ bricklayer. At time of present writing under treatment at the Radium Center in Copenhagen (journal no. 17587) for cancer of the right breast.

MOTHER'S ELDEST SISTER.—Born in Fodby March 31st, 1879. Single. In 1938 treated at the Frederiksberg Hospital, Copenhagen, service F, and died at Frederiksberg the following year, of cancer of the ovary. The diagnosis verified by death certificate.



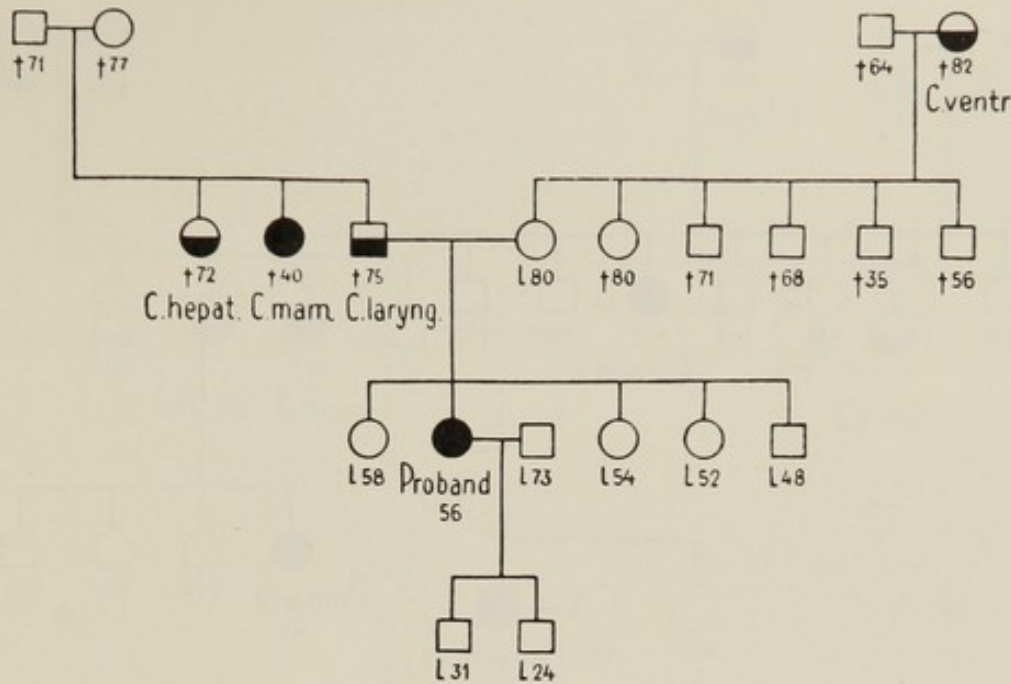
Pedigree 55.

PROBAND (Radium Center, Copenhagen; no. 31947).—○, born in Roskilde June 17th, 1895. ∞ cabinet-maker. Formerly well. Menstruation from fourteenth to forty-third year, regular. Menopause normal. Two childbirths. Lactation normal. Tumor in left breast first noticed six days before admission. Ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma and solid carcinoma.

FATHER.—Born in Frederikssund June 16th, 1848. Farm-overseer. Died in Copenhagen Sep. 9th, 1910, of cancer of the stomach. The diagnosis verified by death certificate.

FATHER'S SISTER.—Born in Frederikssund March 11th, 1853. ∞ inspektor. Died in the Frederiksberg Hospital, Copenhagen, June 14th, 1926, of embolism of pulmonary artery following operation for cancer of the left breast. The diagnosis verified by death certificate.

BROTHER.—Born in Iceland Jan. 31st, 1881. Foreman, married. Died in the Nørre Hospital, Copenhagen, May 29th, 1939, of cancer of the colon. The diagnosis verified by death certificate.



Pedigree 56.

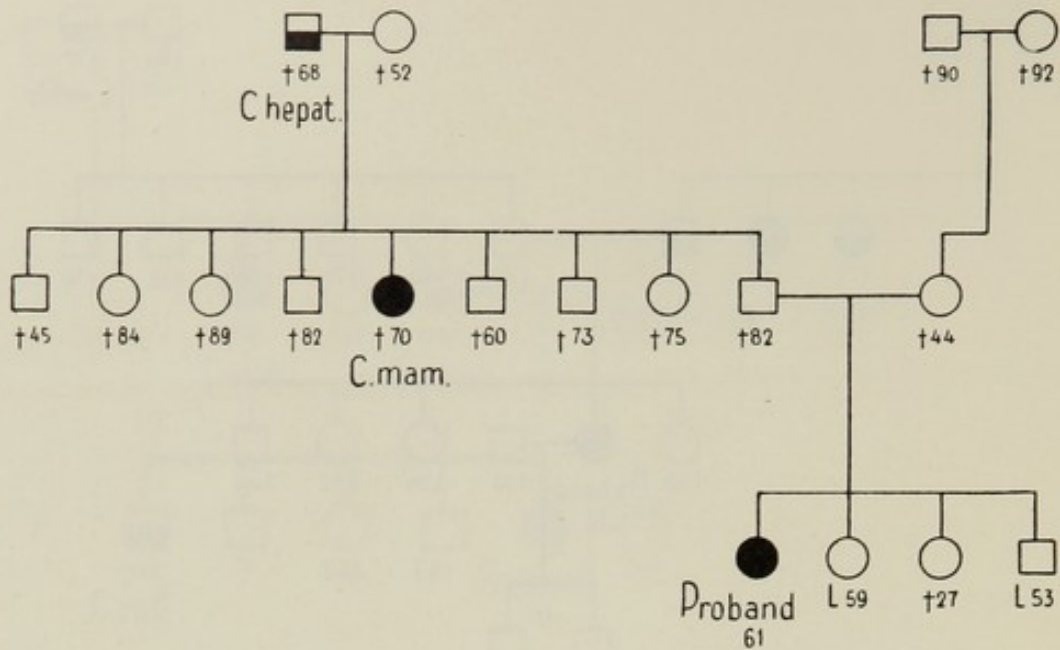
PROBAND (Municipal Hospital, Copenhagen; service 5, no. 1329/42).—  
 ○, born in Helsingø Jan. 15th, 1886. ∞ postmaster. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Two childbirths. Nursed about nine months each time. In the summer, 1940, treated for climacteric disorders with ovex tablets (1000 I.U.), 300 in all. Noticed during this treatment that her breasts were getting larger and heavier. No secretion from the nipples. Two weeks before her admission to hospital Sep. 9th, 1940, she believed that she felt a circumscribed solid area in her left breast. Examination failed to reveal any definable tumor, but she was treated with roentgen, 300 r. on two fields. The treatment was repeated in January, 1941, but not until seventeen months later was a tumor found, and on June 25th, 1942, the left breast and axillary glands were removed. Histologic diagnosis: adenomatous and solid carcinoma.

MOTHER'S MOTHER.—Born in Hillerød Sep. 9th, 1826. Farm-owner's widow. Died at Allingbjerggaard, near Ølstykke, June 9th, 1909, of stomach cancer of about a year's duration, during which time there had been symptoms of pylorostenosis. According to the physician's statement, stomach cancer was the cause of death.

FATHER.—Born in Horslunde Feb. 26th, 1854. Landowner. Died in the County Hospital, Gentofte, Aug. 26th, 1929, of cancer of the larynx. The diagnosis verified by death certificate.

FATHER'S YOUNGEST SISTER.—Born 1842 in Horslunde. ∞ farmer. Operated on in 1881, for mammary cancer (Prof. Howitz's clinic, Copenhagen) and one breast removed. Died Oct. 1882, in Brønderslev, of metastases.

FATHER'S ELDEST SISTER.—Born in Horslunde Dec. 19th, 1857. Cattle-dealer's widow. Died in Maribo Oct. 30th, 1929, of cancer of the liver. The diagnosis verified by death certificate.

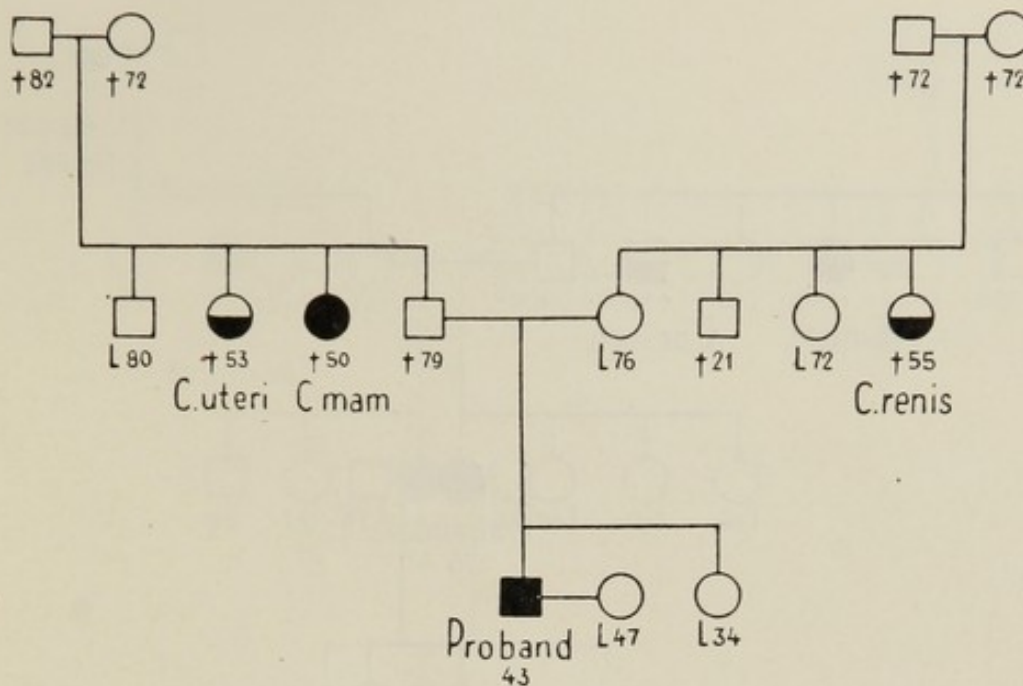


Pedigree 57.

PROBAND (State Hospital, Copenhagen; service D, no. 1440/42).—  
 ○, born in Faaborg July 2nd, 1881. Housekeeper, single. In 1904 treated  
 at the Frederiksberg Hospital, Copenhagen, for pulmonary tuberculosis.  
 Menstruation from fourteenth to fiftieth year. Menopause normal. Never  
 pregnant. Three years before present admission to hospital she had fallen  
 and hurt her left breast against the corner of a table. There had been some  
 pain, but no swelling or extravasation. The tumor first noticed three weeks  
 before admission. Sep. 3rd, 1942, ablation of the breast, with evacuation of  
 the axilla. Histologic diagnosis: solid and adenomatous carcinoma.

FATHER'S SISTER.—Born in Odense March 30th, 1858. Died in Aarhus  
 Jan. 28th, 1929, of inoperable cancer of the breast. The diagnosis verified  
 by the Radium Center for Jutland, in Aarhus.

FATHER'S FATHER.—Born in Odense 1824. Blacksmith. Died in Odense  
 May 1st, 1892, of cancer of the liver. The diagnosis verified by death  
 certificate.



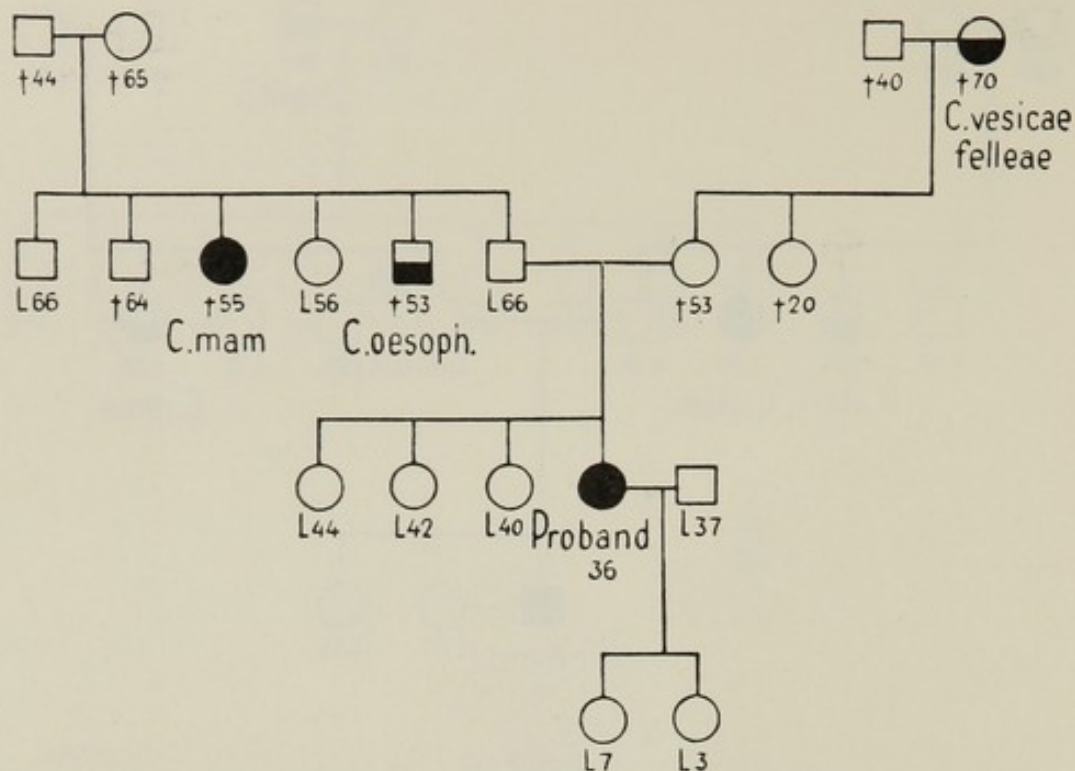
Pedigree 58.

PROBAND (Municipal Hospital, Copenhagen; service 5, no. 1161/42).—  
 □, born in Silkeborg Nov. 27th, 1899. Journalist; married. In 1915, nephritis. In 1920 bilateral pulmonary tuberculosis, treated at the Vejlebjerg Sanatorium. A month before present admission he noticed a small lump in his right breast. May 8th, 1942, extirpation of the tumor, with evacuation of the axilla. Histologic diagnosis: solid, partly scirrhous carcinoma.

FATHER'S YOUNGEST SISTER.—Born 1874 in Copenhagen. ∞ farm-owner, Hedehusene. Died Aug. 20th, 1924, of metastasising cancer of the breast. The diagnosis verified at the St. Maria Hospital, Roskilde, where she had previously been treated.

FATHER'S ELDEST SISTER.—Born 1870 in Copenhagen. Single. Died in Stubbekøbing Aug. 21st, 1923, of uterine and peritoneal cancer. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born 1887 in Copenhagen. Died there June 9th, 1942, of cancer of the kidney. The diagnosis verified by death certificate.



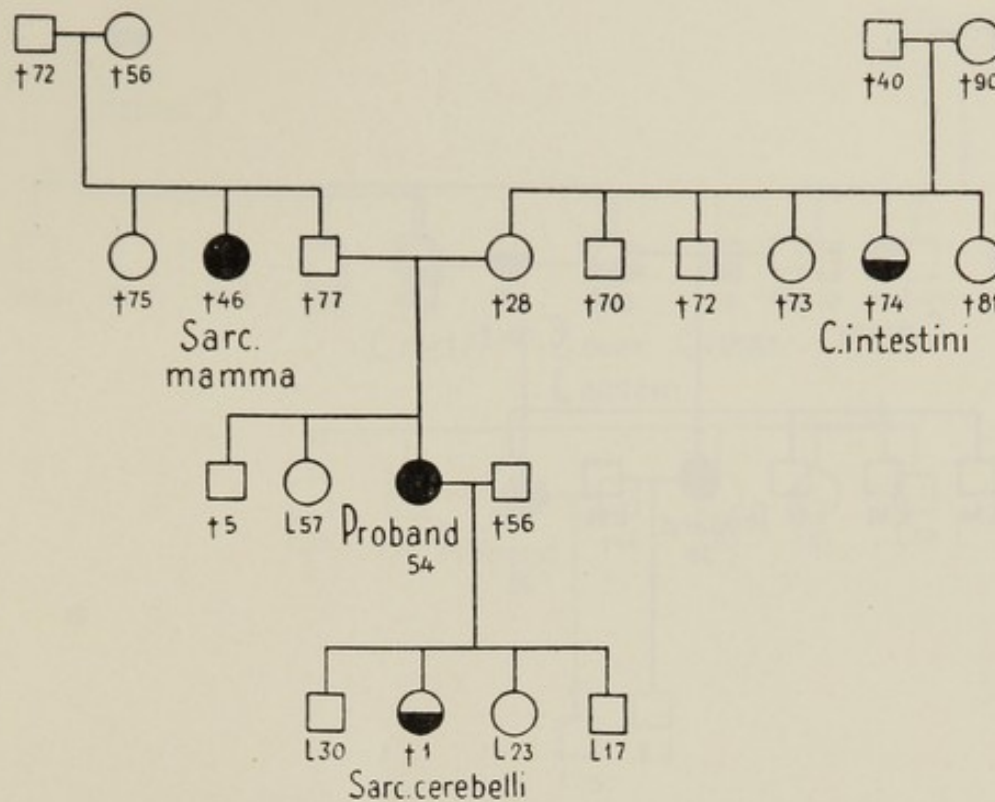
Pedigree 59.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 2149/41).—  
 ○, born in Copenhagen Nov. 18th, 1904. ∞ tobacconist. Formerly well. Menstruation since fifteenth year, regular. Two childbirths. Nursed the first child eight months, the second only three, when she was admitted to the St. Lucas Hospital with suppurating mastitis of the right breast. Treated with incisions. The tumor in the breast first noticed two weeks before present admission. Nov. 17th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER'S ELDEST SISTER.—Born in Copenhagen June 20th, 1881. Manufacturess, single. Died in the Frederiksberg Hospital, Copenhagen, in September 1936, of cancer of the breast. The diagnosis verified by the hospital.

FATHER'S YOUNGEST BROTHER.—Born in Copenhagen Jan. 19th, 1889. Workingman. Died in Copenhagen Aug. 5th, 1942, of cancer of the esophagus. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born in Copenhagen May 7th, 1846. ∞ plumber. Died in the Bispebjerg Hospital, Copenhagen, June 15th, 1916, of cancer of the gall bladder. The diagnosis verified by death certificate.



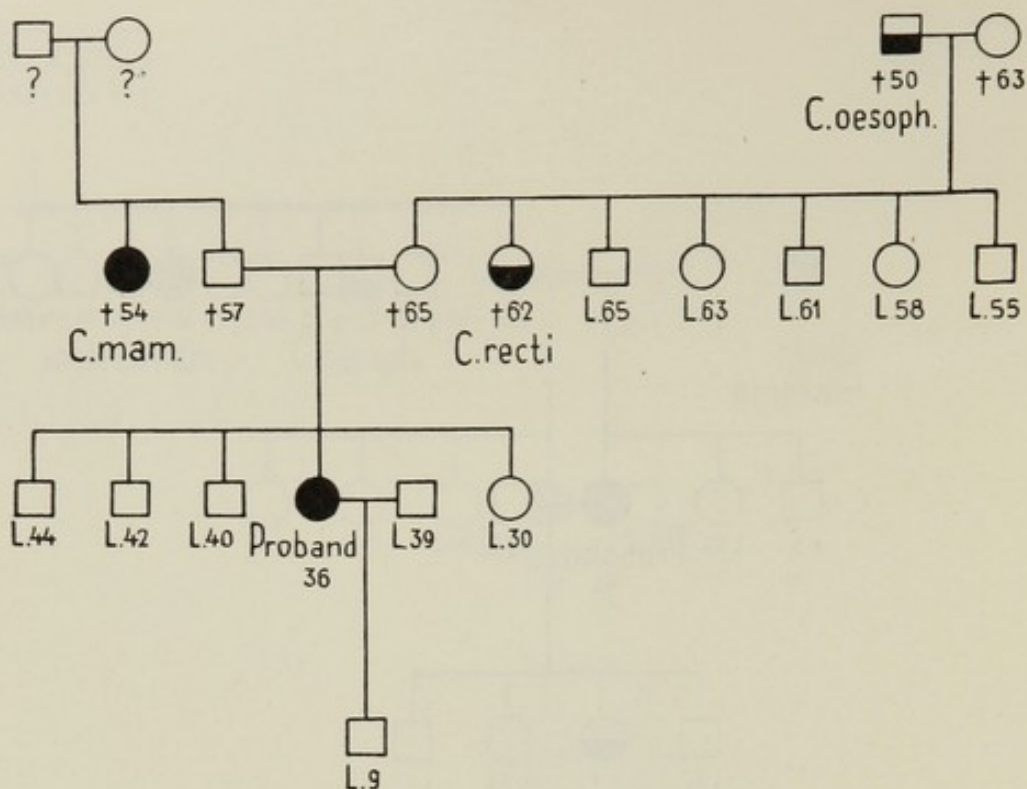
Pedigree 60.

PROBAND (Radium Center, Copenhagen; no. 28471).—○, born in Svendborg Sep. 22nd, 1887. Lawyer's widow. Formerly well. Menstruation from twelfth to fifty-third year, regular. In March 1942 prescribed 100 neurovex tablets (each tablet containing 100 I.U. of estrone) for climacteric disorders. Four childbirths. Lactations normal. Lump in left breast discovered three months before admission to hospital in Svendborg. Aug. 4th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: mammary carcinoma. At present writing under treatment at the Radium Center in Copenhagen since September 1942.

FATHER'S SISTER.—Born in Svendborg Sep. 8th, 1856. ∞ schoolmaster. Died in Horsens Dec. 28th, 1902, of sarcoma of the breast. The diagnosis verified by death certificate.

MOTHER'S SISTER.—Born in Svendborg March 21st, 1856. ∞ musician (violinist). Died in Copenhagen, in 1930, of cancer of the intestine. The diagnosis verified by death certificate.

DAUGHTER.—Born in Copenhagen July 5th, 1918. Died there, in the Queen Louise's Children's Hospital, of cerebral sarcoma. The diagnosis verified by death certificate.



Pedigree 61.

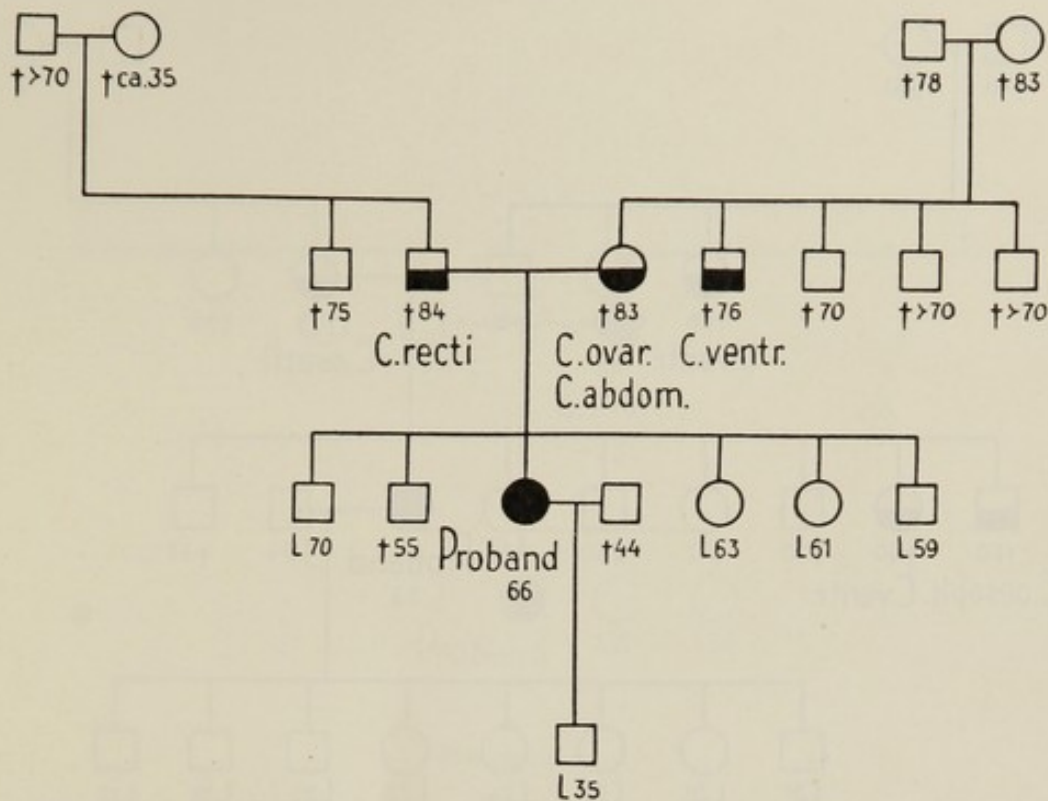
PROBAND (State Hospital, Copenhagen; radiol. service, no. 238/42).—  
 ○, born Nov. 12th, 1905. ∞ chief engineer. Menstruation since fourteenth  
 year, regular. One childbirth. Nursed ten months. Tumor in left breast first  
 noticed one month before admission. Apr. 23rd, 1940, ablation of the breast,  
 with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

MOTHER'S FATHER.—Born in Korsør March 21st, 1852. Fisherman. Died  
 in Korsør Oct. 9th, 1902, of cancer of the esophagus. The diagnosis verified  
 by death certificate.

MOTHER'S ELDEST SISTER.—Born in Korsør July 15th, 1876. ∞ work-  
 ingman. Died in Copenhagen Apr. 4th, 1939, of cancer of the rectum. The  
 diagnosis verified by death certificate.

FATHER'S SISTER.—Born in Korsør Nov. 7th, 1876. ∞ sailorman. Died  
 in Korsør Dec. 9th, 1930, of metastasising cancer of the breast. The diagnosis  
 verified by death certificate.





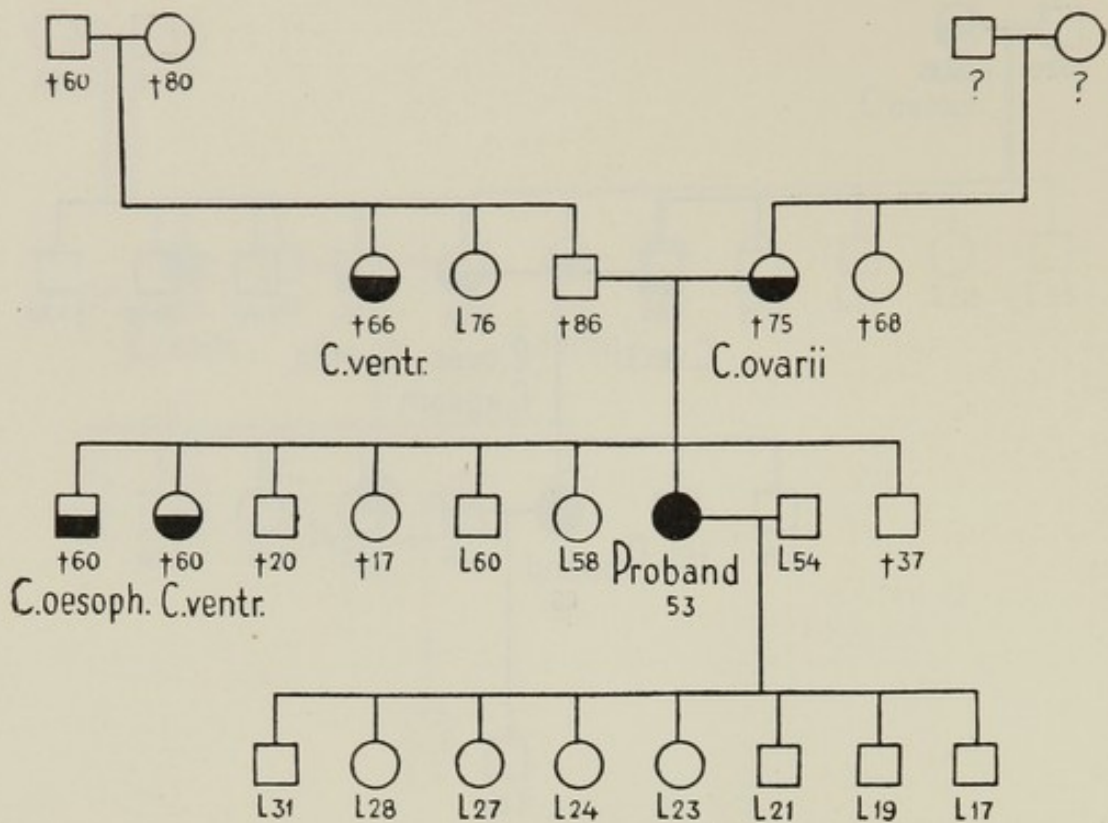
Pedigree 62.

PROBAND (Radium Center, Copenhagen; no. 28639).—○, born in Copenhagen Jan. 25th, 1876. Bank clerk's widow. Formerly well. Menstruation from fifteenth to forty-second year, regular. Menopause normal. One childbirth. Nursed only two months, owing to hypogalactia. Believes herself that the tumor in her right breast has been present for about ten years. Did not seek medical advice, because she did not think that it was growing larger. Sep. 24th, 1942, trephine biopsy. Histologic diagnosis: adenocarcinoma.

MOTHER.—Born in Tingerup March 31st, 1844. Widow. Died in Copenhagen May 4th, 1928, of ovarian and abdominal cancer. The diagnosis verified by death certificate.

MOTHER'S BROTHER.—Born 1842 in Tingerup. Farmer. Died there in 1918. According to the treating physician's statement to the mother of the proband, the death was due to cancer of the stomach.

FATHER.—Born 1843 on Als. Old age pensioner. Died in Copenhagen Aug. 10th, 1927, of cancer of the rectum. The diagnosis verified by death certificate.



Proband 63.

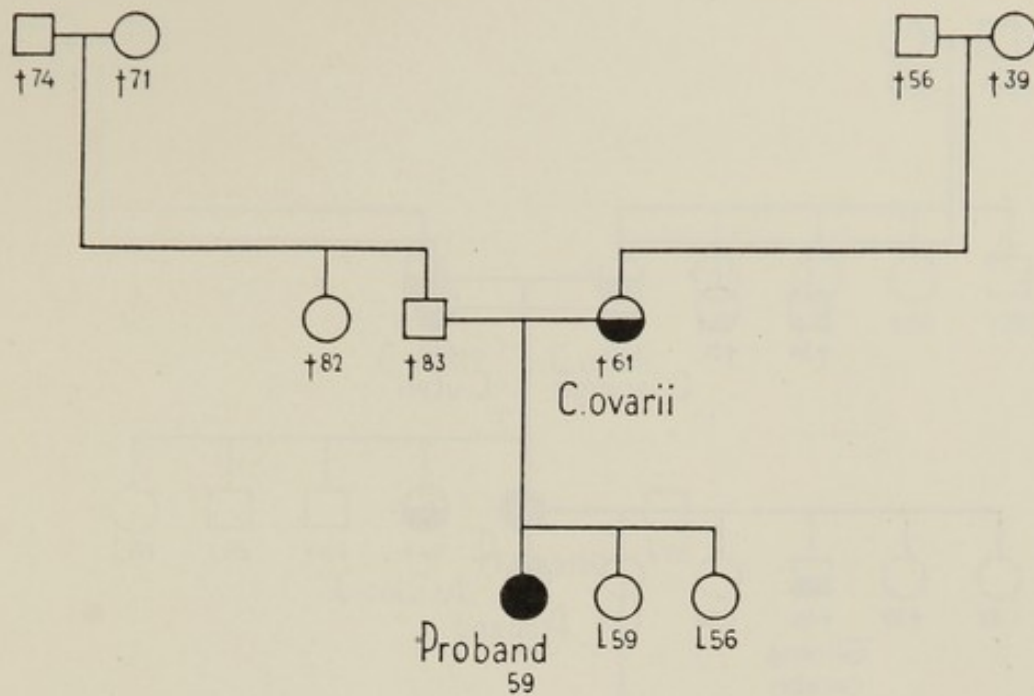
PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 863/42).—○, born in Copenhagen May 14th, 1888. ∞ clerk. Formerly well. Menstruation from fifteenth to forty-eighth year, regular. Eight childbirths. Lactations normal. Tumor in right breast first noticed two weeks before admission. Apr. 14th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Korsør Jan. 12th, 1850. ∞ collector of customs. Died in Randers Dec. 14th, 1925, of cancer of the ovary. The diagnosis verified by death certificate.

FATHER'S SISTER.—Born in Korsør Apr. 26th, 1857. Died in Slagelse March 26th, 1924, of cancer of the stomach. The diagnosis verified by death certificate.

ELDEST BROTHER.—Born in Copenhagen Feb. 27th, 1876. Controller of customs. Died Jan. 10th, 1937, of cancer of the esophagus. The diagnosis verified by death certificate.

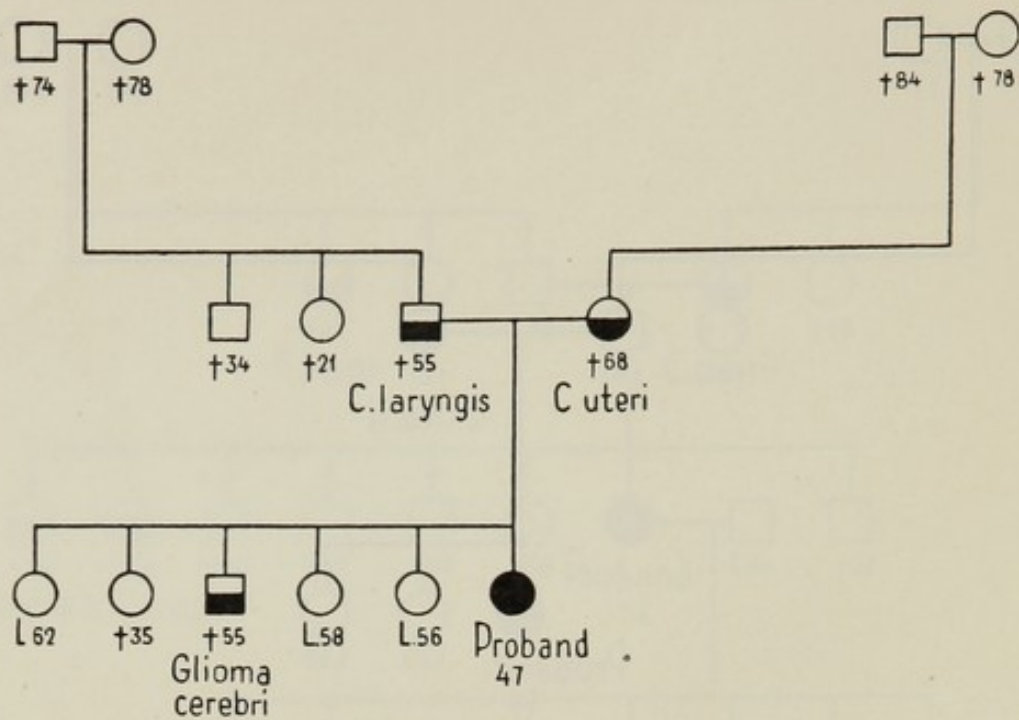
ELDEST SISTER.—Born in Copenhagen June 18th, 1880. Single. Died in Randers March 14th, 1941, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 64.

PROBAND (Radium Center, Copenhagen; no. 25008).—○, born in Copenhagen Oct. 24th, 1881. School inspectress; unmarried. Formerly well. Menstruation from fifteenth to fifteenth year, regular. Menopause normal. From fifty-fourth to fifty-seventh year treated with spargani tablets (folliculin, 100 I.U.), 1 tablet daily. Noticed a slowly growing tumor in her left breast a month before admission. Sep. 1st, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Hillerød Jan. 11th, 1857. ∞ cabinet-maker. Died in the Municipal Hospital, Copenhagen, Sep. 11th, 1918, of cancer of the ovary. The diagnosis verified by death certificate.



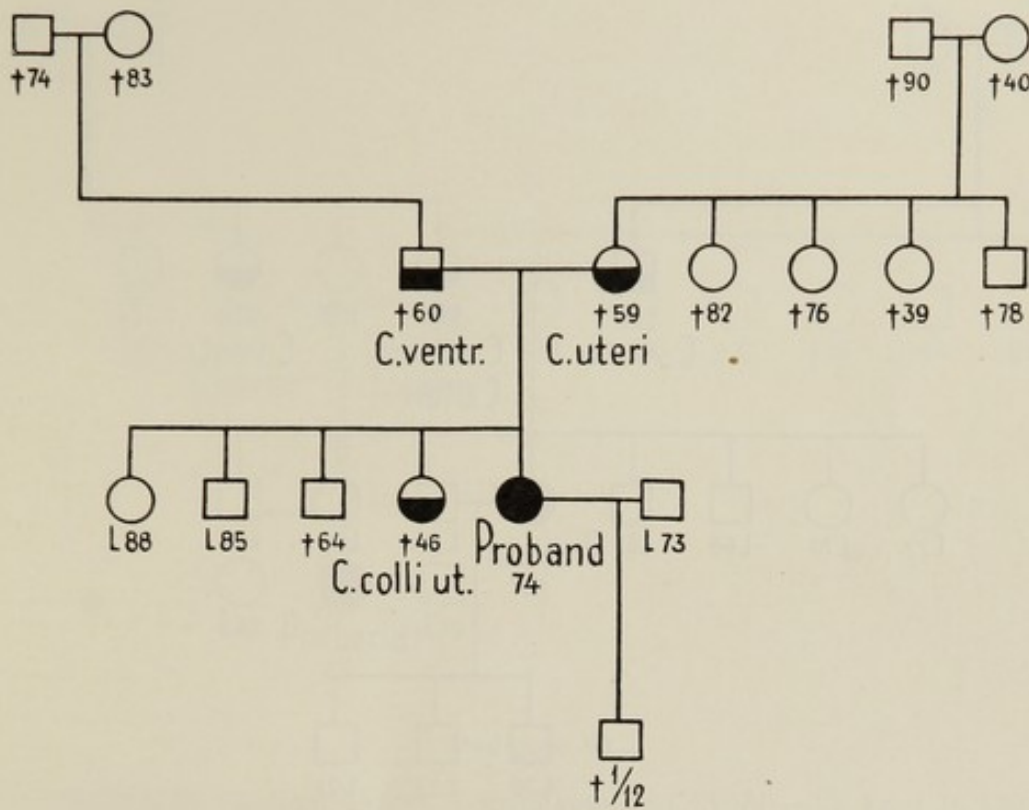
Pedigree 65.

PROBAND (Radium Center, Copenhagen; no. 27247).—○, born in Copenhagen Apr. 22nd, 1895. Bank clerk, single. Formerly well. Menstruation since fifteenth year. The bleedings in the last years less copious, and the intervals longer. Never pregnant. The tumor in the left breast noticed two months before admission. July 6th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid, partly scirrhous carcinoma.

FATHER.—Born in Søllerød Apr. 28th, 1854. Engineer. Died in St. Joseph's Hospital, Copenhagen, Jan. 18th, 1910, of cancer of the trachea. The diagnosis verified by death certificate.

MOTHER.—Born in Copenhagen May 10th, 1859. Died in the Municipal Hospital, Copenhagen, March 18th, 1918, of cancer of the uterus. The diagnosis verified by death certificate.

BROTHER.—Born in Copenhagen Dec. 19th, 1882. Head clerk; married. Died in the Municipal Hospital, Copenhagen, Sep. 26th, 1938, of cerebral glioma. The diagnosis verified by death certificate.

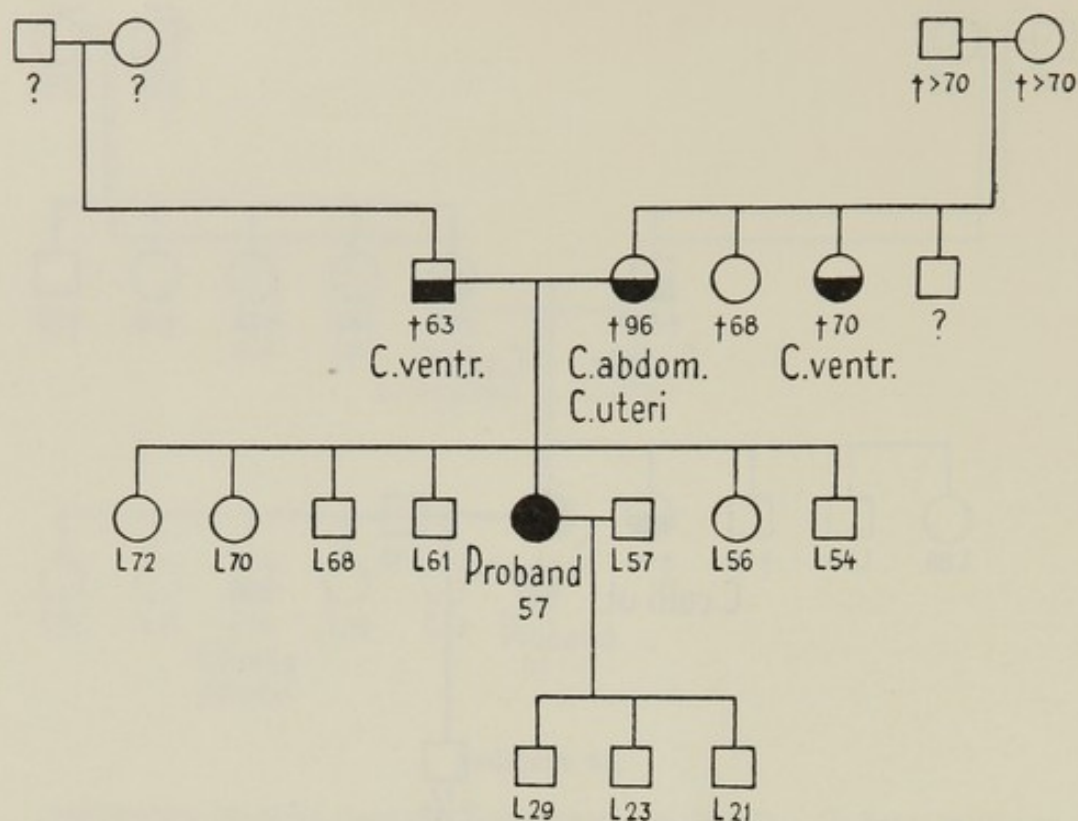


Pedigree 66.

PROBAND (Radium Center, Copenhagen; no. 25953).—○, born in Copenhagen Nov. 26th, 1866. ∞ old age pensioner. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. One childbirth. Nursed until the child died, a month old. Noticed a tumor in her right breast over three years ago, but did not seek the hospital until a slight ulcer appeared, which refused to heal. Biopsy resulted in a histologic diagnosis of adenocarcinoma. Feb. 11th, 1942, mastectomy. Histologic diagnosis: adenocarcinoma.

FATHER.—Born in Sandbjerg June 17th, 1823. Porter. Died in the Hospital for the Poor, Copenhagen, July 26th, 1883, of cancer of the stomach. The diagnosis verified by death certificate.

YOUNGEST SISTER.—Born in Copenhagen March 9th, 1863. ∞ house painter. Died in the Frederiks Hospital, Copenhagen, Jan. 13th, 1910, of cervical cancer. The diagnosis verified by death certificate.



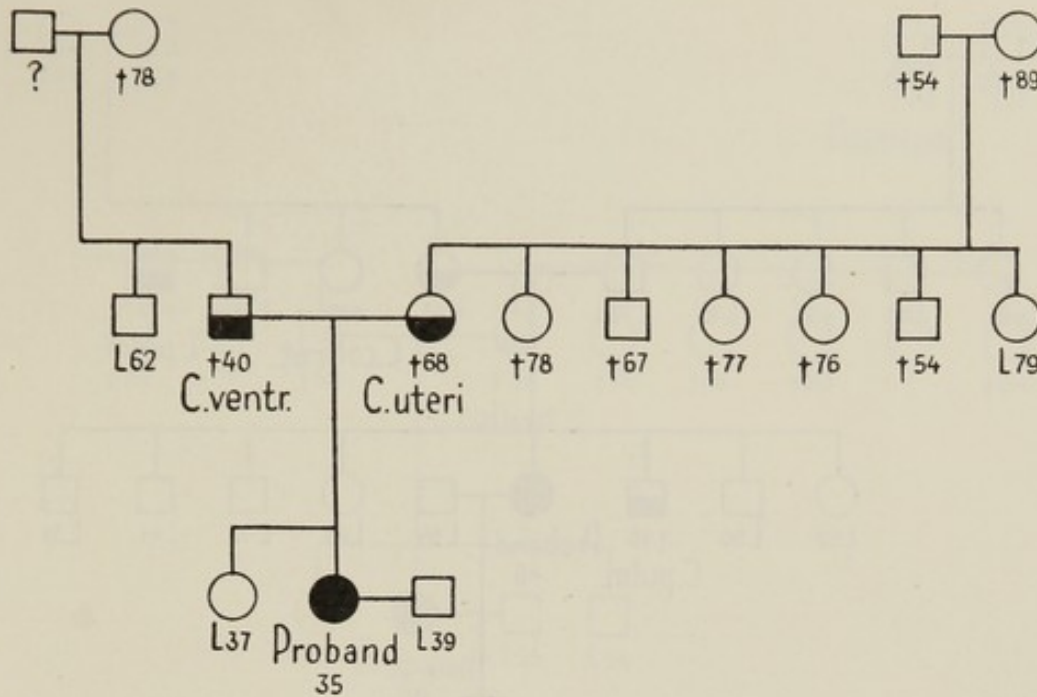
Pedigree 67.

PROBAND (Radium Center, Copenhagen; no. 23212).—○, born in Faarevejle Jan. 30th, 1883. ∞ wood carver. Formerly well. Menstruation from fourteenth to fifty-second year, regular. Menopause normal. Three child-births. Nursed respectively fourteen, nine and ten months. Had for nine months before admission been aware of a slowly growing tumor in her right breast. Dec. 12th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born 1845 in Faarevejle. Tailor. Died in Faarevejle Sep. 9th, 1908, of cancer of the stomach, of about three years' duration, during which time it had manifested itself with increasing symptoms of stenosis, feebleness and emaciation. In the last months before death, icterus.

MOTHER.—Born 1844 in Faarevejle. Died there in April, 1941, of cancer of the uterus and abdomen. The diagnosis verified by death certificate.

MOTHER'S SISTER.—Born 1848 in Faarevejle. Died in Asnæs 1918, of cancer of the stomach. Had been operated on in the hospital in Nykøbing (Sjælland); but only exploratory laparotomy had been done, as metastases to the liver were found.

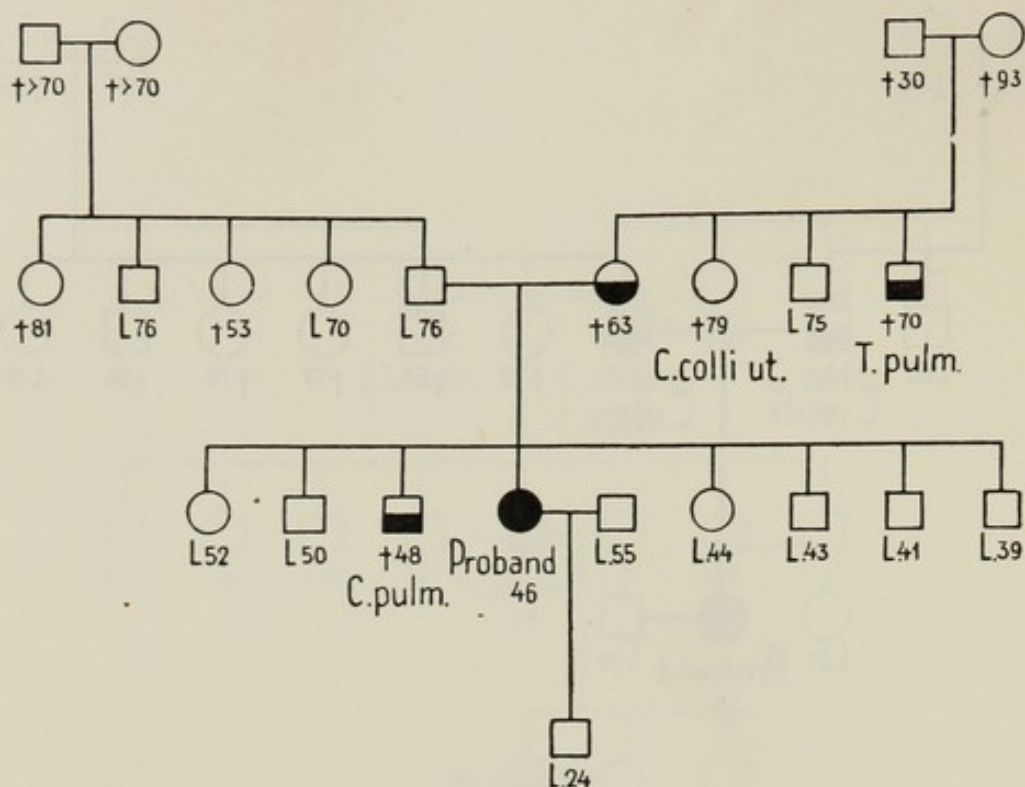


Pedigree 68.

PROBAND (Radium Center, Copenhagen; no. 29674).—○, born in Udbyhøj, near Randers, Jan. 6th, 1908. Publisher's assistant; married. Formerly well. Menstruation since thirteenth year, regular. Never pregnant. Tumor in right breast first noticed a week before admission. Apr. 17th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Assens Jan. 8th, 1877. Barge skipper. Died in the Bispebjerg Hospital, Copenhagen, Feb. 8th, 1917, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER.—Born in Udbyhøj Dec. 25th, 1863. Died in the Bispebjerg Hospital, Copenhagen, Aug. 8th, 1932, of cancer of the uterus. The diagnosis verified by death certificate.



Pedigree 69.

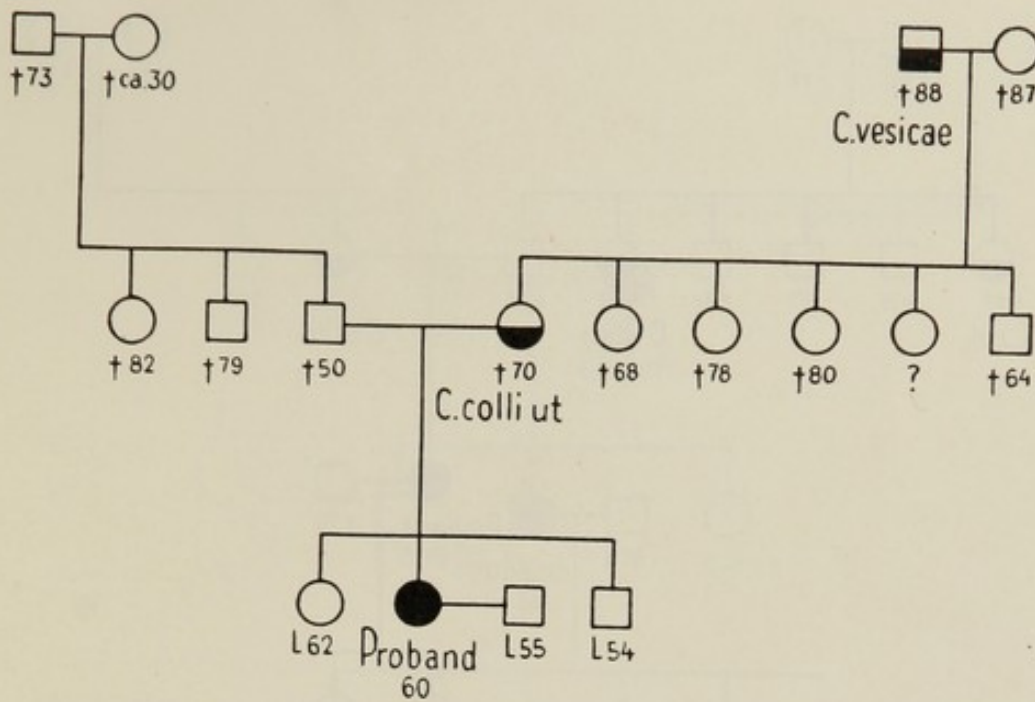
PROBAND (Radium Center, Copenhagen; no. 30395).—○, born in Copenhagen Nov. 5th, 1896. ∞ haulage contractor. Menstruation since fourteenth year, regular. One childbirth. Nursed six months. The tumor in the right breast first noticed two months before admission. May 13th, 1943, extirpation of the tumor. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Birkerød Aug. 17th, 1865. ∞ foreman. Died in Copenhagen Oct. 21st, 1928, of cervical cancer. Treated at the Radium Center (journal no. 3855/26).

BROTHER.—Born in Copenhagen Feb. 2nd, 1894. Tramway employee; married. Died in the Municipal Hospital, Copenhagen, June 4th, 1942, of cancer of the lung. The diagnosis verified by the hospital (service 1).

MOTHER'S BROTHER.—Born 1867 in Birkerød. Farmer. Died in the Usserød Hospital, in 1937, of cancer of the lung. The diagnosis verified by death certificate.



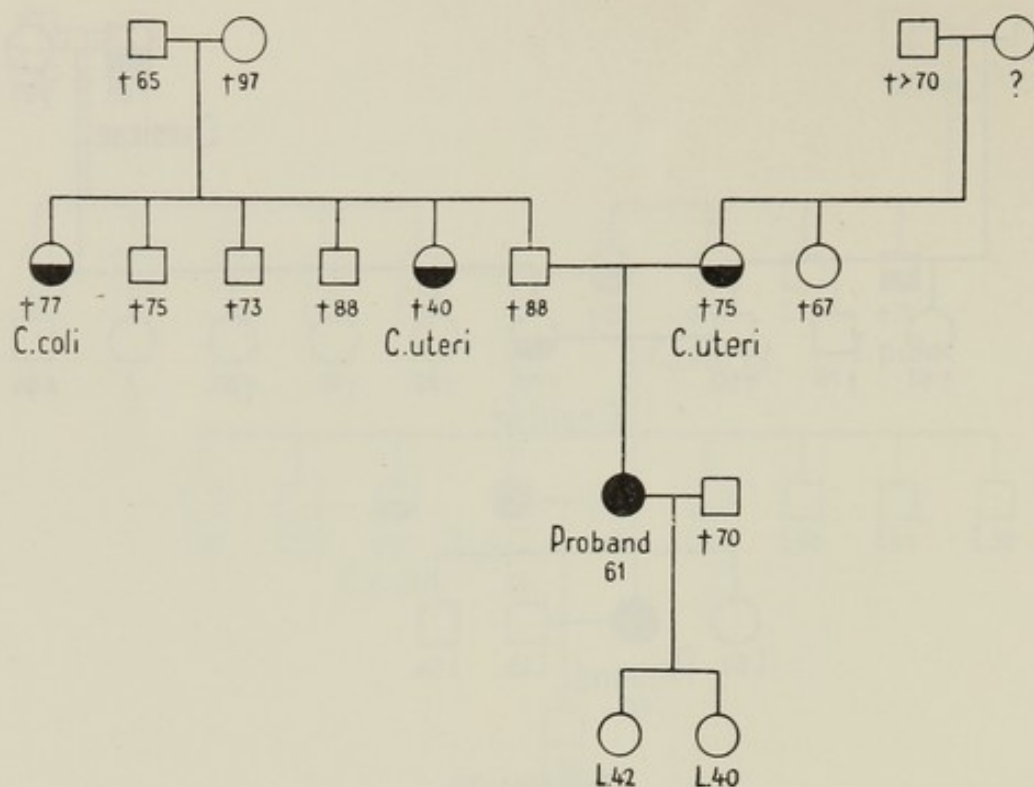


Pedigree 70.

PROBAND (Radium Center, Copenhagen; no. 31101).—○, born in Copenhagen Sep. 6th, 1882. Divorced. Business manageress. Formerly well. Menstruation from fifteenth to forty-sixth year, regular. Menopause normal. Had for five years noticed that her left breast was getting smaller and firmer, and the nipple retracted. Trephine biopsy. Histologic diagnosis: scirrhus carcinoma.

MOTHER.—Born in Elsinore Feb. 25th, 1858. Widow. From 1926 treated at the Radium Center, Copenhagen, (journal 4009/26) for cancer of the uterine cervix. Histologic diagnosis: solid carcinoma. Died in Copenhagen Aug. 31st, 1928.

MOTHER'S FATHER.—Born 1812 in Elsinore. Shipwright. Died 1900 in the Øresunds Hospital, Helsingør, of cancer of the bladder. The diagnosis verified by death certificate.



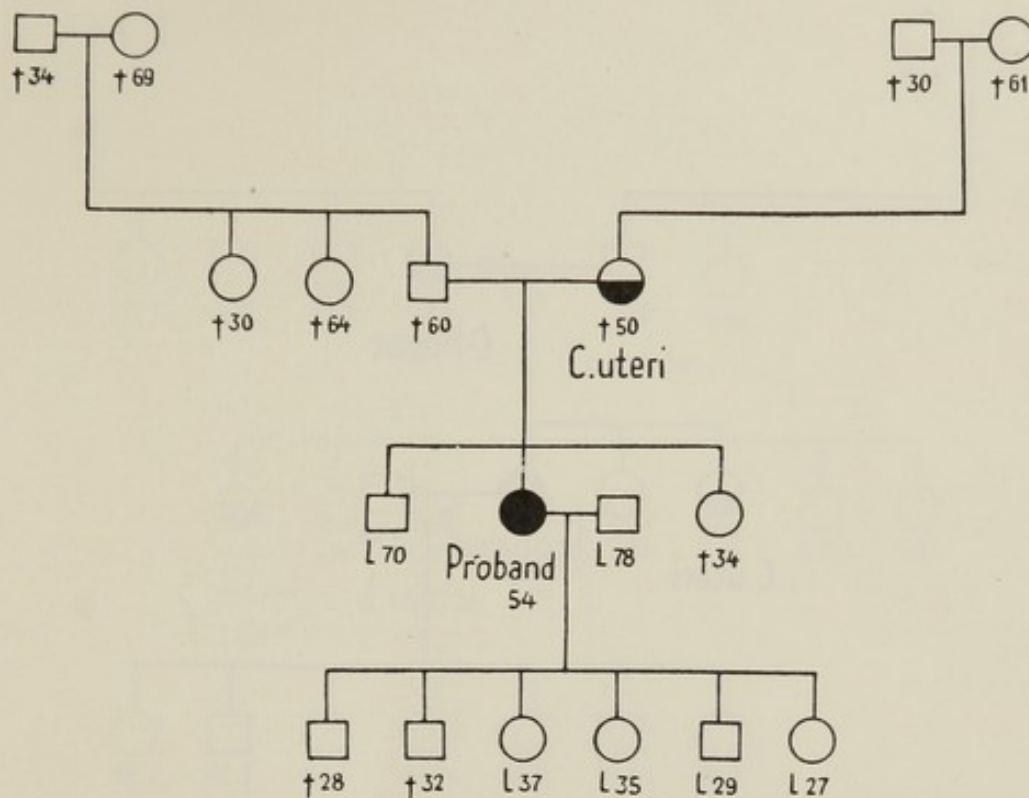
Pedigree 71.

PROBAND (Radium Center, Copenhagen; no. 24368).—○, born in Copenhagen Feb. 6th, 1880. Architect's widow. Menstruation from fifteenth to thirty-ninth year, regular. Menopause normal. Two childbirths. Nursed only a few weeks on each occasion, owing to hypogalactia. Has for thirty years been aware of a small lump, the size of a pea, in her right breast. It never changed until a year ago, when it without any external cause began to grow larger. Apr. 5th, 1941, it was extirpated and histologically diagnosed as adenocarcinoma. June 23rd, same year, ablation of the breast, with evacuation of the axilla.

MOTHER.—Born in Nakskov Aug. 30th, 1850. ∞ clerk. Died in the Øresunds Hospital, Copenhagen, Nov. 16th, 1925, of uterine cancer and pulmonary tuberculosis. The diagnosis verified by death certificate.

FATHER'S ELDEST SISTER.—Born 1845. Broker's widow. Died in Copenhagen July 24th, 1923; according to the death certificate of cancer of the colon.

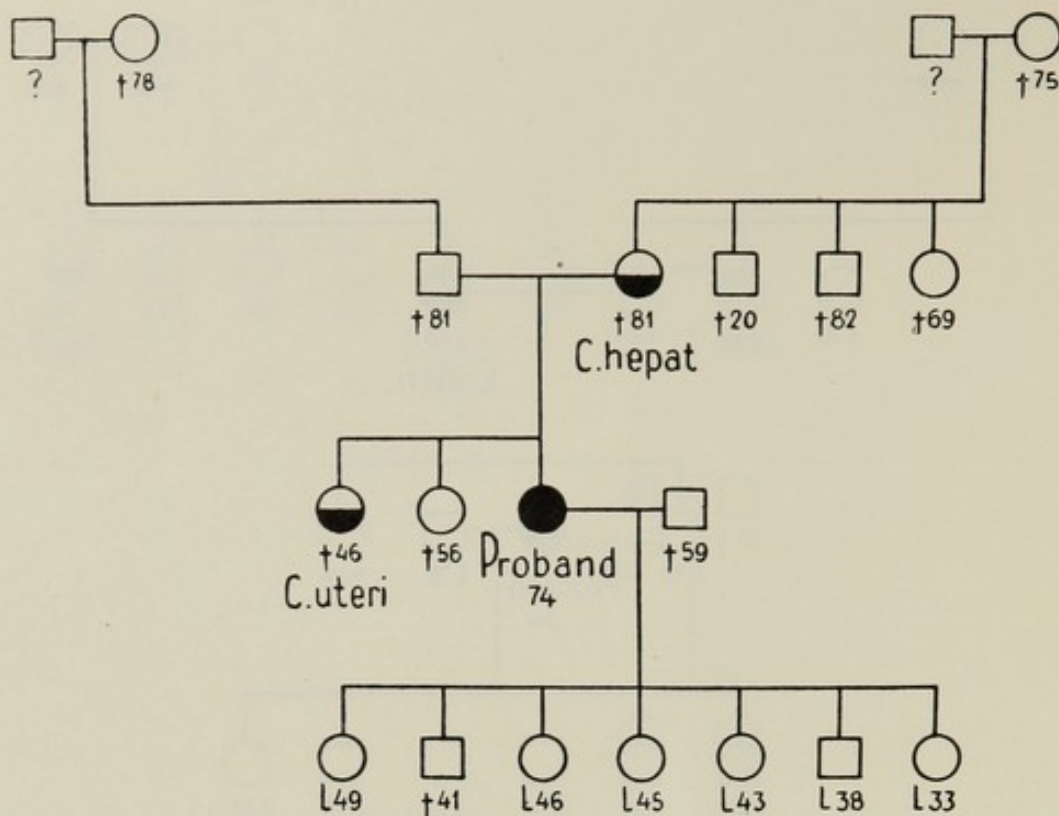
FATHER'S YOUNGEST SISTER.—Born 1856. Single. Died in Copenhagen Oct. 5th, 1896; according to the death certificate of uterine cancer.



Pedigree 72.

PROBAND (State Hospital, Copenhagen; service 5, no. 1784/42).—○, born in Copenhagen July 9th, 1875. Embroidery designer; divorced. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Six childbirths. Nursed for about a year each time. Belives herself that the tumor in her right breast, which she first noticed three months before admission, is due to pressure of a corset stay that had hurt her for a long time. Nov. 27th, 1942, ablation of the breast. Histologic diagnosis: solid, partly scirrhus carcinoma.

MOTHER.—Born in Vintersbølle July 10th, 1849. ∞ railway functionary. In 1901, treated at St. Joseph's Hospital, Copenhagen, for cancer of the uterus. The diagnosis verified by the hospital. Died on Amager 1902.

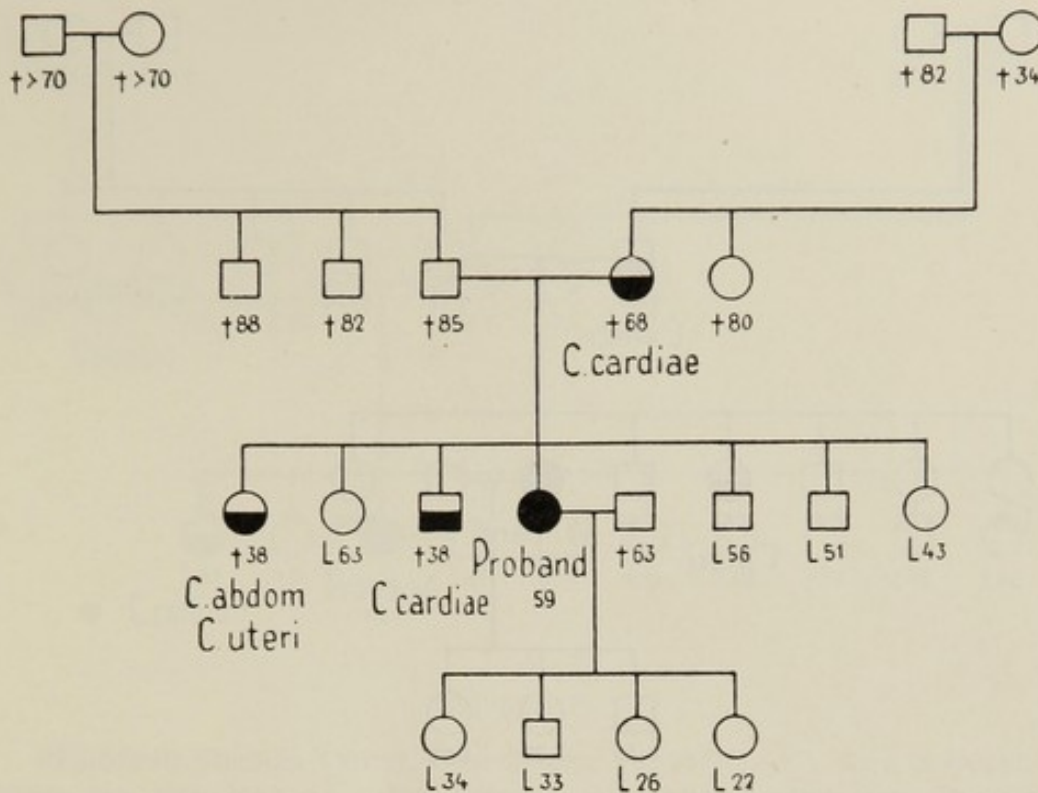


Pedigree 73.

PROBAND (Radium Center, Copenhagen; no. 31285).—○, born in Struer Jan. 29th, 1869. Widow. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Seven childbirths. Never able to nurse for longer than three months, owing to hypogalactia. Fifteen years ago she fell and hurt her left breast, which was tender for a long while afterwards, but there was no swelling or extravasation. A month before admission she noticed a lump in the breast. Trephine biopsy. Histologic diagnosis: carcinoma.

MOTHER.—Born in Stege Apr. 19th, 1837. Widow. Died in Copenhagen (Frederiksberg) Nov. 28th, 1918, of cancer of the liver. The diagnosis verified by death certificate.

ELDEST SISTER.—Born in Struer Apr. 17th, 1861. ∞ waggoner. Died in the Municipal Hospital, Copenhagen, June 16th, 1907, of perforating uterine cancer and peritonitis. The diagnosis verified by the hospital.



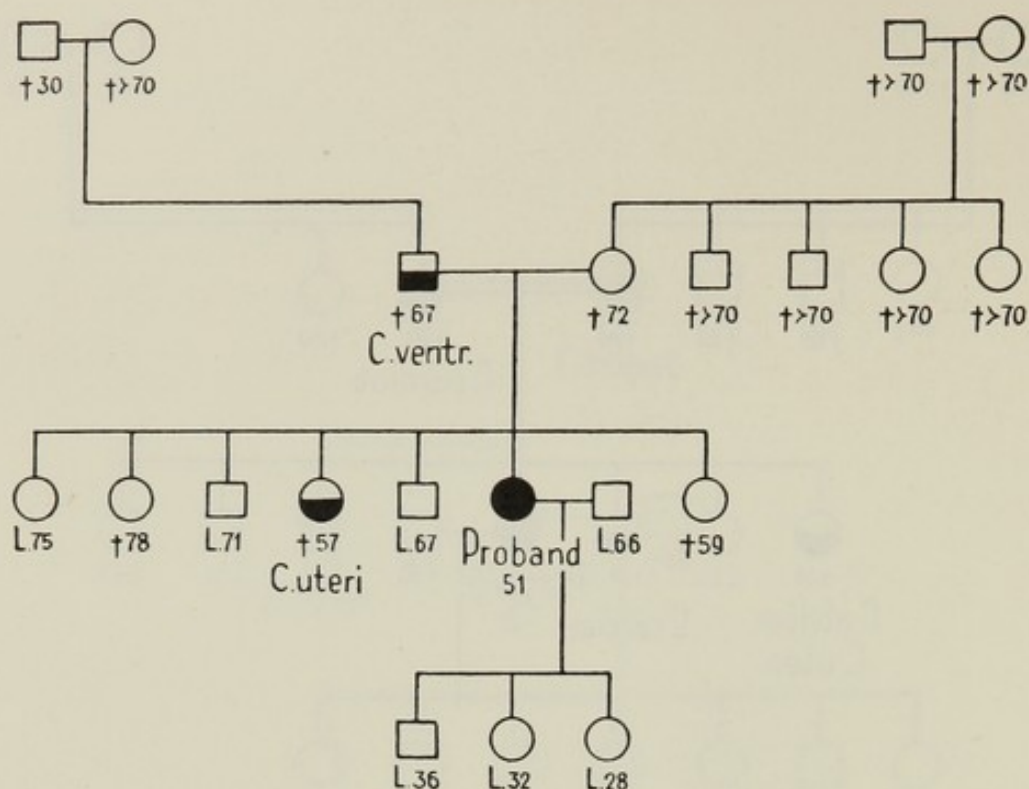
Pedigree 74.

PROBAND (Radium Center, Copenhagen; no. 31814).—○, born in Copenhagen Feb. 13th, 1884. Haulage contractor's widow. Formerly well. Menstruation from twelfth to fiftieth year. Menopause normal. Four childbirths. Nursed respectively four, eight, ten and eighteen months. Tumor in the left breast noticed five days before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER.—Born 1856 in Lille Værlose. ∞ brewer. Died in the Frederiksberg Hospital, Copenhagen, 1924, of cardiac cancer. The diagnosis verified by the hospital records (service B, no. 937/24).

ELDEST SISTER.—Born in Copenhagen July 21st, 1878. ∞ tramway employee. Died in the Bispebjerg Hospital, Copenhagen, March 8th, 1917, of uterine and abdominal cancer. The diagnosis verified by the hospital's death register.

ELDEST BROTHER.—Born in Copenhagen Dec. 21st, 1882. Tramway employee. Died in the Municipal Hospital, Copenhagen, of cardiac cancer. The diagnosis verified by the hospital's death register.

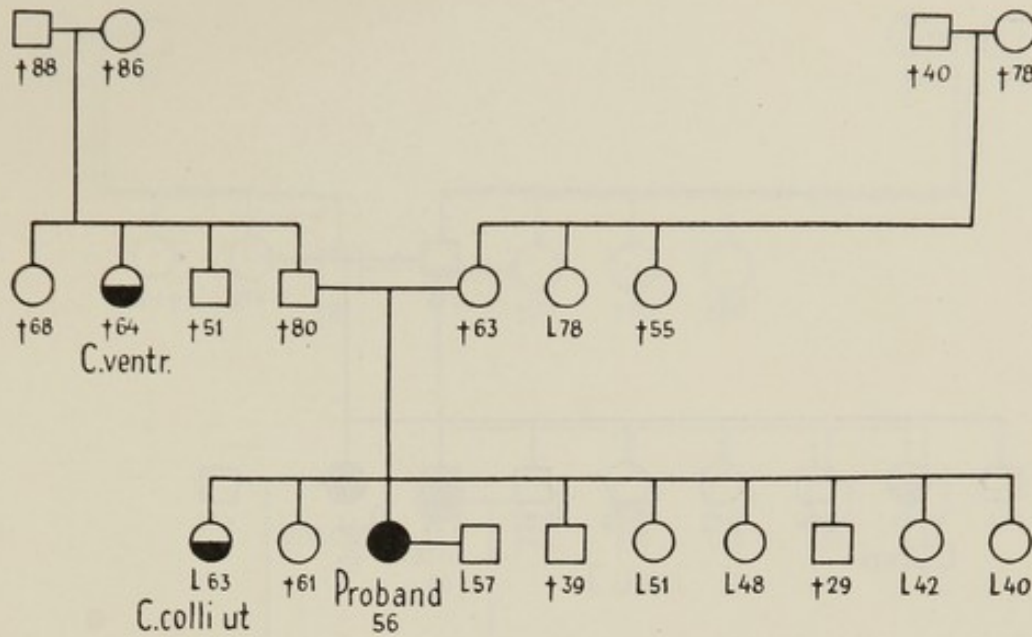


Pedigree 75.

PROBAND (Radium Center, Copenhagen; no. 22184).—○, born in Skævinge June 4th, 1887. ∞ surveyor. Menstruation from sixteenth to fortieth year, regular. Menopause normal. Three childbirths. Nursed nine months on each occasion, but during the second lactation galactophoritis of the right breast set in. In 1929, she was operated on at the Frederiksberg Hospital, Copenhagen, and the right breast ablated. 1940, local recurrence, and she has since been treated at the Radium Center. Histologic diagnosis: scirrhus carcinoma.

FATHER.—Born on Møen 1835. Provision dealer. Died in Skævinge Jan. 14th, 1902, of cancer of the stomach. The diagnosis verified by death certificate.

SISTER.—Born in Skævinge 1872. Housekeeper, single. Died in Copenhagen Jan. 20th, 1930, of cancer of the uterus. The diagnosis verified by death certificate.

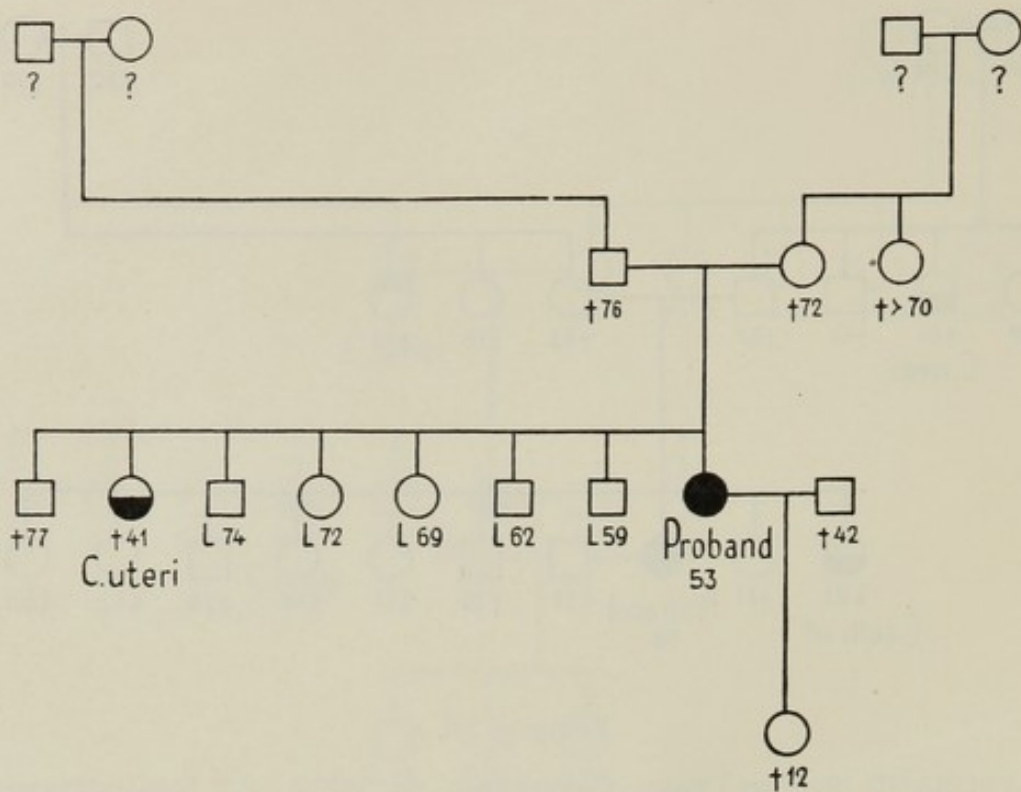


Pedigree 76.

PROBAND (Radium Center, Copenhagen; no. 28720).—○. born in Copenhagen Jan. 30th, 1882. ∞ waiter. Formerly well. Menstruation from fifteenth to fifty-second year. Menopause normal. Never pregnant. In 1938, operated on at the Sundby Hospital, Copenhagen, for cancer of the left breast. Histologic diagnosis: solid carcinoma. Some time afterwards she noticed a tumor in her right breast, for which she was operated on, in 1939, in a private clinic. September, 1942, local recurrence in right side.

FATHER'S NEXT ELDEST SISTER.—Born in Torpe July 28th, 1862. ∞ shopkeeper. Died Dec. 31st, 1926, in St. Joseph's Hospital, Copenhagen, of cancer of the stomach. The diagnosis verified by death certificate.

ELDEST SISTER.—Born 1880 in Copenhagen. ∞ workingman, Faxe Ladeplads. At present writing being treated at the Radium Center, Copenhagen, for cancer of the uterine cervix. The diagnosis verified by the Hospital.

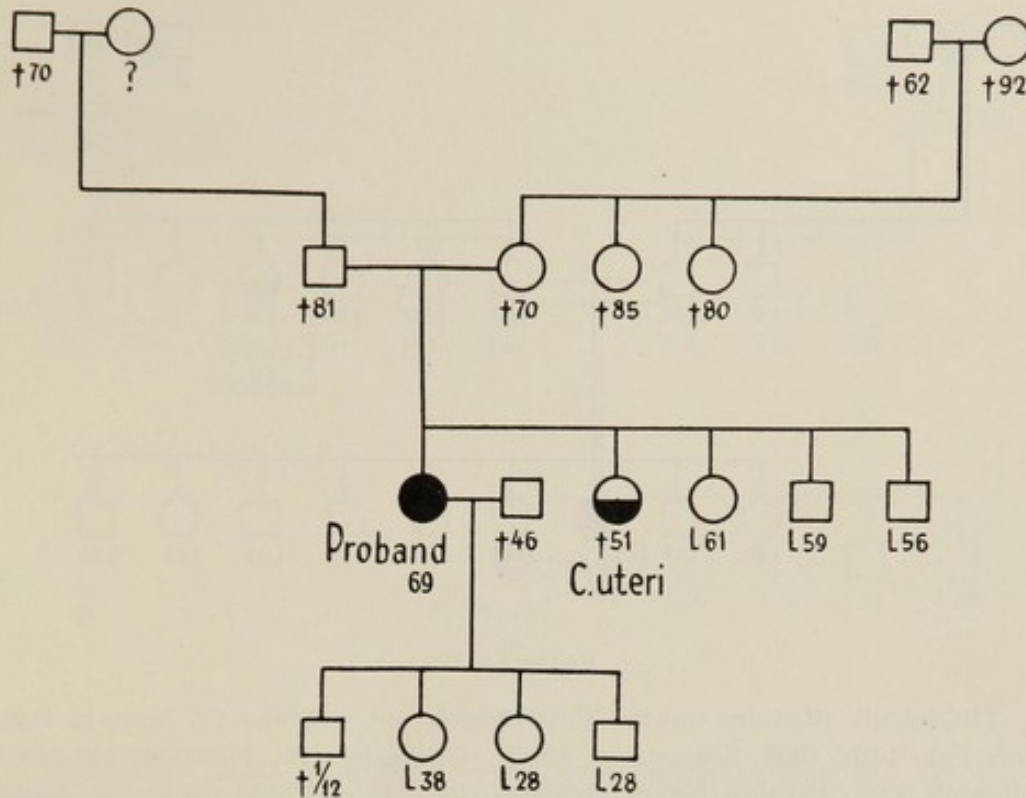


Pedigree 77.

PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Middelfart Apr. 30th, 1885. Waiter's widow. Formerly well. Menstruation from eighteenth to forty-fourth year, regular. Menopause normal. One child-birth. Nursed only a few weeks, owing to hypogalactia. Thinks that a corset which she wore for several years pressed on her breasts. In 1934 treated at the Radium Center, Copenhagen, for cancer of the uterine cervix. In 1938, ablation of the left breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma. April, 1942, glandular recurrence.

SISTER.—Born in Middelfart Sep. 12th, 1866. ∞ carpenter. Died in Copenhagen May 24th, 1907, of uterine cancer. The diagnosis verified by death certificate.

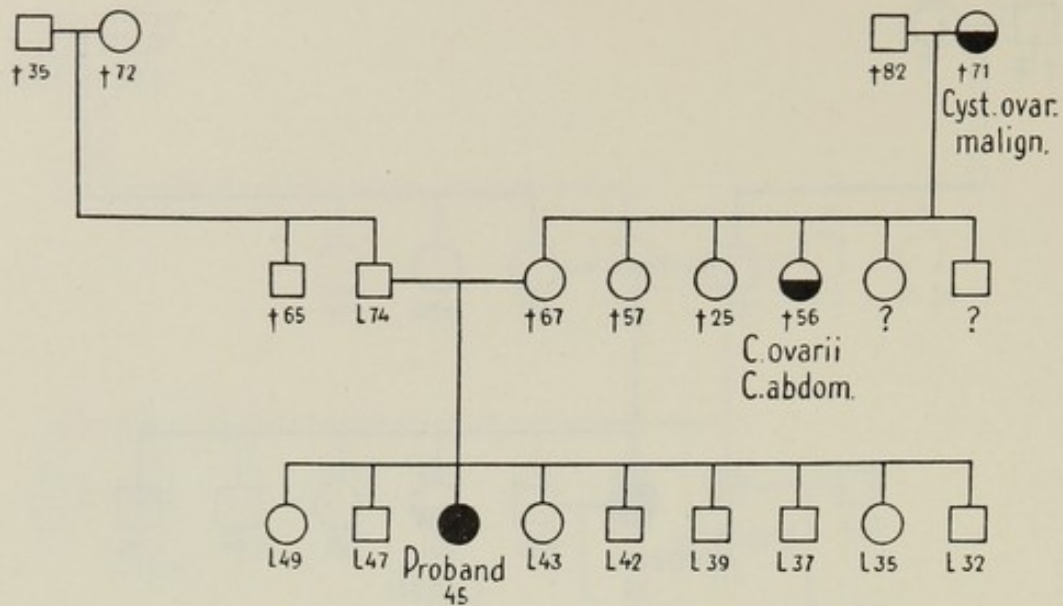




Pedigree 78.

PROBAND (Radium Center, Copenhagen; no. 28772).—○, born in Odense Nov. 10th, 1873. Widow. In 1906 treated in St. Joseph's Hospital, Copenhagen, for ovarian cyst. Otherwise formerly well. Menstruation from fourteenth to thirty-ninth year, regular. Three childbirths. Nursed respectively six weeks, twelve months and one week. Three months before admission she was the victim of a collision and fractured two ribs on the right side. When the bandage was removed she noticed a lump in the left breast. March 10th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

SISTER.—Born in Odense July 3rd, 1876. ∞ wholesale merchant. Died in the State Hospital, Copenhagen, 1927, of uterine cancer. The diagnosis verified by death certificate.

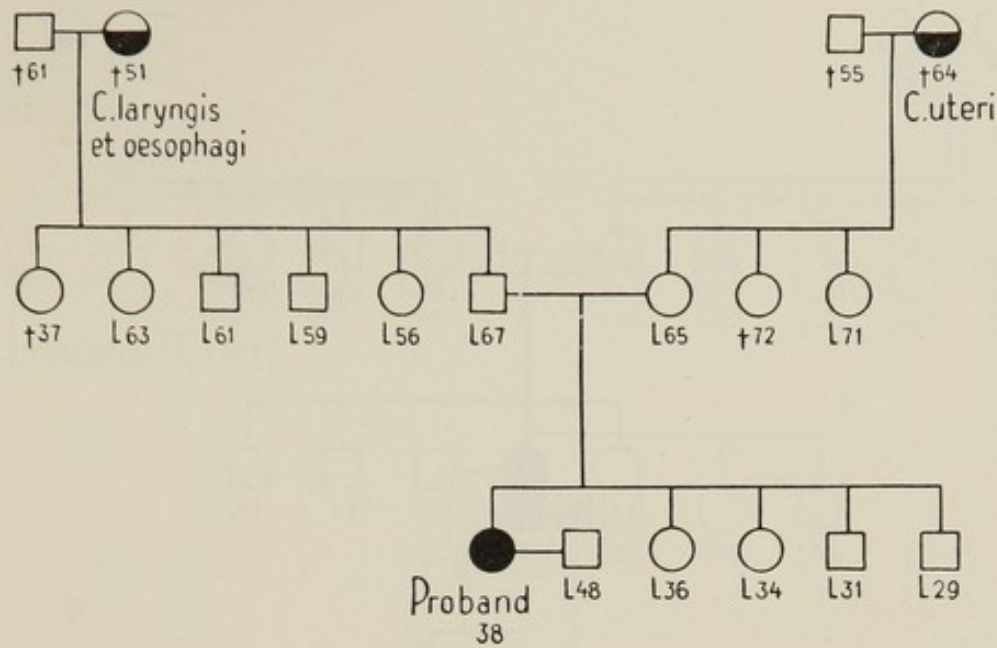


Pedigree 79.

PROBAND (Radium Center, Copenhagen; no. 31670).—○, born in Randers Feb. 13th, 1898. Seamstress; single. Formerly well. Menstruation since fifteenth year, regular. Never pregnant. In 1935 operated on in the Bispebjerg Hospital, Copenhagen, service D, for fibroadenoma of the right breast. In the last year before her present admission to the Radium Center, Sep. 14th, 1943, she had noticed that the tissue underneath and about the cicatrix in her right breast became firmer and firmer; hence she addressed herself to the surgical policlinic of the Municipal Hospital, where a trephine biopsy was done. Histologic diagnosis: solid carcinoma, in fibromatous, partly cystic.

MOTHER'S MOTHER.—Born in Udby Mark June 8th, 1837. ∞ carpenter. Died 1908 in hospital in Randers, of malignant ovarian cystoma. The diagnosis verified by death certificate.

MOTHER'S NEXT YOUNGEST SISTER.—Born in Holbæk Sep. 25th, 1861. Died in Randers Sep. 14th, 1918, of cancer of the ovary. The diagnosis verified by death certificate.

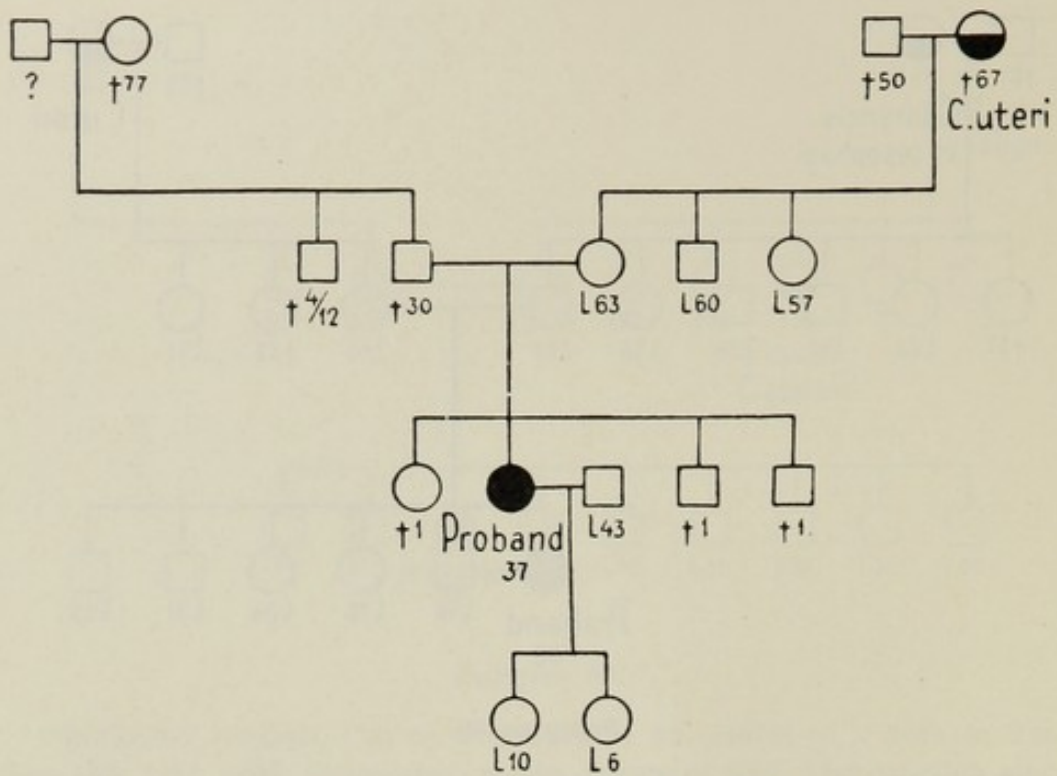


Pedigree 80.

**PROBAND** (State Hospital, Copenhagen; radiol. service, no. 578/43).—  
 ○, born in Copenhagen Feb. 10th, 1905. ∞ brewery-workman. Formerly  
 well. Menstruation since fifteenth year, regular. Never pregnant. Two years  
 ago treated with injections of estibilin for frigidity (12 injections of 1 mg.  
 each). The tumor in the right breast noticed three months before admission.  
 Trephine biopsy. Histologic diagnosis: solid carcinoma.

**FATHER'S MOTHER.**—Born Nov. 10th, 1846. ∞ ship's carpenter. Died in  
 Copenhagen Aug. 9th, 1898, of cancer of the larynx and esophagus. The  
 diagnosis verified by death certificate.

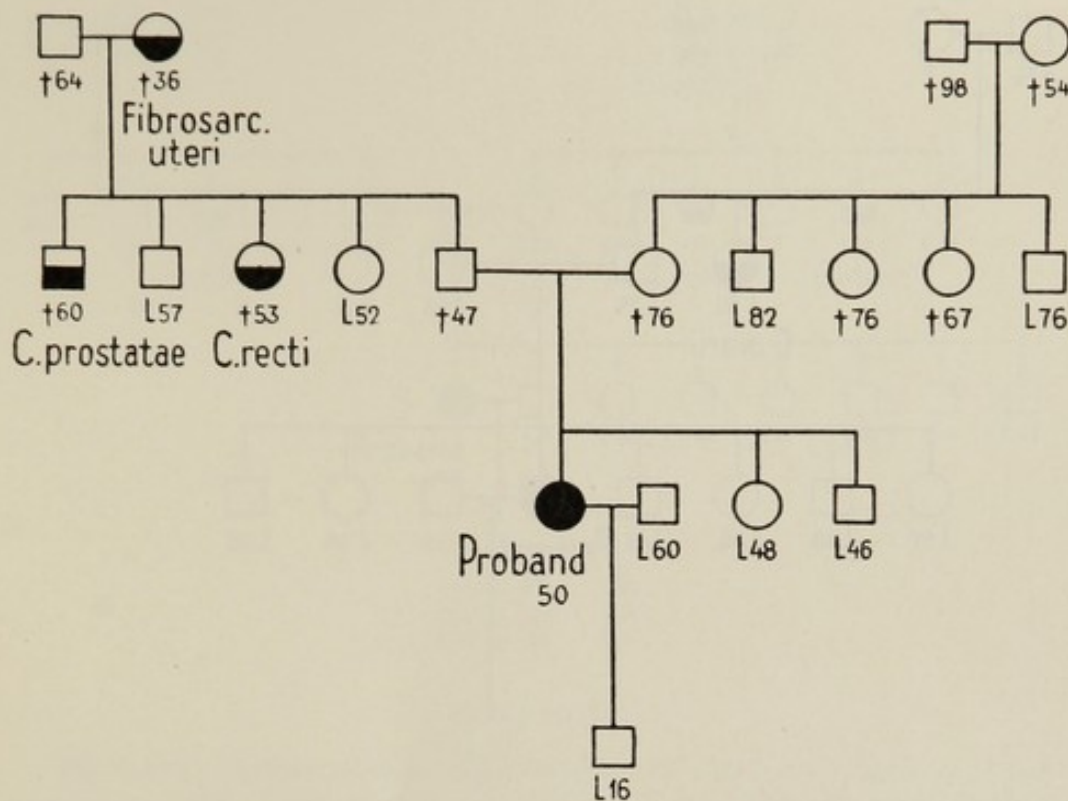
**MOTHER'S MOTHER.**—Born in Køge Jan. 6th, 1844. Shoemaker's widow.  
 In 1908 treated at the Frederiks Hospital, Copenhagen, for cancer of the  
 uterus. Died Sep. 20th, same year. The diagnosis verified by death certificate.



Pedigree 81.

PROBAND (Radium Center, Copenhagen; no. 31557).—○, born in Copenhagen June 21st, 1906. ∞ fruiterer. Formerly well. Menstruation since fifteenth year, regular. Two childbirths. Did not nurse, owing to hypogalactia. Aware of a lump in her left breast for over a year before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER'S MOTHER.—Born in Sweden Oct. 10th, 1855. Died in Copenhagen (Frederiksberg) Dec. 25th, 1922, of uterine cancer. The diagnosis verified by death certificate.



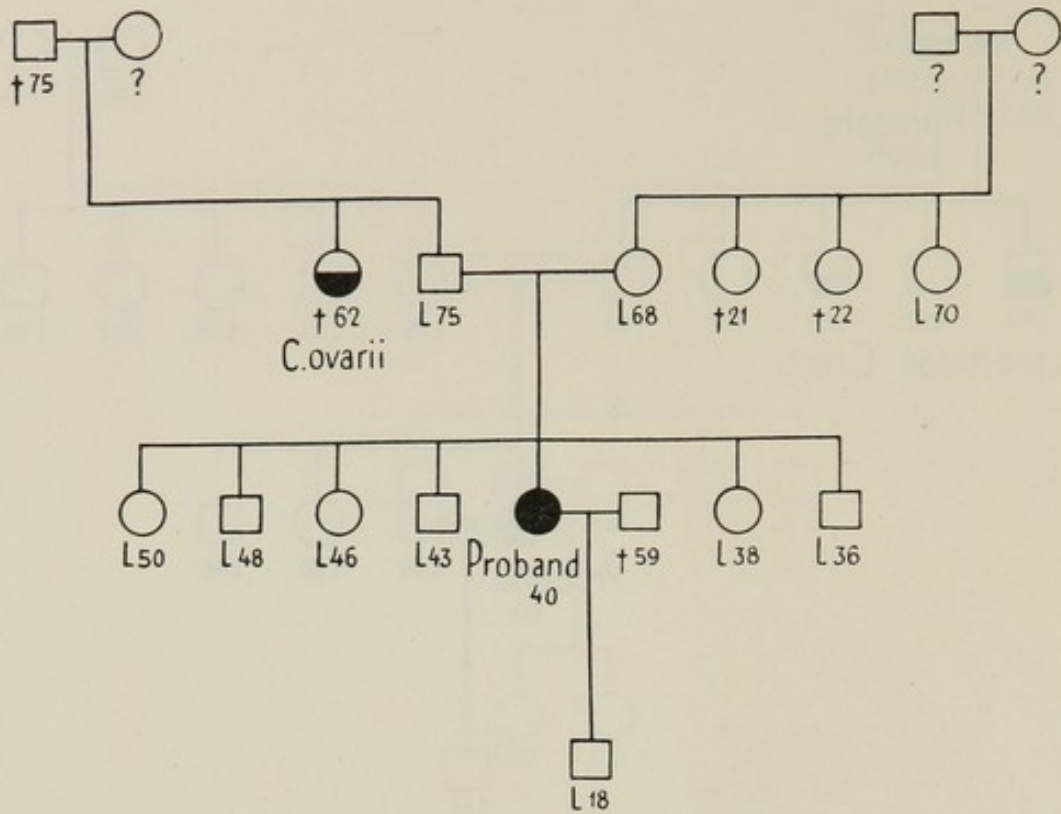
Pedigree 82.

PROBAND (Radium Center, Copenhagen; no. 28566).—○, born in Copenhagen Sep. 17th, 1892. ∞ house painter. Menstruation since fourteenth year, regular. One childbirth. Nursed fully six months. Since her thirty-fourth year treated for diabetes mellitus, in the first years getting along with dieting, now getting protamine insulin, 12 units daily. Tumor in right breast first noticed two weeks before admission. Dec. 9th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

FATHER'S MOTHER.—Born in Copenhagen Jan. 8th, 1844. ∞ custom-house agent. Died in Copenhagen Jan. 18th, 1880, of fibroma of the uterus. The diagnosis verified by death certificate.

FATHER'S ELDEST BROTHER.—Born in Copenhagen June 13th, 1879. Head clerk. Died in the Frederiksberg Hospital, Copenhagen, July 4th, 1939, of cancer of the prostate. The diagnosis verified by death certificate.

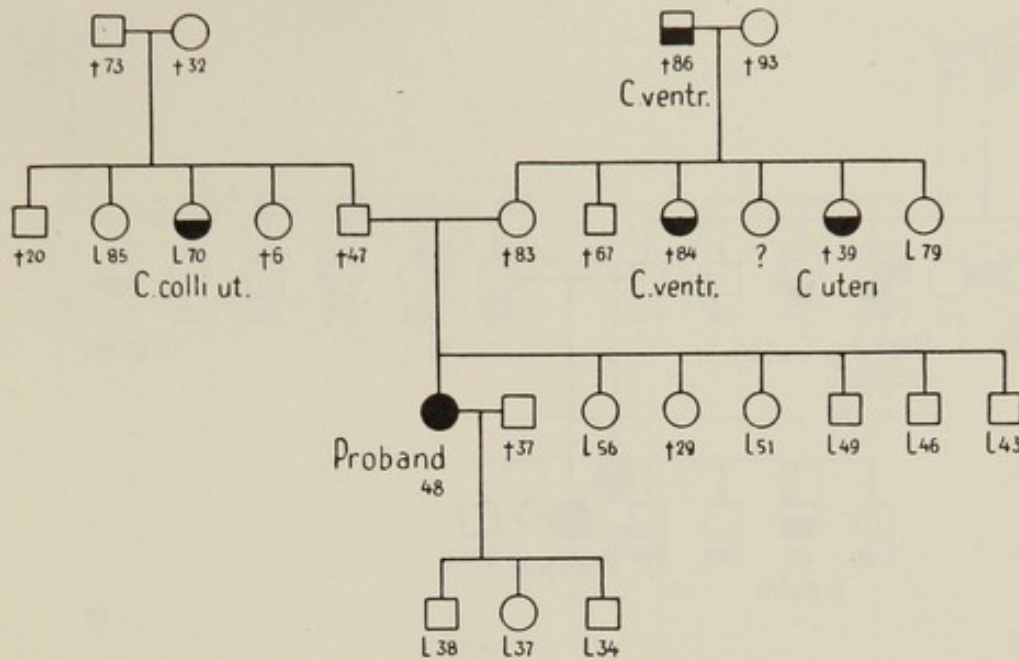
FATHER'S ELDEST SISTER.—Born in Copenhagen Apr. 30th, 1888. ∞ civil engineer. Died in Copenhagen April 1941, of cancer of the rectum. The diagnosis verified by death certificate.



Pedigree 83.

PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 845/41).—  
 ○, born in Slagelse Apr. 8th, 1901. Restaurant-keeper's widow. Formerly well. Menstruation since fifteenth year, regular. One childbirth. Did not nurse, because the child had to be put out to be cared for outside the home. The tumor in the right breast first noticed a month before admission. Dec. 20th, 1941, ablation of the breast and evacuation of the axilla.

FATHER'S SISTER.—Born in Odense 1865. ∞ waiter. Died in Copenhagen March 11th, 1928, of cancer of the ovary. The diagnosis verified by death certificate.



Pedigree 84.

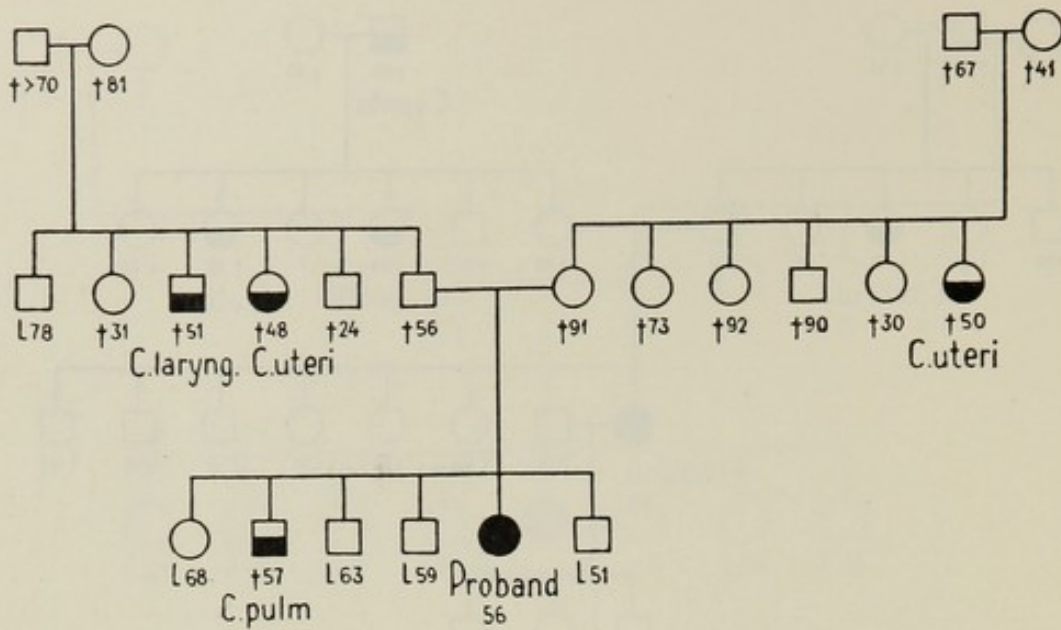
PROBAND (Radium Center, Copenhagen; no. 24543).—○, born in Copenhagen Jan. 19th, 1884. Widow. Formerly well. Menstruation from fifteenth to fifteenth year, regular. Menopause normal. Three childbirths. Nursed respectively seven, seven and four months. During the first lactation, abscess of the right breast, treated by incision. 1930, extirpation of the breast. 1932, local recurrence. Histologic diagnosis: adenomatous carcinoma. 1941, metastases in axillary lymph glands. Trephine biopsy. Histologic diagnosis: metastasis from adenocarcinoma and solid carcinoma of the breast.

MOTHER'S ELDEST SISTER.—Born Oct. 28th, 1850. Died 1934, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S NEXT YOUNGEST SISTER.—Born Feb. 22nd, 1863. Died in the Sundby Hospital, Copenhagen, Jan. 11th, 1903, of uterine cancer. The diagnosis verified by death certificate.

MOTHER'S FATHER.—Born in Elsinore Nov. 23rd, 1817. Rural smallholder. Died in Tikøb Aug. 9th, 1904, after being ill for about two years. According to the statement of the treating physician to the proband's mother, the death was due to malignant tumor in the stomach. Besides, there had in the last months been increasing icterus.

FATHER'S SISTER.—Born Sep. 14th, 1862. ∞ head clerk. At the time of present writing under treatment at the Radium Center in Copenhagen, for uterine cancer.



Pedigree 85.

PROBAND (Radium Center, Copenhagen; no. 30297).—○, born in Havrslev May 25th, 1886. Schoolteacher, single. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Never pregnant. The tumor in the left breast noticed over a year before admission. Histologic diagnosis: solid carcinoma.

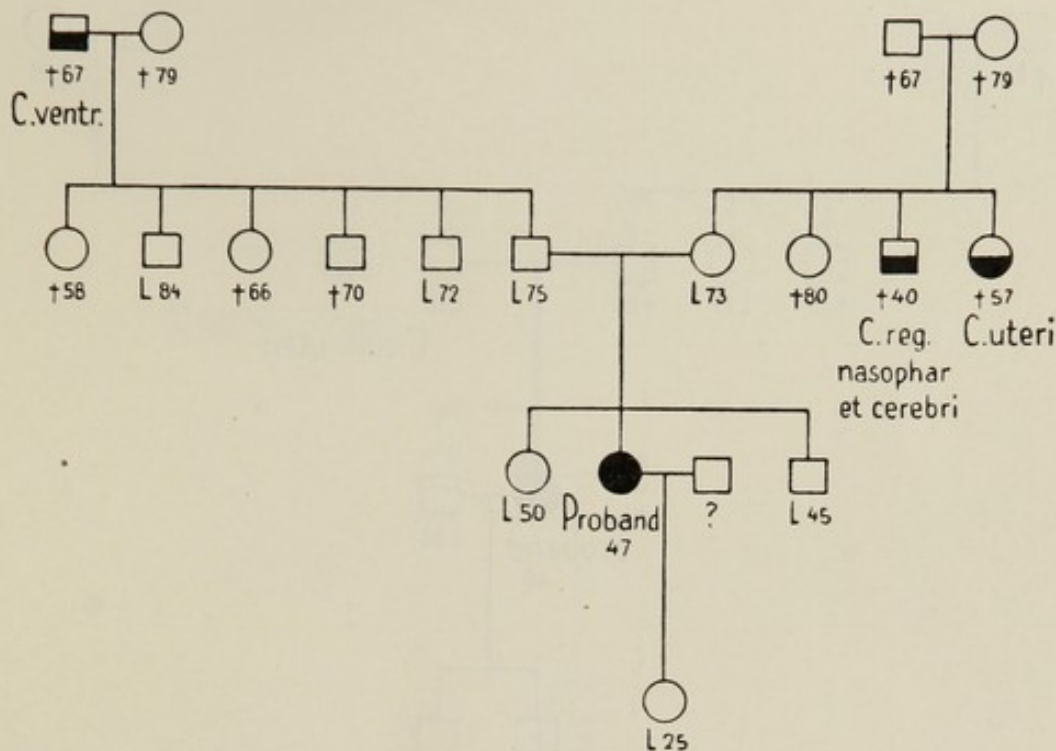
MOTHER'S SISTER.—Born in Mellerup March 3rd, 1846. ∞ master carpenter. Died in Copenhagen July 22nd, 1896, of uterine cancer. The diagnosis verified by death certificate.

FATHER'S NEXT ELDEST BROTHER.—Born 1844, in Restrup. Schoolteacher. Died 1896 in Copenhagen, of cancer of the larynx. The diagnosis verified by death certificate.

FATHER'S YOUNGEST SISTER.—Born 1848, in Restrup. Single. Died in Randers July 22nd, 1896, of uterine cancer. The diagnosis verified by death certificate.

ELDEST BROTHER.—Born in Havrslev July 3rd, 1877. Pharmacist. Died in Glumsø Nov. 25th, 1935, of cancer of the lung. The diagnosis verified by death certificate.





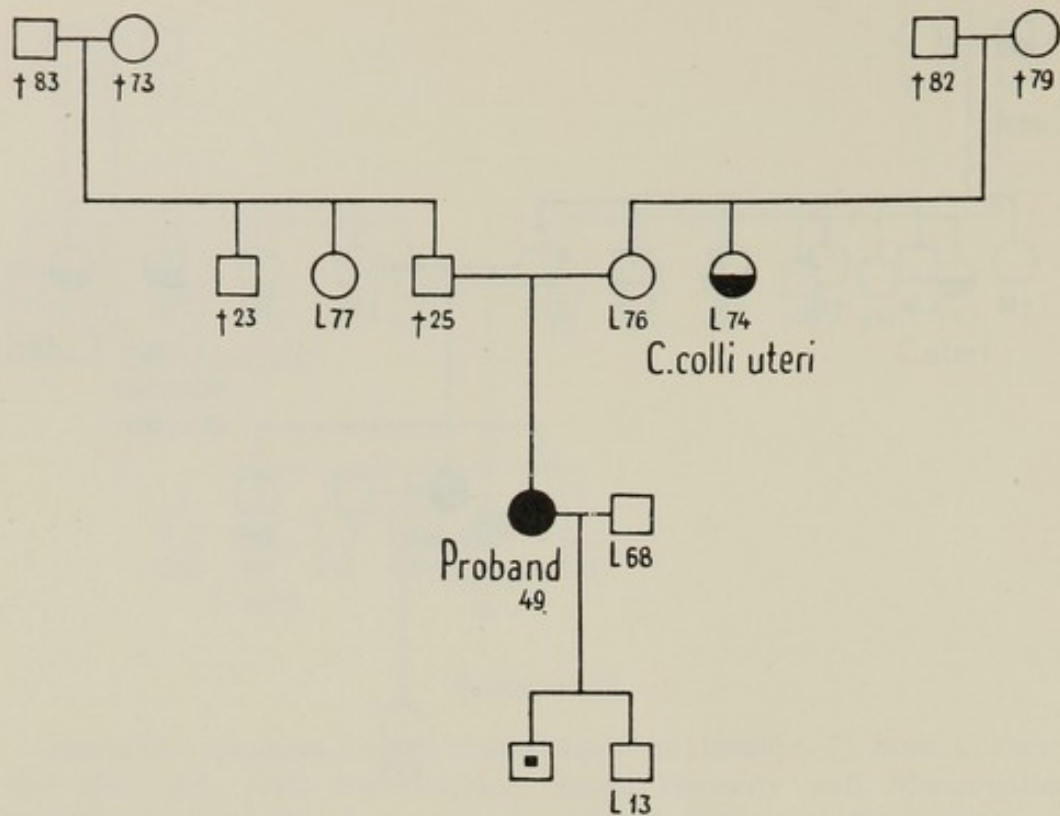
Pedigree 86.

PROBAND (Radium Center, Copenhagen; no. 24683).—○, born in Copenhagen May 10th, 1894. Seamstress; divorced. Formerly well. Menstruation since twelfth year, regular until last year, since when the bleedings have been somewhat more profuse. Dec., 1940, to March, 1941, treated with estibilin tablets (0.1 mg.), 1 tablet three times daily. One childbirth. Did not nurse, owing to papillary aplasia. Thinks that she has had a hazelnut-sized lump in her right breast for about ten years. It had never troubled her, only in the last months before admission she thought that it was getting a little bigger, and at the examination at entrance it was found to be as large as a hen's egg. July 11th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma and solid carcinoma.

FATHER'S FATHER.—Born in Bulbjerg May 5th, 1829. Pavier. Died in Svendborg March 10th, 1897, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S BROTHER.—Born 1864 in Copenhagen. Telegraph foreman. Died in St. Joseph's Hospital, Copenhagen, Oct. 23rd, 1906, of nasopharyngeal and cerebral cancer. The diagnosis verified by death certificate.

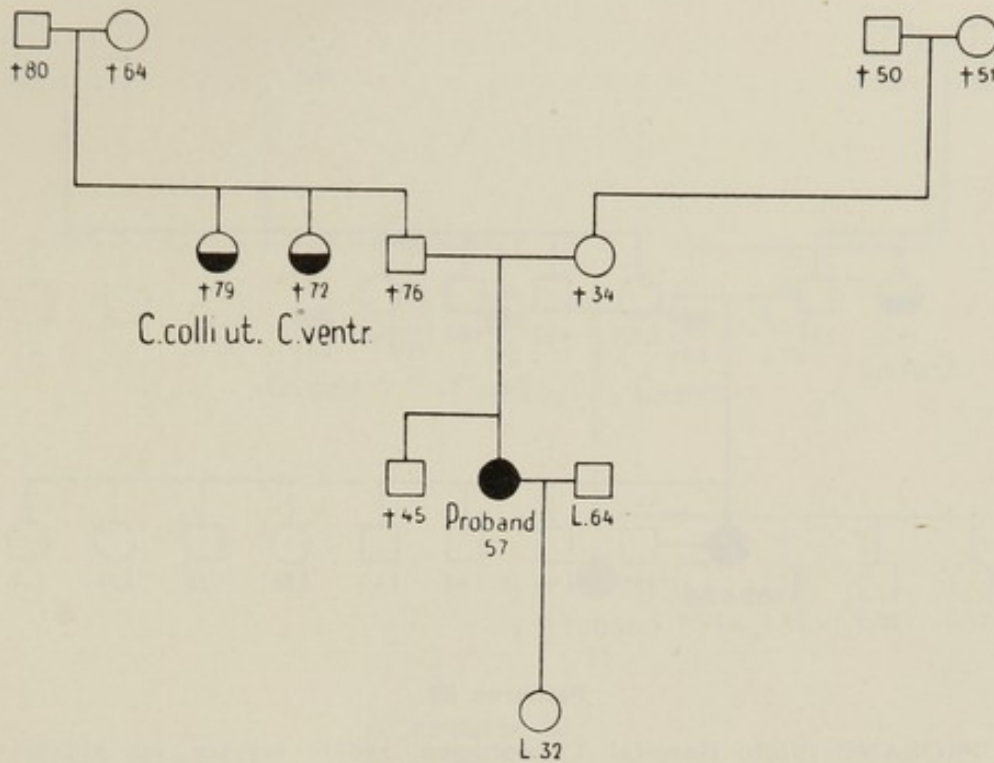
MOTHER'S YOUNGEST SISTER.—Born 1854 in Copenhagen. Widow. Died in Copenhagen Jan. 8th, 1912, of cancer of the uterus. The diagnosis verified by death certificate.



Pedigree 87.

PROBAND (Radium Center, Copenhagen; no. 24381).—○, born in Copenhagen February 26th, 1892. ∞ restaurant keeper. Formerly well. Menstruation since fourteenth year, regular. Two childbirths. First child stillborn. Nursed the second only one month, owing to hypogalactia. The tumor in the right breast noticed a month before admission. June 16th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid medullary carcinoma.

MOTHER'S SISTER.—Born in Nærum Jan. 13th, 1874. Waggoner's widow. At present writing under treatment at the Radium Center, Copenhagen (journal no. 18313), for cancer of the uterine cervix.

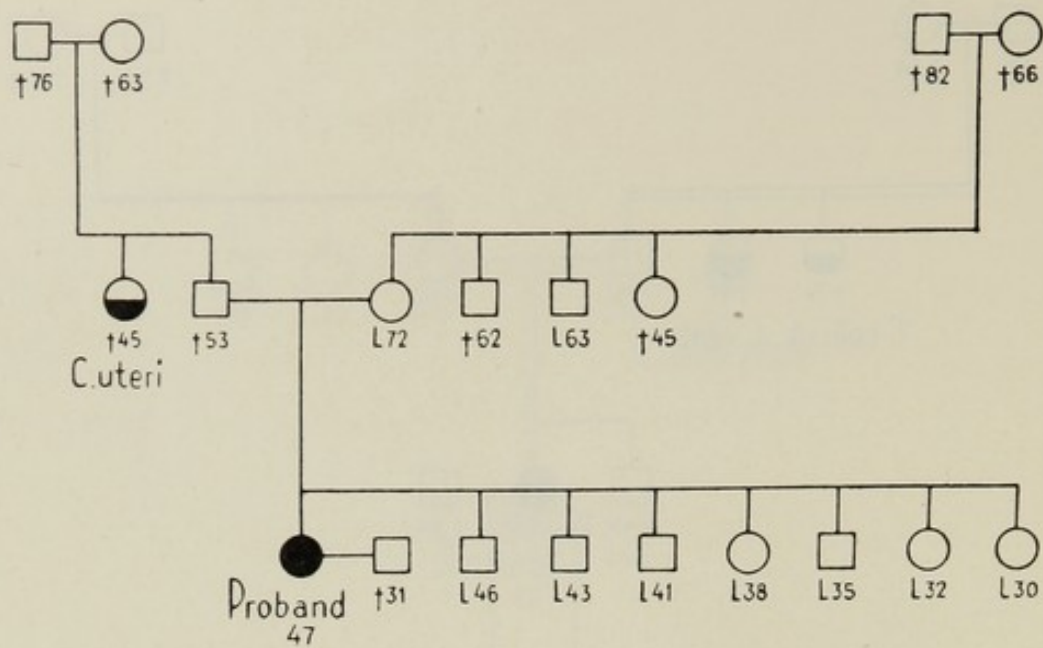


Pedigree 88.

PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Copenhagen Feb. 16th, 1885. ∞ house painter. Menstruation from fourteenth to fifty-second year, regular. Menopause normal. One childbirth. Nursed only two months, owing to hypogalactia. Tumor in the left breast noticed a month before admission. Sep. 3rd, 1936, ablation of the breast, with evacuation of the axilla, at the surgical clinic of the State Hospital, Copenhagen. Histologic diagnosis: scirrhous carcinoma.

FATHER'S ELDEST SISTER.—Born in Korsør June 23rd, 1859. ∞ pattern maker. Died in the Odense County Hospital June 25th, 1939, of cancer of the uterine cervix. The diagnosis verified by inquiry to the radiologic service of the hospital. Histologic diagnosis: papillomatous and solid carcinoma.

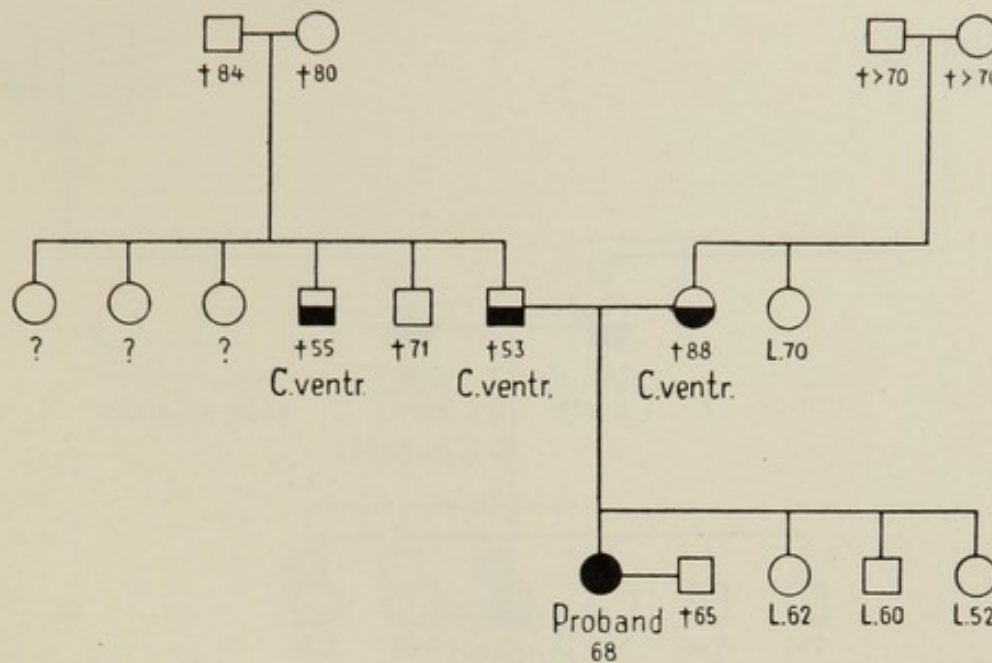
FATHER'S YOUNGEST SISTER.—Born in Korsør Apr. 13th, 1865. ∞ carpenter. Died in St. Joseph's Hospital, Odense, Feb. 17th, 1938; according to information from the hospital of stomach cancer and pylorostenosis.



Pedigree 89.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 412/43).—  
 ○, born in Copenhagen Sep. 21st, 1895. Waiter's widow. Formerly well. Menstruation from fourteenth to forty-fifth year, regular until a year ago, when the bleeding became irregular and protracted. Treated with hormone injections, ovex, 10,000 units, three times. No effect; therefore in 1941 admitted to the Municipal Hospital, Copenhagen, where curettage of the uterine mucosa was done. Never pregnant. Noticed a lump in her left breast a year ago and immediately consulted a physician, who thought it best to wait until the tumor grew larger before deciding about surgical intervention. July 10th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenomatous carcinoma.

FATHER'S SISTER.—Born 1878 in Copenhagen. Single. Died in Copenhagen Sep. 1st, 1923, of cancer of the uterus. The diagnosis verified by death certificate.



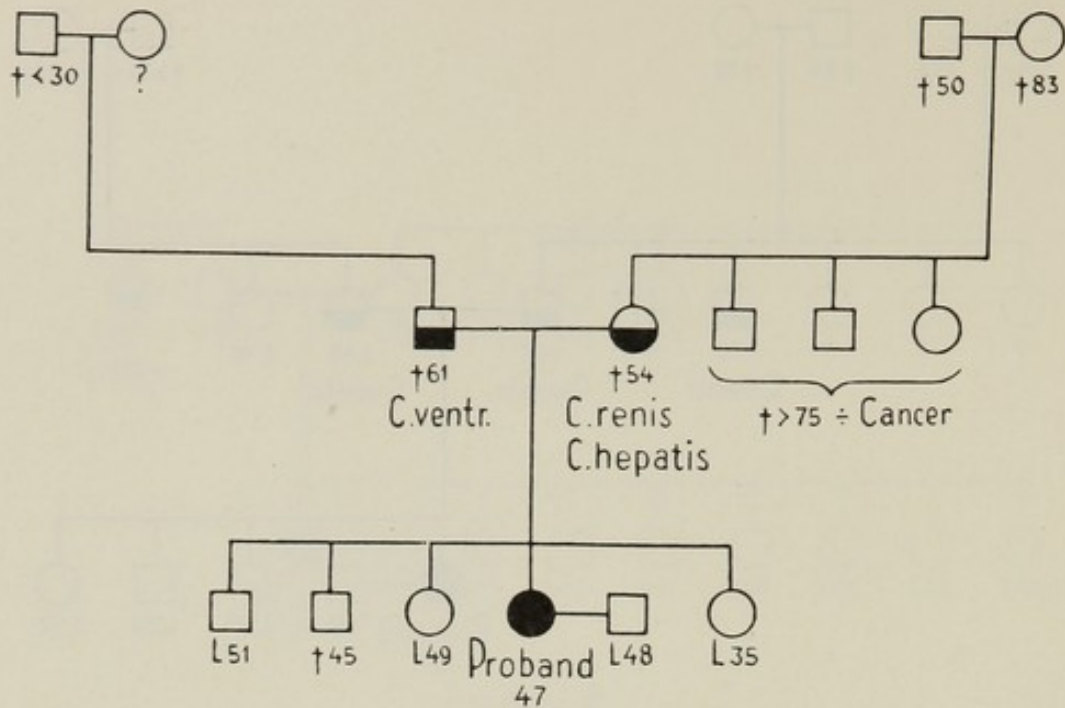
Pedigree 90.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 969/42).—○, born in Aalborg Aug. 1st, 1874. Waiter's widow. Menstruation from fifteenth to fifteenth year, regular. Menopause normal. Never pregnant. In 1940 treated in same hospital, service B, for diabetes insipidus. A slowly growing tumor in right breast noticed five months before present admission. Apr. 17th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Nørre Tranders Aug. 17th, 1842. House-owner, Aalborg. Died there March 14th, 1896, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER.—Born in Aalborg July 15th, 1851. Died there Oct. 26th, 1939, of cancer of the stomach. The diagnosis verified by death certificate.

FATHER'S BROTHER.—Born 1844 in Nørre Tranders. Farmer. Died 1899, of stomach cancer of about a year's duration. According to the treating physician's statement to the family the case was inoperable. The anamnesis was typical for stenosing tumor of the pylorus.

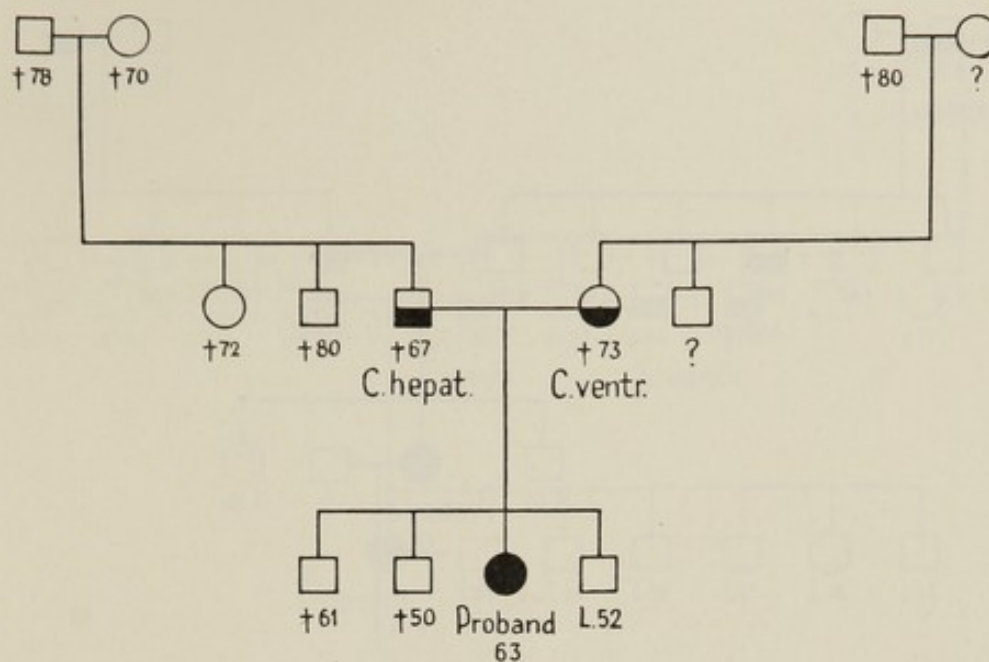


Pedigree 91.

PROBAND (Radium Center, Copenhagen; no. 31248).—○, born in Randers June 30th, 1896. ∞ riveter. When twelve years old operated on in Randers Hospital, for nodular struma. Menstruation from thirteenth to forty-fourth year, regular. Menopause normal. Never pregnant. Had for three months before admission noticed an increasing retraction of the nipple of her right breast, but had not herself felt the formation of a lump there. Trephine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Randers Oct. 13th, 1867. ∞ workingman. Died in Randers Oct. 23rd, 1921, of cancer of the kidney and liver. The diagnosis verified by death certificate.

FATHER.—Born in Randers May 10th, 1867. Workingman. Died in the Randers Hospital March 7th, 1929, of cancer of the stomach. The diagnosis verified by death certificate.

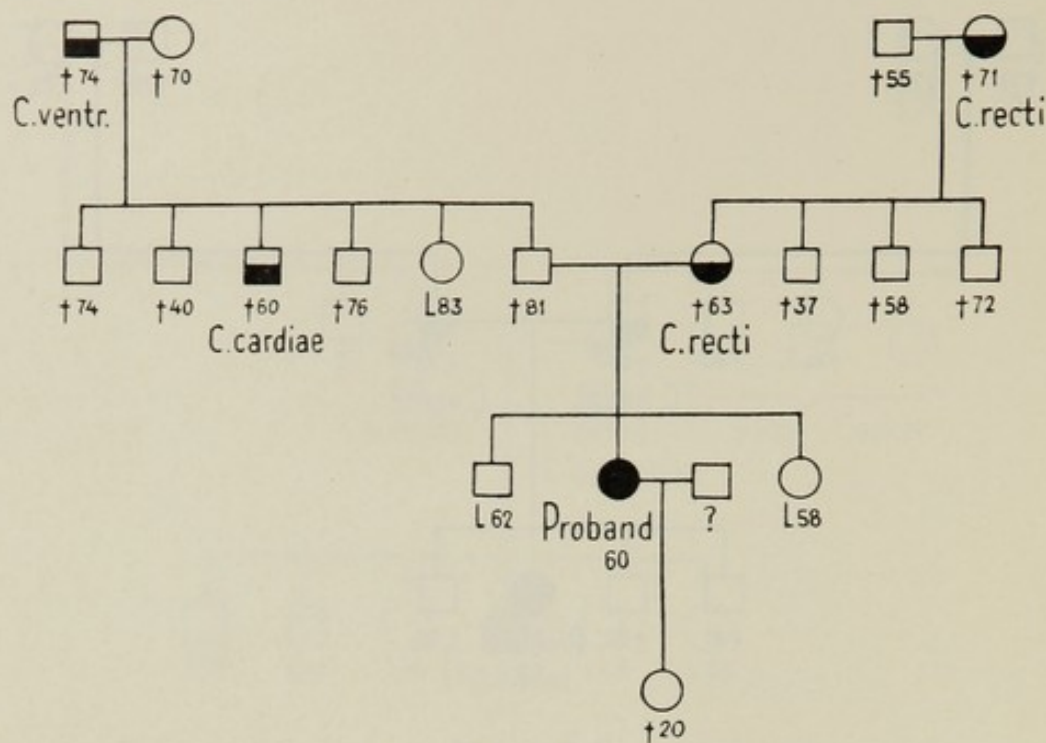


Pedigree 92.

PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Vissenbjerg Nov. 10th, 1879. Seamstress; single. Menstruation from fourteenth to fifty-second year, regular. Treated in the neurologic service of the Municipal Hospital, Copenhagen, for climacteric nervousness. Never pregnant. The tumor in the left breast noticed three months before hospitalisation. July 5th, 1935, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Vejleby Aug. 11th, 1847. Railway foreman. Died in Middelfart Aug. 7th, 1914, of cancer of the liver. The diagnosis verified by death certificate.

MOTHER.—Born in Vemb March 31st, 1845. Died in Røjle Dec. 11th, 1919, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 93.

PROBAND (Radium Center, Copenhagen; no. 27023).—○, born in Nakskov June 15th, 1872. Caretaker; divorced. Menstruation from fifteenth to forty-third year, regular. In 1925 treated in the State Hospital, Copenhagen, (gynecologic service), for cancer of the uterine cervix. Was given a series of roentgen treatments and radium (3 sittings). One childbirth. Nursed only a few weeks, owing to hypogalactia. After a slight injury sustained a year before admission, she became aware of the tumor in her right breast, she had noticed a slight bloody exudation from the nipple. March 24th, 1932, extirpation of the breast. Histologic diagnosis: solid carcinoma. 1942, local recurrence. Trepine biopsy. Histologic diagnosis, adenocarcinoma.

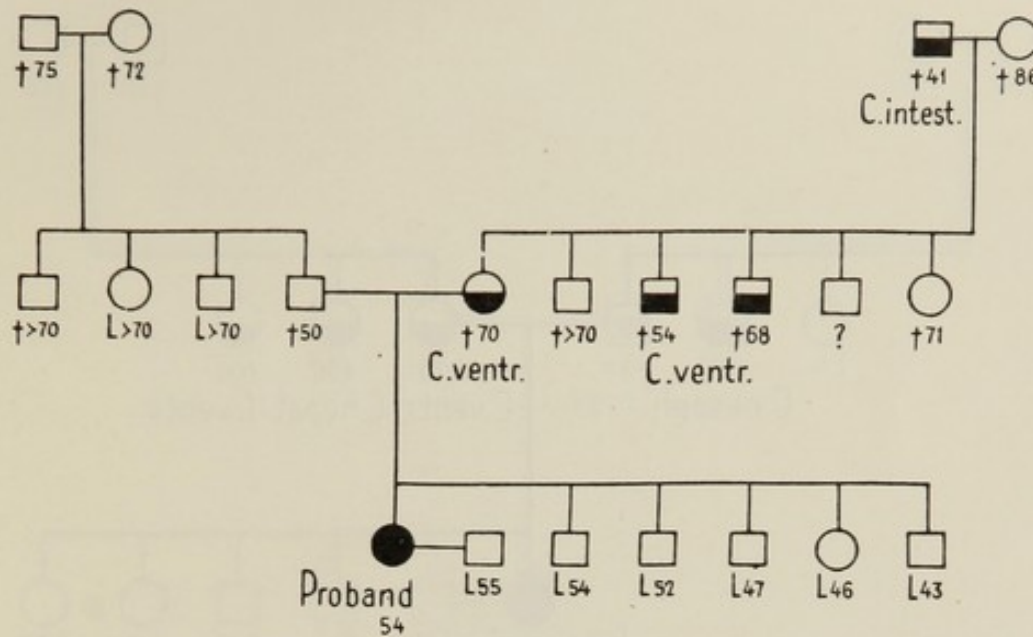
MOTHER.—Born in Nakskov July 24th, 1859. ∞ shoemaker. Died in Copenhagen Oct. 21st, 1922, of cancer of the rectum. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born on Langeland Oct. 12th, 1826. ∞ flour-dealer. Died in Nakskov Dec. 20th, 1897, of cancer of the rectum. The diagnosis verified by death certificate.

FATHER'S BROTHER.—Born in Nakskov Jan. 28th, 1849. Died there in 1909, of cancer of the heart. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born in Nakskov Aug. 11th, 1812. Shoemaker. Died in Nakskov May 20th, 1887, of cancer of the stomach. The diagnosis verified by death certificate.





Pedigree 94.

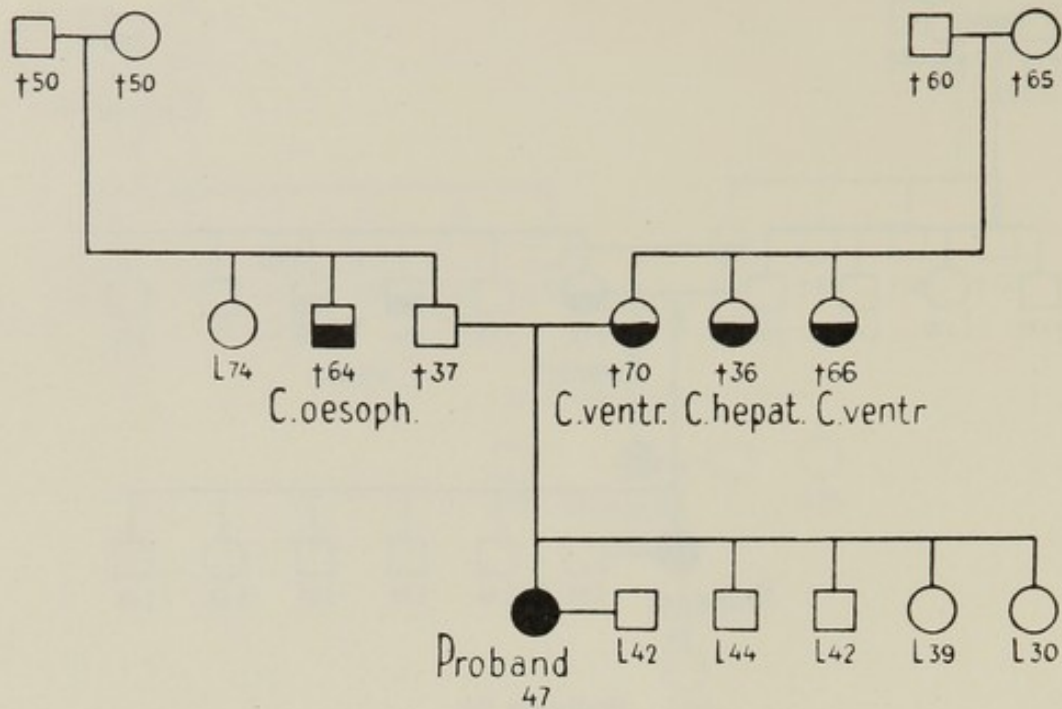
PROBAND (Radium Center, Copenhagen; no. 25993).—○, born in Copenhagen Oct. 11th, 1887. ∞ cabinet maker. Formerly well. Menstruation from fifteenth to fiftieth year, regular. Menopause normal. Never pregnant. Had for over a year before admission a suppurating sore below the nipple of the left breast, but did not consult a physician, treating herself instead with lapis ointment, without effect. Jan. 13th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid scirrhus carcinoma.

MOTHER.—Born in Copenhagen March 3rd, 1864. Died Dec. 23rd, 1934, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S FATHER.—Born in Copenhagen 1830. Chief engineer. Died there 1871. About a year before, he had become ill, with increasing signs of intestinal stenosis, which eventually developed into ileus and cachexia. The attending physician diagnosed the case as intestinal tumor and advised hospitalisation, but the patient refused and was in the last months treated with morphine. Though there is no fully satisfactory proof of the malignancy of the disease, the most likely diagnosis seems to be cancer of the intestine.

MOTHER'S NEXT ELDEST BROTHER.—Born in Copenhagen Oct. 6th, 1855. Machinist. Died in Copenhagen Aug. 1910, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S NEXT YOUNGEST BROTHER.—Born in Copenhagen Dec. 22nd, 1853. Machinist. Died in the Municipal Hospital, Copenhagen, Apr. 20th, 1922, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 95.

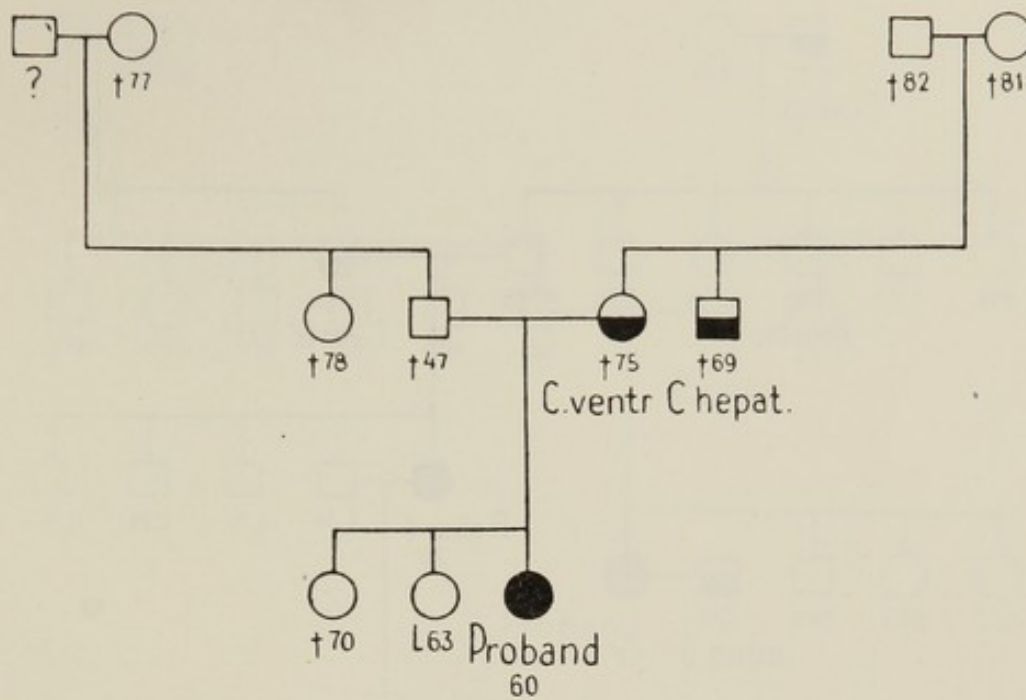
PROBAND (Radium Center, Copenhagen; no. 26428).—○, born in Copenhagen Sep. 3rd, 1894. ∞ ship's officer. Formerly well. Menstruation from fourteenth to forty-seventh year, regular. Menopause normal. Never pregnant. Tumor in left breast first noticed four months before admission. March 3rd, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

MOTHER.—Born in Copenhagen Sep. 18th, 1872. Widow. Died in Copenhagen Dec. 31st, 1942, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S ELDEST SISTER.—Born in Copenhagen 1869. ∞ non-commissioned officer. Died in Copenhagen March 15th, 1905, of cancer of the liver. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born 1875. ∞ blacksmith. Died in the Bispebjerg Hospital, Copenhagen, June 8th, 1941, of cancer of the stomach. The diagnosis verified by death certificate.

FATHER'S BROTHER.—Born in Stege 1874. Typographer. Died in the Sundby Hospital, Copenhagen, Dec. 27th, 1938, of cancer of the esophagus. The diagnosis verified by the hospital.

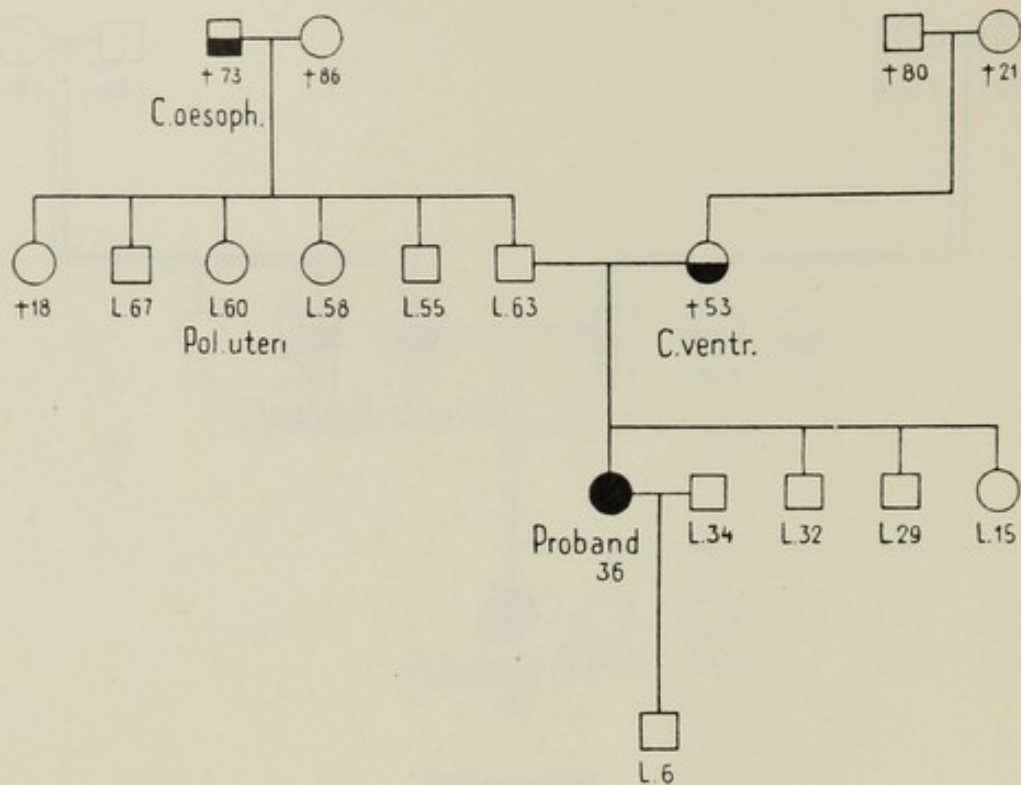


Pedigree 96.

PROBAND (Radium Center, Copenhagen; no. 31015).—○, born in Copenhagen Jan. 8th, 1883. Dressmaker; single. Formerly well. Menstruation from fourteenth to forty-ninth year, regular. Menopause normal. Never pregnant. A year before admission she had noticed a small lump in her right breast; later others had developed, forming like a ring about the first, and there was a slight secretion of bloody, serous fluid from the nipple. Trephine biopsy. Histologic diagnosis: solid medullary carcinoma.

MOTHER.—Born in Copenhagen Feb. 10th, 1848. Fuller's widow. Died in Copenhagen Apr. 29th, 1923, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S BROTHER.—Born 1854 in Copenhagen. Haulage contractor. Died in Copenhagen Sep. 21st, 1924, of cancer of the liver. The diagnosis verified by death certificate.

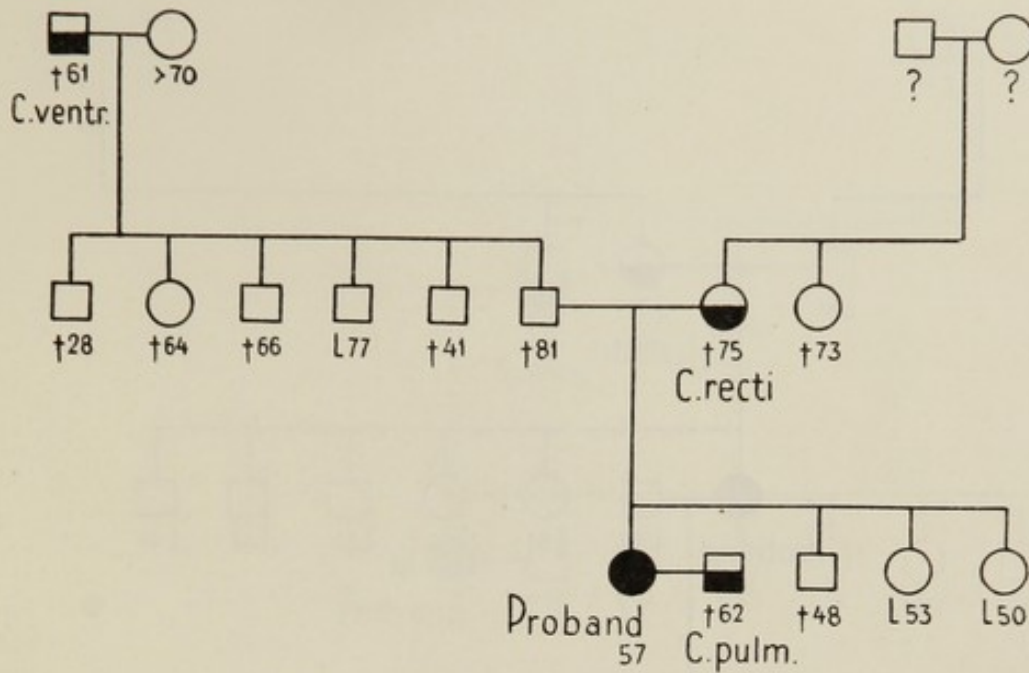


Pedigree 97.

PROBAND (Radium Center, Copenhagen; no. 29211).—○, born in Copenhagen May 28th, 1906. ∞ cabinet maker. Menstruation from fourteenth to thirty-sixth year, regular. One childbirth. Nursed nine months. Tumor in the right breast noticed six months before admission. Jan. 12th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

MOTHER.—Born in Vordingborg Jan. 8th, 1883. ∞ cabinet maker. Died in the Bispebjerg Hospital (service A), Copenhagen, June 14th, 1936, of cancer of the stomach. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born in Copenhagen Dec. 30th, 1846. Carpenter. Died 1919, in the Frederiksberg Hospital, Copenhagen, of cancer of the esophagus. The diagnosis verified by death certificate.

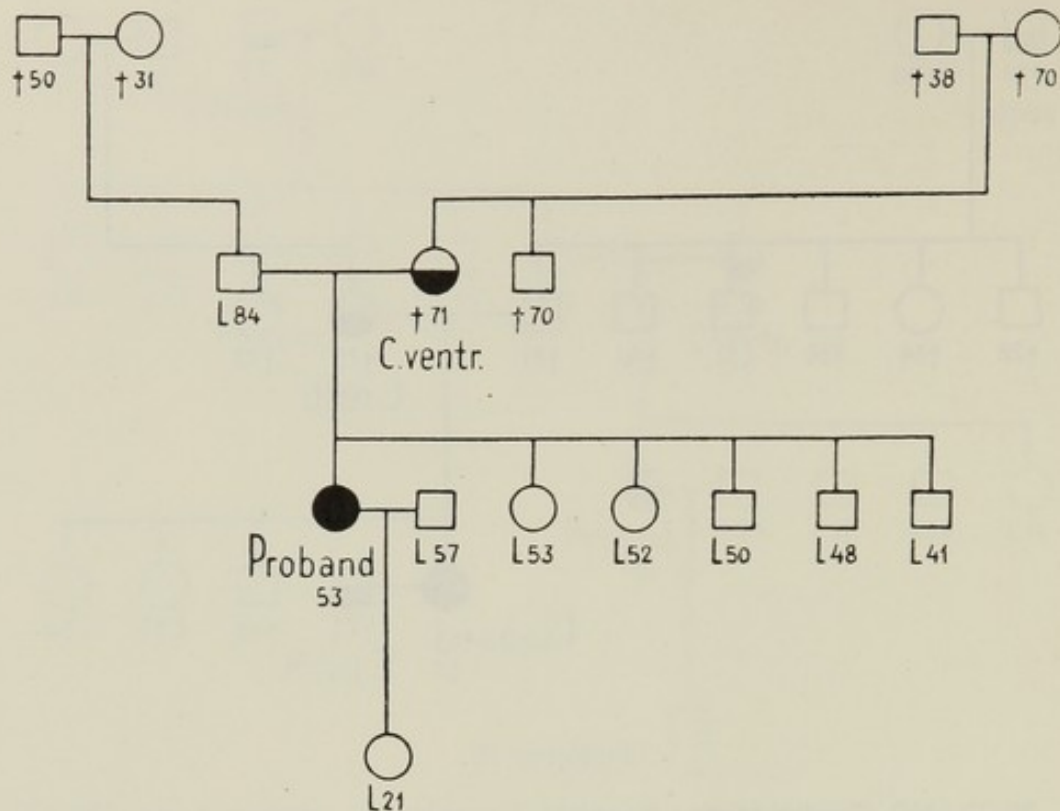


Pedigree 98.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 228/42). —○, born in Copenhagen Oct. 17th, 1885. Bicycle dealer's widow. Formerly well, with exception many years' suffering from rheumatic pains. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Never pregnant. In November 1941, she fell while riding in a tram and hurt her right breast against the edge of a seat. No pain or swelling following the injury, but a month afterwards she noticed that the nipple of the breast was getting retracted, and a hard lump below it. Jan. 14th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous carcinoma.

MOTHER.—Born in Copenhagen Jan. 18th, 1861. ∞ baker. Died Apr. 27th, 1936, of cancer of the rectum. The diagnosis verified by Dr. Otto Møller (private clinic), Copenhagen.

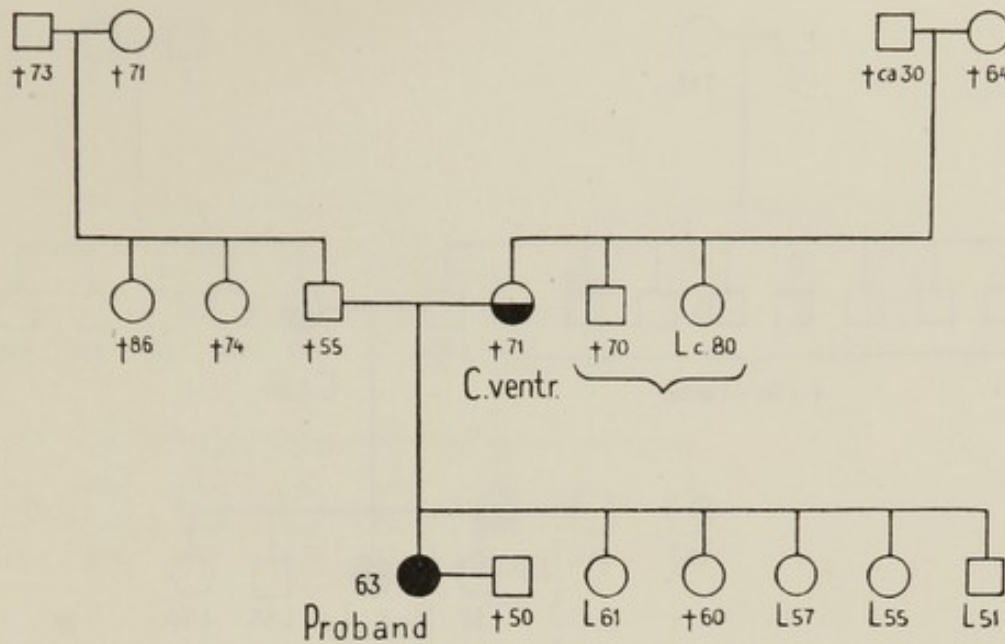
FATHER'S FATHER.—Born in Aalborg Jan. 11th, 1832. Died Oct. 26th, 1893, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 99.

PROBAND (Deaconesses' Hospital, Copenhagen; service B, no. 171/42).—  
 ○, born in Copenhagen Oct. 21st, 1888. ∞ masseur. Formerly well. Menstruation from fifteenth to forty-fifth year, regular. Menopause normal. One childbirth. Did not nurse, owing to hypogalactia. In 1924, operated on for appendicitis and retroflexion of the uterus. Tumor in the right breast noticed ten years before admission. For nine years it did not grow larger and did not cause any discomfort, but as it in the last year rapidly increased in size, and there at the same time had come some stitchy pains in the breast, she finally sought medical advice. Jan. 23rd, 1942, ablation of the breast. Histologic diagnosis: solid carcinoma.

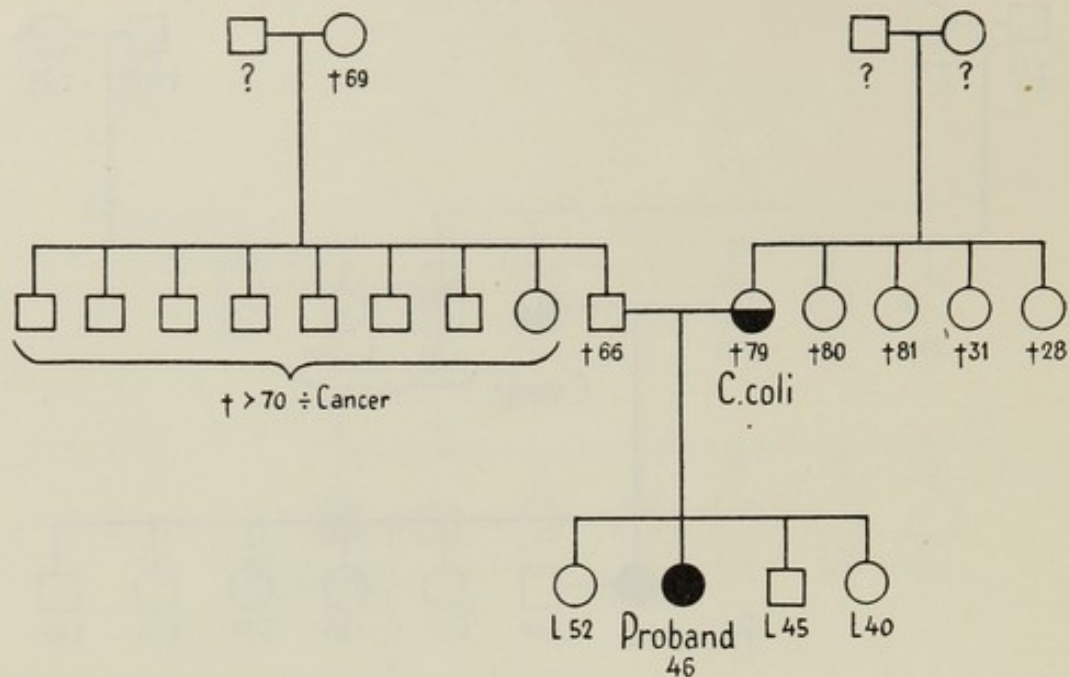
MOTHER.—Born in Roskilde Feb. 18th, 1864. ∞ naval architect. Died in Copenhagen Aug. 25th, 1935, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 100.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1186/42).—  
 ○, born in Næstved June 3rd, 1879. Restaurant-keeper's widow. Menstruation from fifteenth to forty-third year, regular. Menopause normal. Never pregnant. In 1923 treated in the same hospital for fibroma of the uterus, and the supravaginal portion of the latter resected. The tumor in the left breast first noticed four days before admission. Ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid and scirrhus carcinoma.

MOTHER.—Born Nov. 6th, 1856. ∞ stone cutter. Died in Copenhagen Dec. 22nd, 1927, of cancer of the stomach. The diagnosis verified by death certificate.

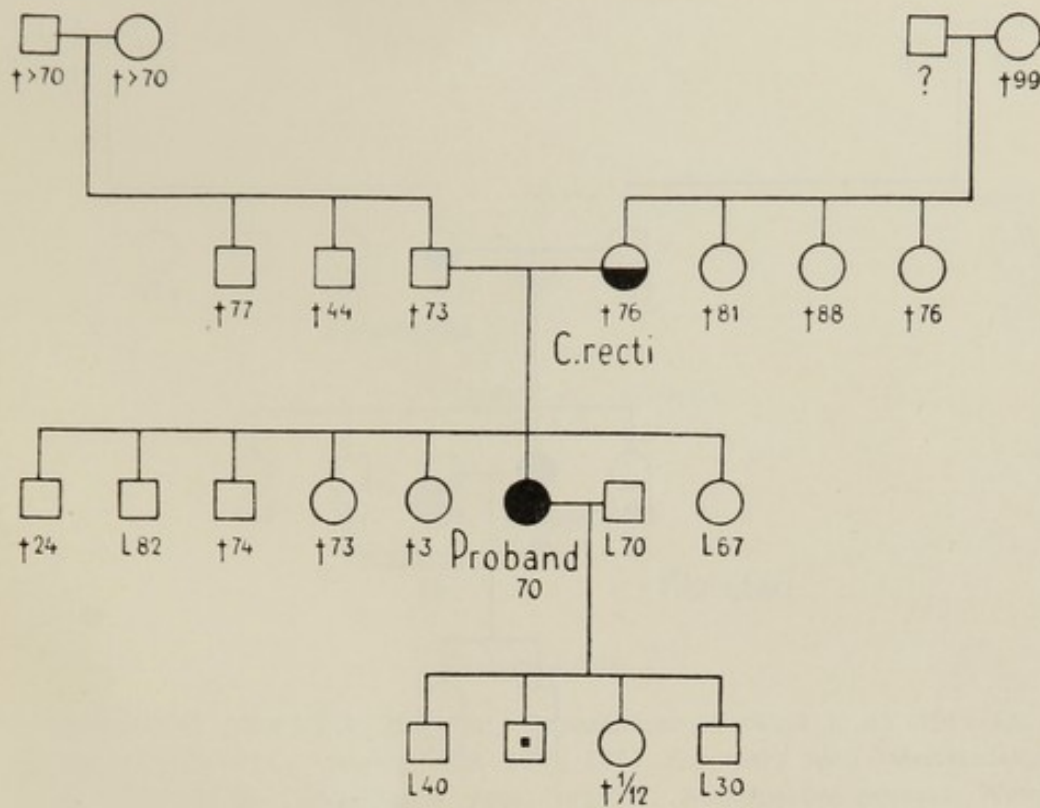


Pedigree 101.

PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Copenhagen Feb. 22nd, 1892. Housekeeper; single. Formerly well. Menstruation from thirteenth to forty-eight year, regular. Menopause normal. Never pregnant. Tumor in right breast noticed two months before admission. Sep. 14th, 1938, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

MOTHER.—Born in Copenhagen July 28th, 1861. Widow. Died in Copenhagen 1941, of cancer of the colon. The diagnosis verified by death certificate.

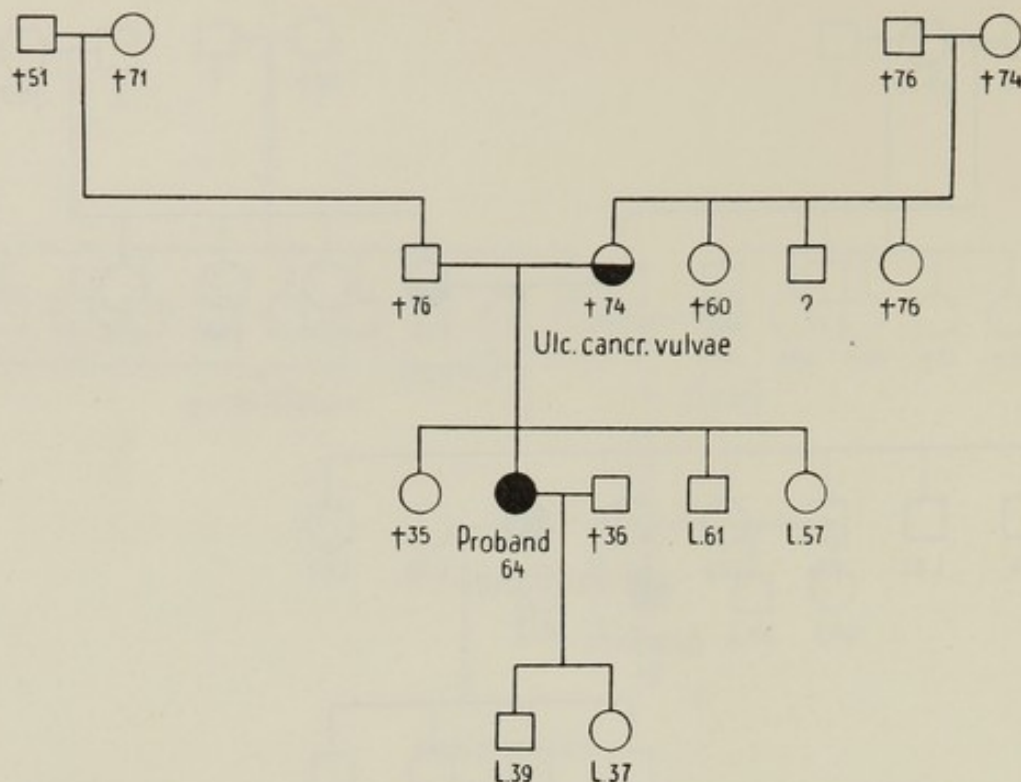




Pedigree 102.

PROBAND (Radium Center, Copenhagen; no. 31665).—○, born in Skive June 26th, 1873. ∞ old age pensioner. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Four childbirths; one child stillborn, another died 1 month old. Nursed the two others respectively two and four months. The tumor in the left breast noticed three days before admission. Trephine biopsy. Histologic diagnosis: scirrhus carcinoma.

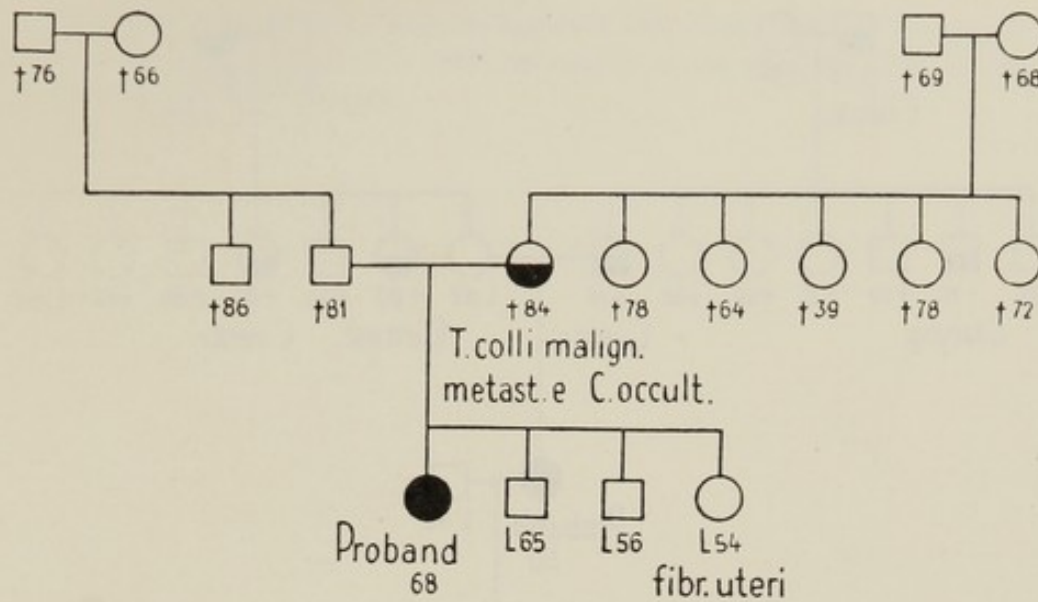
MOTHER.—Born 1837 in Skive. ∞ rural smallholder. In 1912 admitted to the Skive Hospital, for cancer of the rectum, where it was found that radical operation was impossible, and artificial anus therefore made. Died in Højslev Sep. 1913.



Pedigree 103.

PROBAND (Radium Center, Copenhagen; no. 30046).—○, born in Odense March 22nd, 1879. ∞ engineer. During twenty-five years treated for chronic rheumatic polyarthritis and chronic bronchitis. Menstruation from fourteenth to fiftieth year. In 1927, abrasion of uterine mucosa, for menorrhagia. Two normal pregnancies and childbirths. On both occasions normal lactation for about a year. For seven or eight years occasional slight, clear secretion from the nipple of the right breast, for which she sought medical advice and thereafter has been under constant observation for cancer; but only when retraction of the nipple was noticed was a lump felt underneath it. Trepine biopsy resulted in the diagnosis of solid cancer.

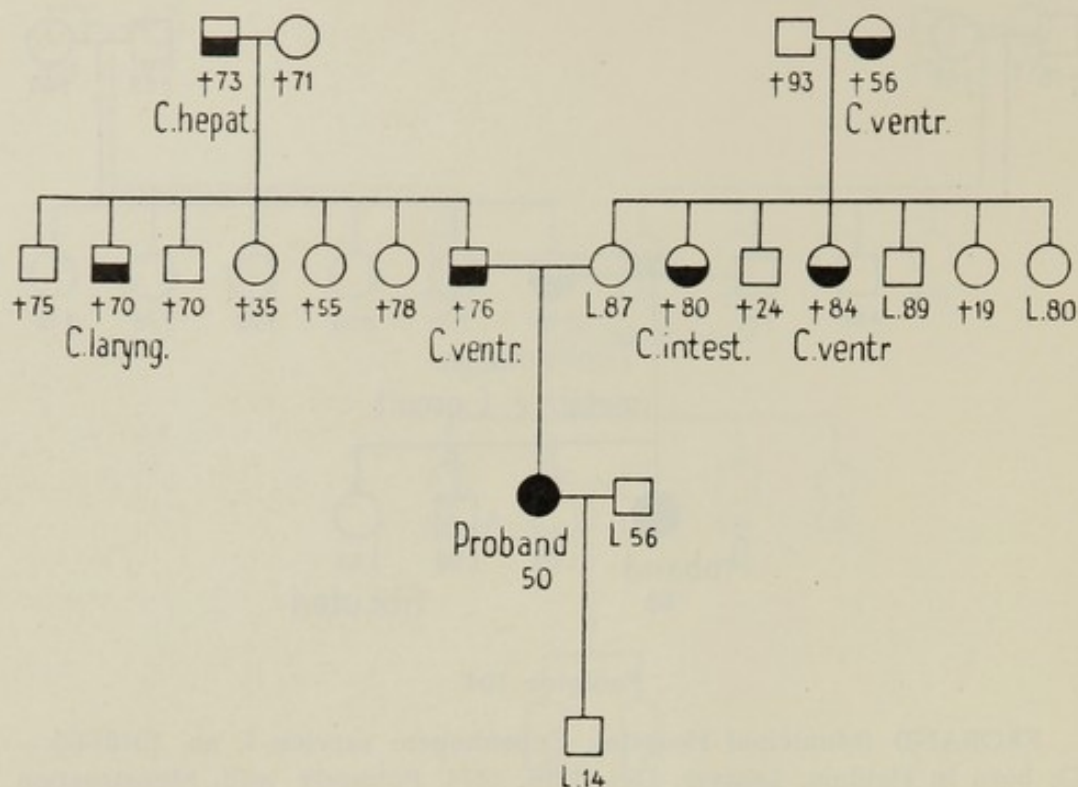
MOTHER.—Born in Langesø Nov. 28th, 1874. ∞ factory manager. Died of old age Feb. 23rd, 1921. Cancer wound in the groin. The diagnosis, according to the death certificate: cancerous ulcer of the vulva.



Pedigree 104.

FROBAND (Municipal Hospital, Copenhagen; service I, no. 1918/42).—  
 ○, born in Heldum, Lemvig, Oct. 13th, 1874. Formerly well. Menstruation  
 from fifteenth to forty-eighth year, regular. Menopause normal. Never  
 pregnant. Lump in left breast noticed a month before admission. Ablation  
 of the breast, with evacuation of the axilla. Histologic diagnosis: solid,  
 partly adenomatous cancer.

MOTHER.—Born in Flynder June 7th, 1846. ∞ farmer. Died in Heldum  
 July 15th, 1930, of malignant tumor of the uterine cervix, metastasis from  
 occult cancer. The diagnosis verified by death certificate.



Pedigree 105.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 877/42).—○, born in Holbæk June 8th, 1892. ∞ civil engineer. Menstruation since twelfth year, in the last two years copious and irregular. In Dec. 1940, abrasion of uterine mucosa; repeated Apr. 10th, 1942, owing to recurrence. Histologic diagnosis: climacteric endometrium. One childbirth (forceps delivery). Nursed only three months, owing to hypogalactia. Tumor in left breast noticed ten days before admission. June 16th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid and adenomatous carcinoma.

FATHER.—Born in Kerteminde Nov. 28th, 1853. Cashier. Died in Holbæk May 21st, 1933, of cancer of the stomach. The diagnosis verified by death certificate.

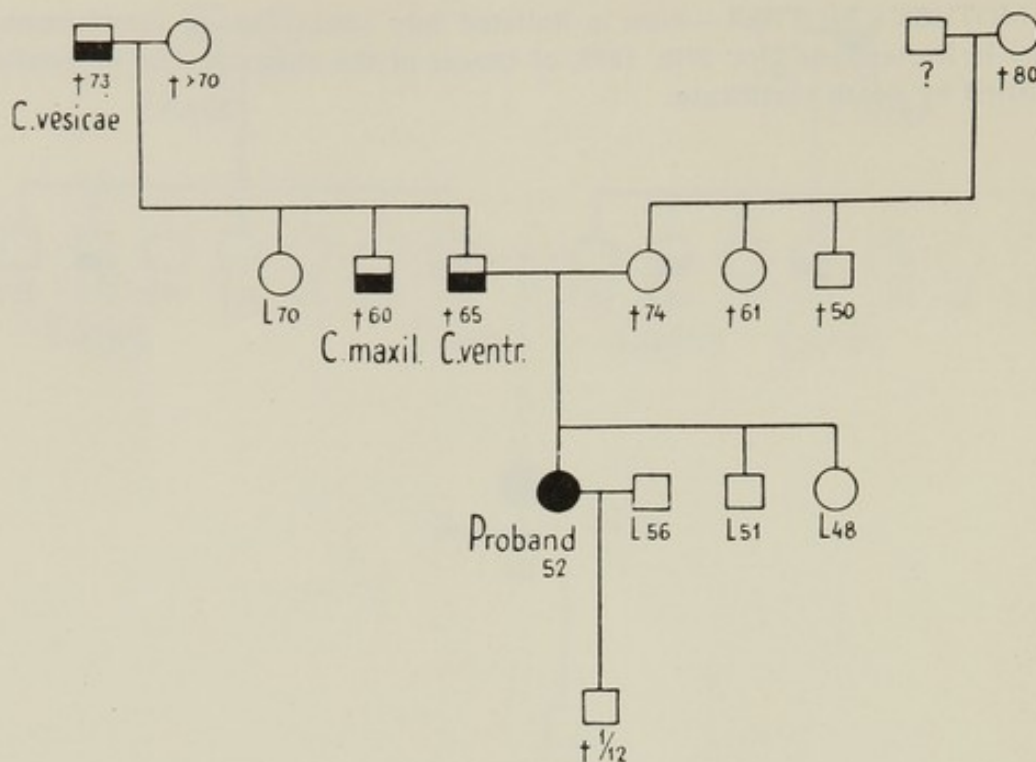
FATHER'S BROTHER.—Born in Kerteminde Aug. 4th, 1856. Saddler. Died in Copenhagen Aug. 14th, 1929, of cancer of the larynx. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born Apr. 23rd, 1816. Baker. Died in Copenhagen Sep. 13th, 1899, of cancer of the liver. The diagnosis verified by death certificate.

MOTHER'S ELDEST SISTER.—Born in Kerteminde Oct. 30th, 1840. ∞ sea-captain. Died in Copenhagen Aug. 31st, 1921, of intestinal cancer. The diagnosis verified by death certificate.

MOTHER'S NEXT ELDEST SISTER.—Born in Kerteminde May 16th, 1851. Died in Odense Sep. 26th, 1936, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born in Rolsted July 22nd, 1819. ∞ foundryman. Died in Kerteminde Oct. 27th, 1875, of cancer of the stomach. The diagnosis verified by death certificate.



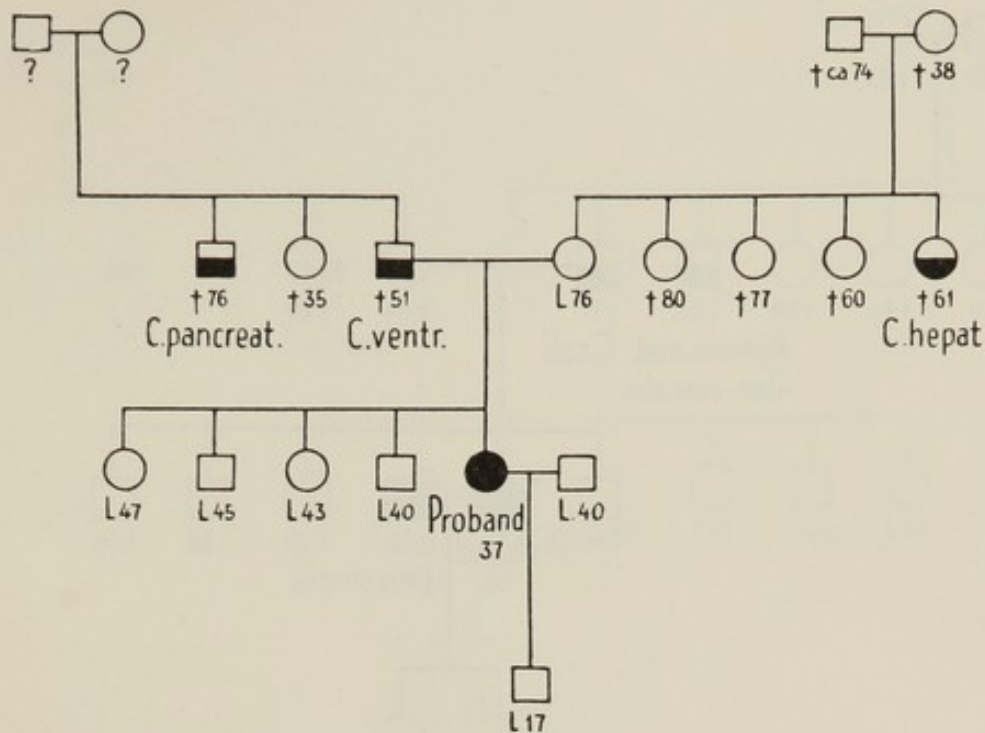
Pedigree 106.

PROBAND (Radium Center, Copenhagen; no. 25598).—○, born in Copenhagen Aug. 23rd, 1889. ∞ commercial agent. Menstruation from fourteenth to fifty-third year, regular. Menopause normal. One childbirth; the baby lived only five days. In 1935 operated on in St. Joseph's Hospital, Copenhagen, for cholelithiasis. The tumor in the left breast noticed three months before present admission to hospital. Aug. 24th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Stege July 15th, 1861. Wholesale merchant. Died in Copenhagen March 15th, 1926, of cancer of the stomach. The diagnosis verified by death certificate.

FATHER'S FATHER.—Born in Stege Apr. 9th, 1835. Provision dealer. Died in Copenhagen March 23rd, 1909, of cancer of the bladder. The diagnosis verified by death certificate.

FATHER'S BROTHER.—Since early youth domiciled in England. Died there, at the age of 60, according to the information received by the family of cancer of the maxilla, for which he had for twelve years been treated with roentgen after it had been found that an attempted radical operation could not be carried through.



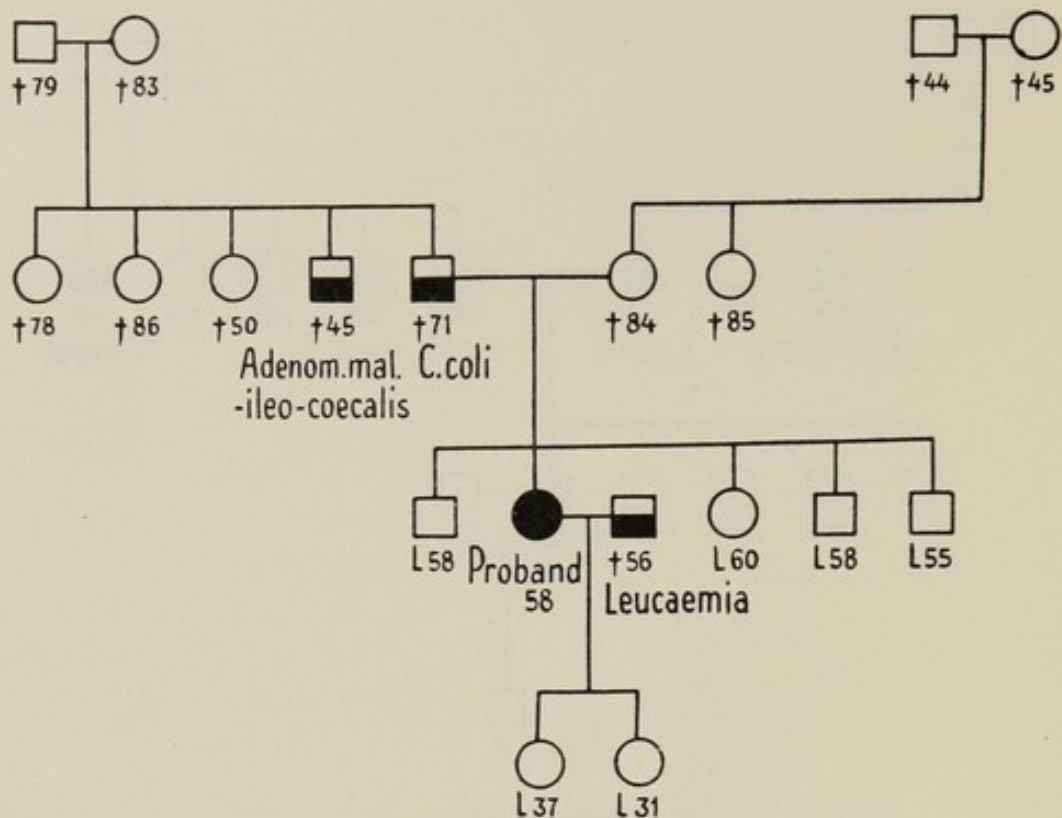
Pedigree 107.

PROBAND (Sundby Hospital, Copenhagen; surg. service. J. no. 2126/42).  
 —○, born in Copenhagen Aug. 2nd, 1905. ∞ cabinet maker. Three times rheumatic fever; no complications from the heart. Menstruation since fourteenth year, regular. One childbirth. Nursed seven months. Tumor in the left breast noticed two weeks before admission. Aug. 24th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Elsinore Apr. 24th, 1865. Sanitary-service workman. In March 1916, treated in the Bispebjerg Hospital, Copenhagen, service A, for cancer of the stomach. Died in Copenhagen June 14th, same year. The diagnosis of cancer verified by death certificate.

FATHER'S BROTHER.—Born in Asminderød March 8th, 1847. Shipyard workman. Died in Elsinore Hospital March 20th, 1923, of cancer of the pancreas. The diagnosis verified by death certificate.

MOTHER'S YOUNGEST SISTER.—Born in Saunte Sep. 19th, 1874. Died in Esbønderup Hospital Sep. 11th, 1936, of cancer of the liver. The diagnosis verified by death certificate.



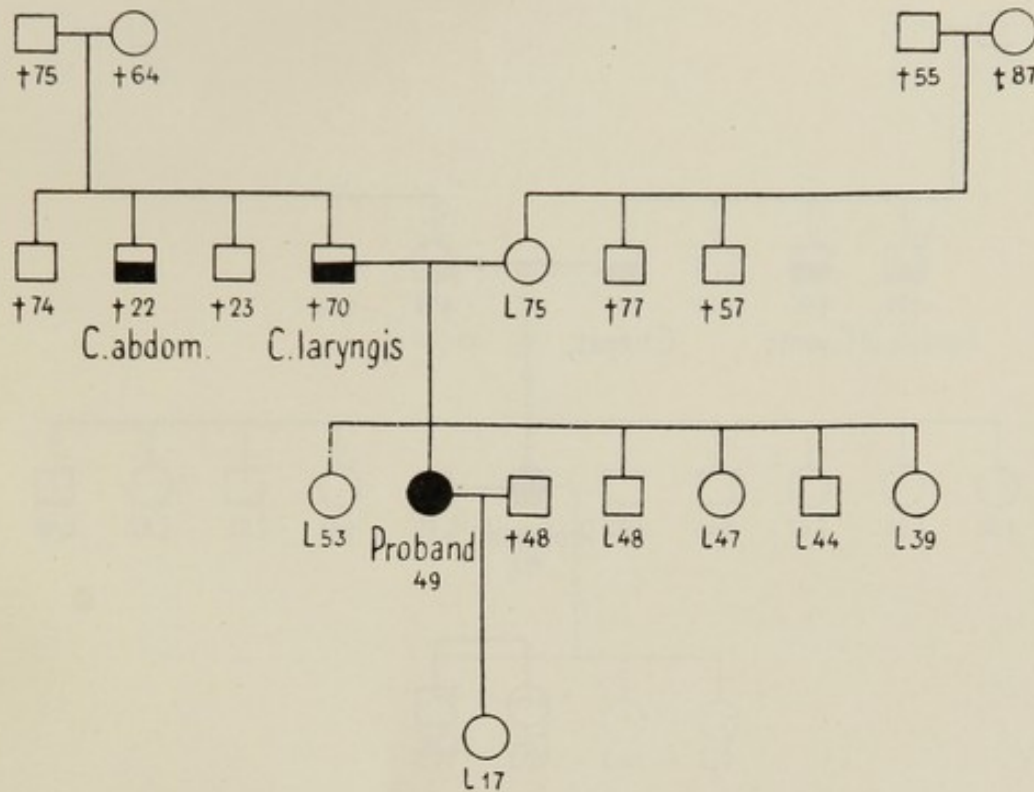
Pedigree 108.

PROBAND (Radium Center, Copenhagen; no. 19879).—○, born in Copenhagen Jan. 21st, 1881. Housepainter's widow. Formerly well. Menstruation from fourteenth to fifteenth year, regular. Menopause normal. Two child-births. Nursed the first child eight months, the second only two months, owing to hypogalactia. Four and a half years before admission she had fallen while riding her bicycle, and had hurt her left breast badly against the handle-bar, resulting in strong swelling and large extravasations. The tumor in the breast was first noticed about six months before admission. June 1939, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma. In 1943 increasing lumbar pains, and roentgen examination showed metastases to the lumbar portion of the spine.

FATHER.—Born in Aarhus March 23rd, 1853. Office assistant. Died in the Bispebjerg Hospital, Copenhagen, Jan. 11th, 1925, of cancer of the colon. The diagnosis verified by death certificate.

FATHER'S BROTHER.—Born 1860 in Aarhus. Head clerk. In 1905 operated on in St. Joseph's Hospital, Copenhagen, for malignant ileocecal adenoma (Journal no. 619/05). Died 1906 in Gentofte, of cancer of the colon.



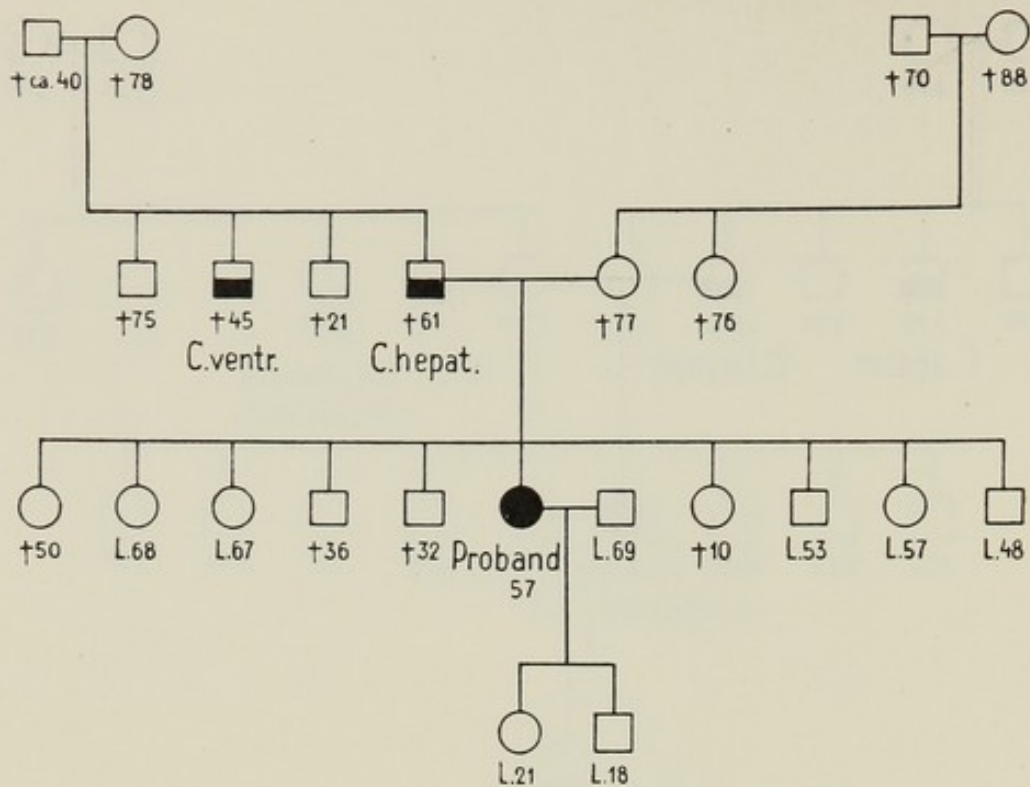


Pedigree 109.

PROBAND (Radium Center, Copenhagen; no. 25331).—○, born in Sorø May 2nd, 1892. Widow. Menstruation from fifteenth to forty-eighth year, regular. Menopause normal. One childbirth. Nursed ten months. A year before admission she hurt her right breast severely against the handle-bar of a bicycle, resulting in swelling and extravasation, which did not disappear until after two weeks. The tumor in the breast noticed nine months before admission. Trepine biopsy. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Copenhagen March 6th, 1856. Contractor. Died in Copenhagen July 8th, 1926, of cancer of the larynx. The diagnosis verified by death certificate.

FATHER'S NEXT ELDEST BROTHER.—Born 1863 in Sorø. Business manager. Died in Sorø June 15th, 1885, of cancer of the abdomen. The diagnosis verified by death certificate.

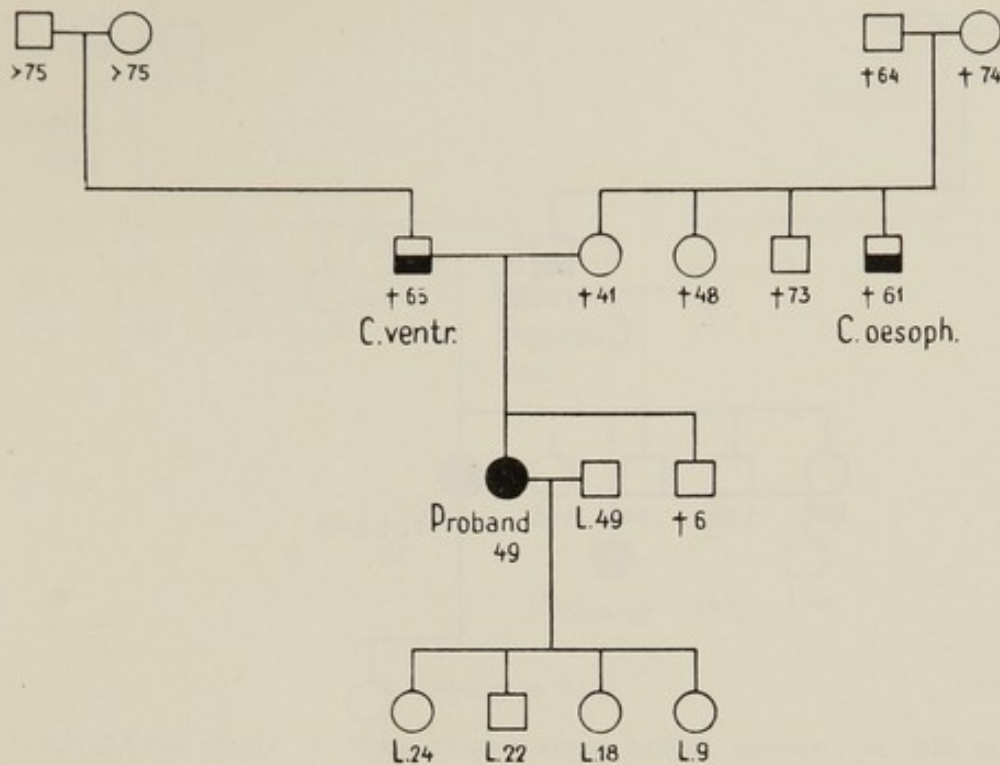


Pedigree 110.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 511/42).—  
 ○, born in Copenhagen Dec. 13th, 1884. ∞ cabinetmaker. Menstruation  
 from fifteenth to forty-seventh year, regular. Menopause normal. Two child-  
 births. Nursed respectively six and eight months. For several years pain  
 in left breast. Did not herself notice any tumor, but went to the surgical  
 policlinic of the State Hospital for advice, and at examination there a tumor  
 the size of a hen's egg was found. June 17th, 1942, ablation of the breast,  
 with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born 1850. Restaurant-keeper. Died in St. Joseph's Hospital,  
 Copenhagen, July 7th, 1911; according to the hospital journal (no. 1395/11)  
 of cancer of the liver.

FATHER'S BROTHER.—Born 1853 in Copenhagen. Died in St. Joseph's  
 Hospital, Copenhagen, Jan. 25th, 1898, of cancer of the stomach. The diag-  
 nosis verified by the hospital journal.

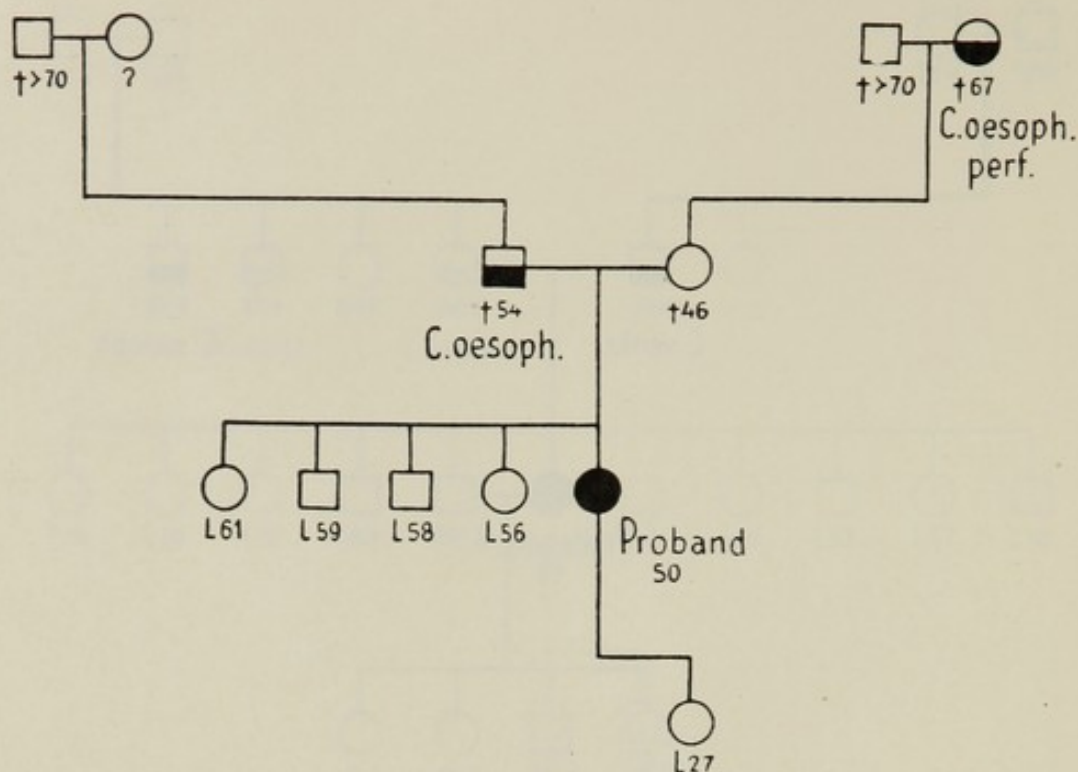


Pedigree 111.

PROBAND (Radium Center, Copenhagen; no. 28328).—○, born in Hobro Oct. 20th, 1893. ∞ furniture dealer. Menstruation from fifteenth to forty-ninth year, regular. Climacterial troubles, with headaches and hot flushes. Four childbirths. Nursed respectively six, eight, eleven and three months. In 1937, she fell down some stairs, and in falling hurt her right breast against the bannister. No extravasation. The tumor in the breast first noticed two months before admission. Aug. 29th, 1942, Trephine biopsy. Histologic diagnosis: solid carcinoma.

FATHER.—Born 1838 in Hobro. Land-owner. Died 1903 in Lerbjerg, near Randers, after about a year's illness, during which time there had been increasing attacks of stenosis and icterus. According to the statement of the treating physician, death was due to malignant tumor of the stomach. Diagnosis: cancer of the stomach.

MOTHER'S BROTHER.—Born 1872 in Hobro. Shoemaker. Died in the Municipal Hospital, Copenhagen, Feb. 7th, 1933, of cancer of the esophagus. The diagnosis verified by the journal of the hospital (journal no. 7812).

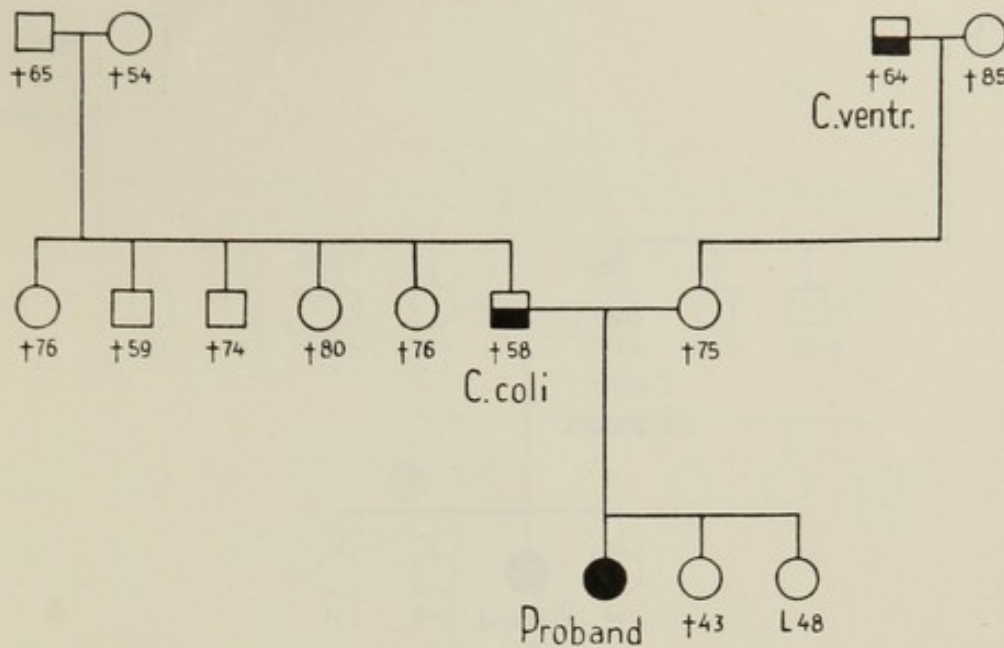


Pedigree 112.

PROBAND (Radium Center, Copenhagen; no. 27928).—○, born in Nyborg July 7th, 1892. Weaveress, single. Formerly well. Menstruation from fourteenth to forty-seventh years, regular. Menopause normal. One childbirth. Nursed only a few days, owing to hypogalactia. Remembers that twenty-eight years ago she hurt her left breast by falling against a stone post. The tumor in the breast noticed nine months before admission. Sep. 29th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid medullary carcinoma.

FATHER.—Born in Kalundborg July 4th, 1854. Engine driver. Died in the Frederiksberg Hospital, Copenhagen, Nov. 7th, 1908, of cancer of the esophagus. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born 1831. ∞ ship's carpenter. Died in the Municipal Hospital, Copenhagen, Apr. 24th, 1898, of perforated cancer of the esophagus. The diagnosis verified by the necropsy journal of the hospital.

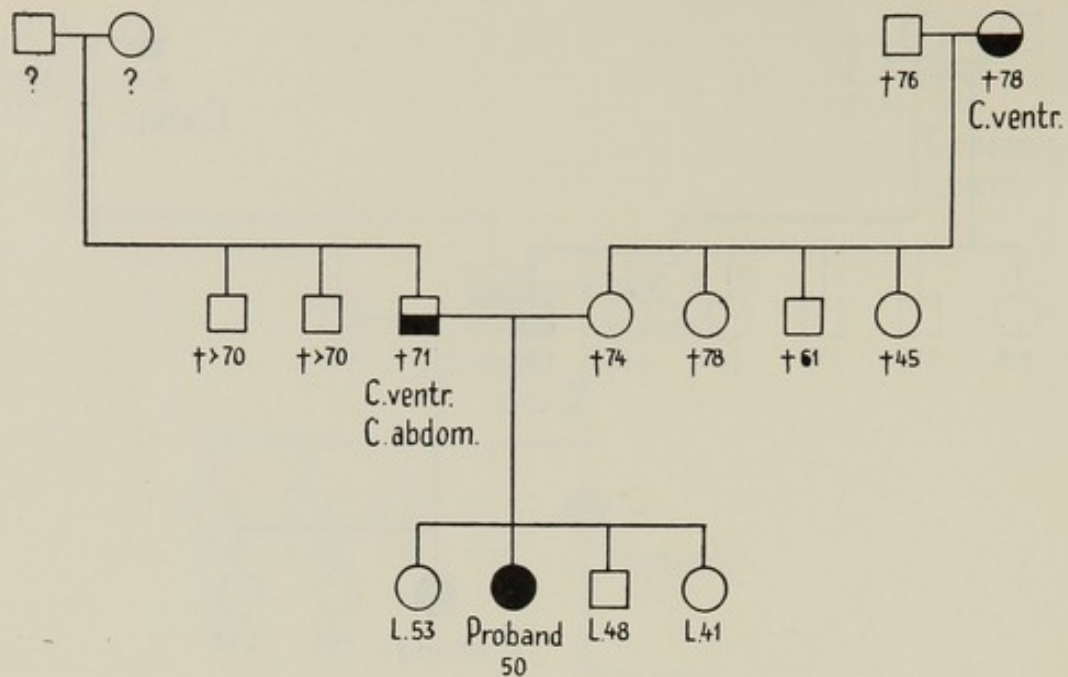


Pedigree 113.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 349/42).—  
 ○, born in Copenhagen Nov. 9th, 1887. Dressmaker, single. Formerly well.  
 Menstruation from fifteenth to forty-eight year, regular. Menopause normal.  
 Never pregnant. Tumor in right breast first noticed two weeks before  
 admission. May 25th, 1942, ablation of the breast, with evacuation of the  
 axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Copenhagen June 2nd, 1856. Baker. Died in the  
 Sundby Hospital, Copenhagen, Aug. 31st, 1914, of cancer of the colon. The  
 diagnosis verified by death certificate.

MOTHER'S FATHER.—Born 1822. Sergeant major. Died in Copenhagen  
 Apr. 2nd, 1886, of cancer of the stomach. The diagnosis verified by death  
 certificate.

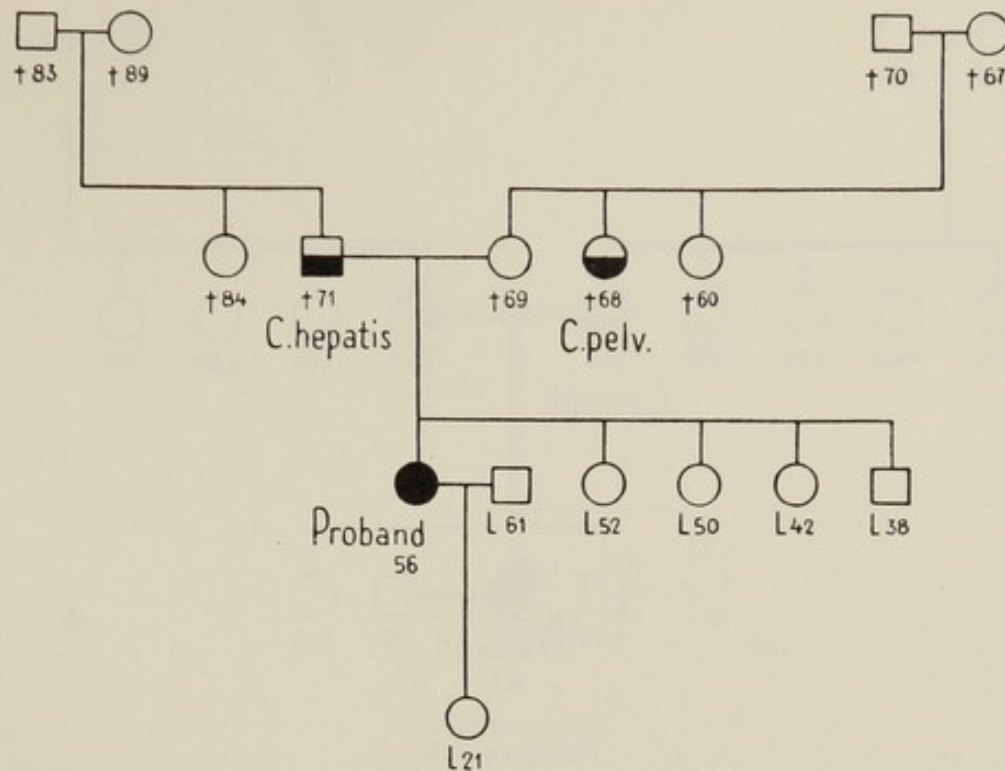


Pedigree 114.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 124/42).—  
 ○, born in Copenhagen Feb. 1st, 1892. Business manageress; single. Formerly well. Menstruation since thirteenth year, regular. In the last two years subject to headaches, dizziness and hot flushes, for which she has for over six months been treated with estibilin tablets (dose 1 mg. twice daily). Never pregnant. Tumor in right breast noticed a month before admission. Feb. 12th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma in fibrosis of the breast.

FATHER.—Born in Copenhagen Sep. 11th, 1864. Pensioner. Died in Copenhagen Feb. 24th, 1936, of cancer of the stomach and abdomen. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born 1826 in Bandholm. Fisherman's widow. Died in Copenhagen Oct. 20th, 1907, of cancer of the stomach. The diagnosis verified by death certificate.

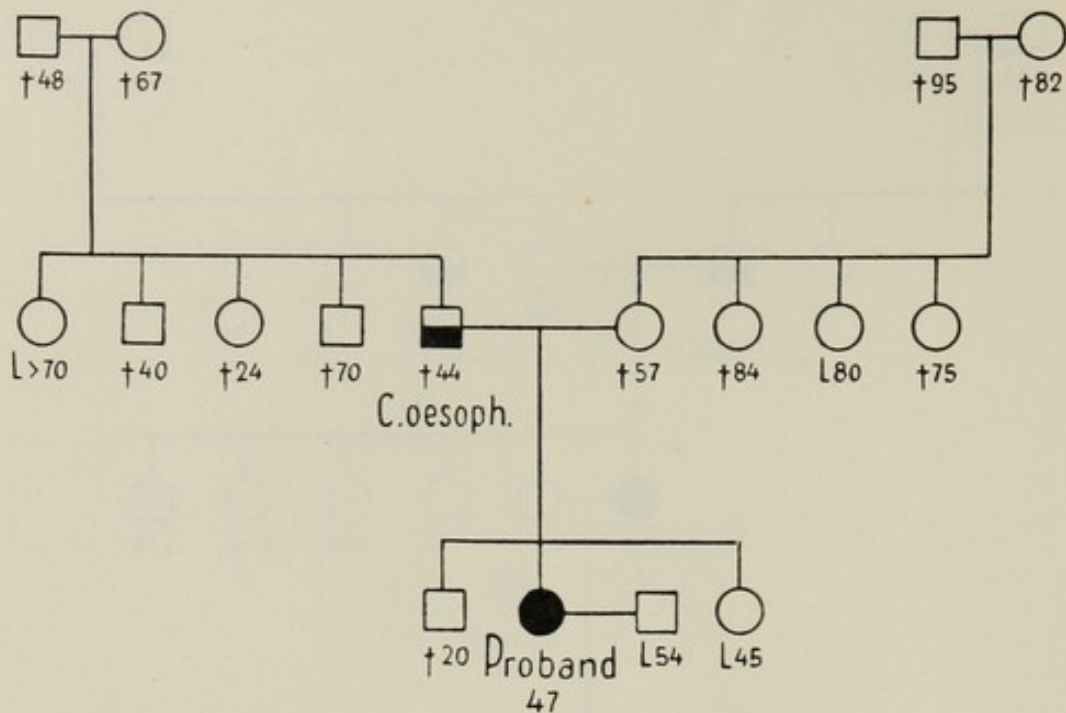


Pedigree 115.

PROBAND (Radium Center, Copenhagen; no. 30252).—○, born in Copenhagen May 18th, 1886. ∞ head railway-porter. Menstruation from seventeenth to fifty-second year, regular. Menopause normal. One childbirth. Nursed only four weeks, owing to hypogalactia. Tumor in right breast noticed nine months before admission. Trephine biopsy. Histologic diagnosis: adenocarcinoma and solid carcinoma.

FATHER.—Born in Rye May 1st, 1860. Policeman. Died in Copenhagen Nov. 26th, 1931, of cancer of the liver. The diagnosis verified by death certificate.

MOTHER'S SISTER.—Born in Aulum Jan. 27th, 1870. ∞ janitor. Died in Copenhagen Nov. 13th, 1938, of cancer of the pelvis. The diagnosis verified by death certificate.

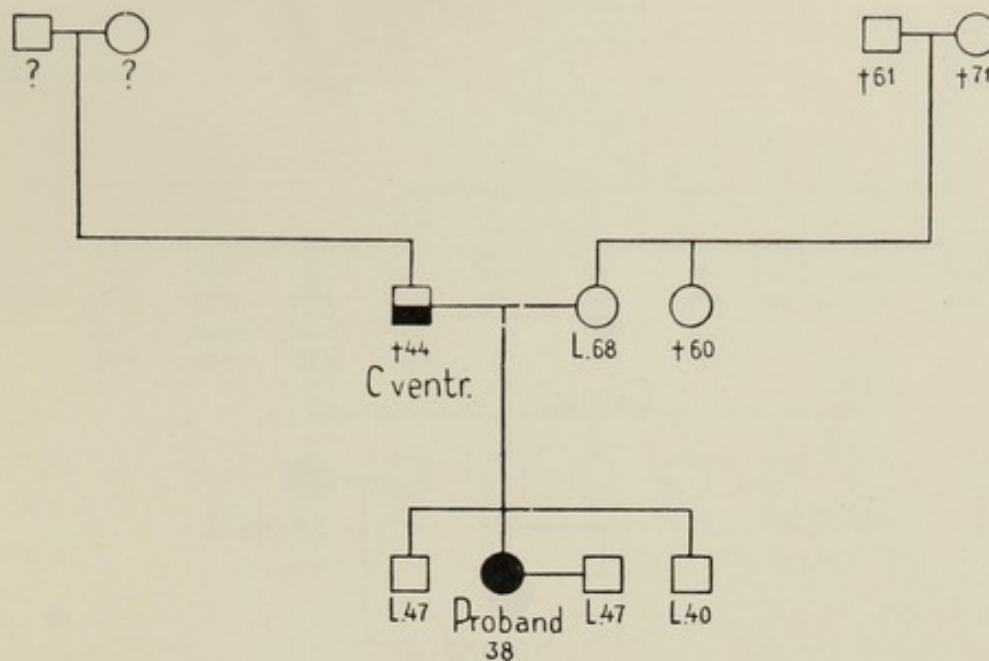


Pedigree 116.

PROBAND (Radium Center, Copenhagen; no. 30474).—○, born in Kristianstad, Sweden, July 7th, 1895. ∞ tinsmith. Frail since birth; congenital luxation of the hip. In 1924 treated in the Nakkebølle Sanatorium for tuberculosis of left lung. Menstruation from thirteenth to forty-third year, regular. Menopause normal. Never pregnant. A year before admission to the Radium Center she had fallen and hurt her left breast against a piano. No tumefaction or extravasation. Four weeks before admission she noticed that pressure on the left breast caused a slight exudation of serous, bloody fluid from the nipple. Apr. 10th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: carcinoma.

FATHER.—Born in Kristianstad May 28th, 1866. Restaurant-keeper. Died 1910 in Kristianstad, after barely a year's illness, marked by increasing difficulty of deglutition. The treating physician stated to the proband that death was due to an inoperable, malignant tumor of the esophagus.

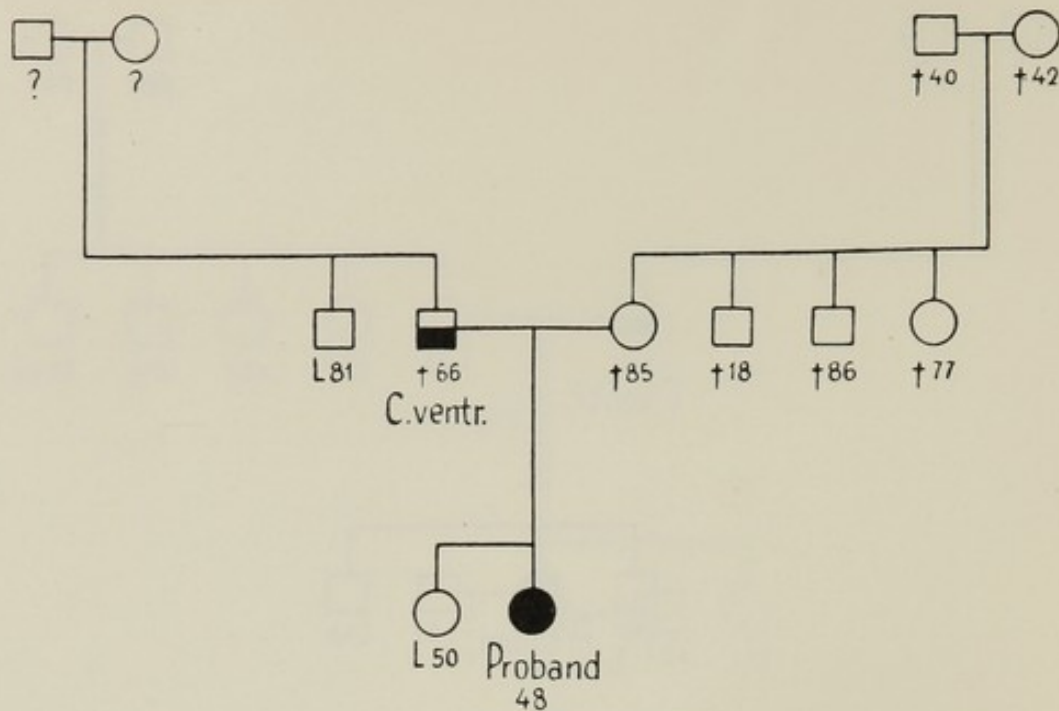




Pedigree 117.

PROBAND (Radium Center, Copenhagen; no. 16938).—○, born in Haderslev March 8th, 1899. ∞ confidential clerk. Menstruation from thirteenth to forty-second year. Never pregnant. In 1936, she noticed a small tumor in her left breast. A year afterwards it had not become larger, and was considered to be benign, but was nevertheless extirpated. The histologic diagnosis was carcinoma, and she was given roentgen treatment. In 1940, local recurrence and renewed roentgen treatment. In 1942, roentgenologically demonstrable metastases in the vertebral column.

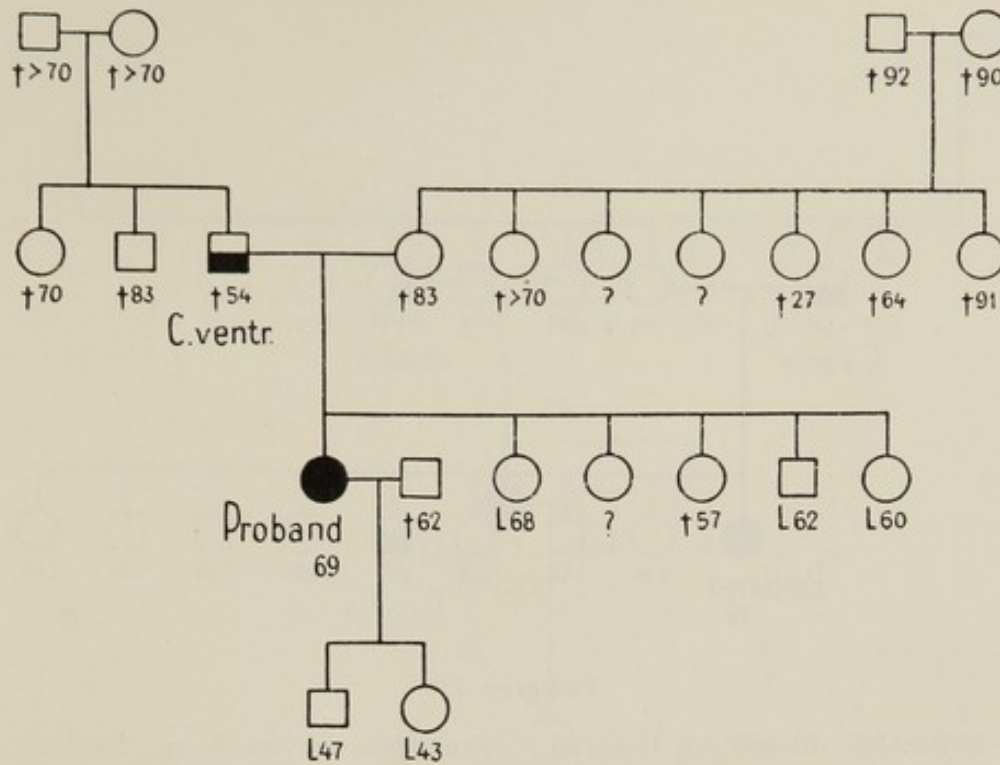
FATHER.—Born 1859 in Posen, Germany. Secretary. Died in Haderslev Feb. 4th, 1904, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 118.

PROBAND (Radium Center, Copenhagen; no. 30947).—○, born in Copenhagen Nov. 6th, 1895. Translatress; single. As child and young well. Menstruation from thirteenth to forty-fifth year; regular until she was forty-four, when the bleeding became irregular and very strong. A year later she was admitted to the Bispebjerg Hospital, suffering from menorrhagia, and as uterine fibroma was found she was operated on. Since then no bleeding. Never pregnant. In May-June, 1943, she was given 3 injections of ovex (10,000 I.U. each) on account of climacteric rises of temperature. Tumor in left breast noticed five days before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.

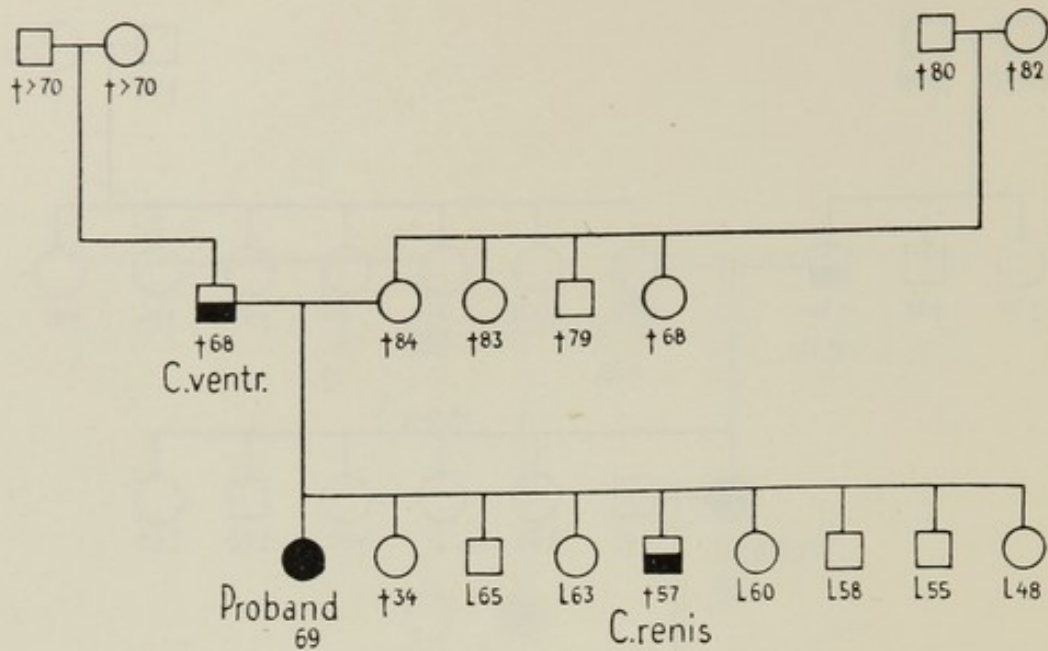
FATHER.—Born in Tillitze March 21st, 1864. Retired farmer. Died in the Bispebjerg Hospital, Copenhagen, Sep. 5th, 1931, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 119.

PROBAND (Bispebjerg Hospital, Copenhagen; service D, no. 1893/42).—  
 ○, born in Copenhagen Dec. 12th, 1872. Cigarmaker's widow. Formerly well.  
 Menstruation from fourteenth to fifty-second year, regular. Menopause  
 normal. Two childbirths. Lactation on both occasions normal. Four years  
 ago she had fallen while riding her bicycle, and had hurt her right breast,  
 but there had been no swelling or extravasation. The tumor in the breast  
 noticed ten days before admission. June 3rd, 1942, ablation of the breast,  
 with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Sindal Oct. 24th, 1845. Harnessmaker. Died in the  
 Municipal Hospital, Copenhagen, Nov. 22nd, 1899, of cancer of the stomach.  
 The diagnosis verified by death certificate.

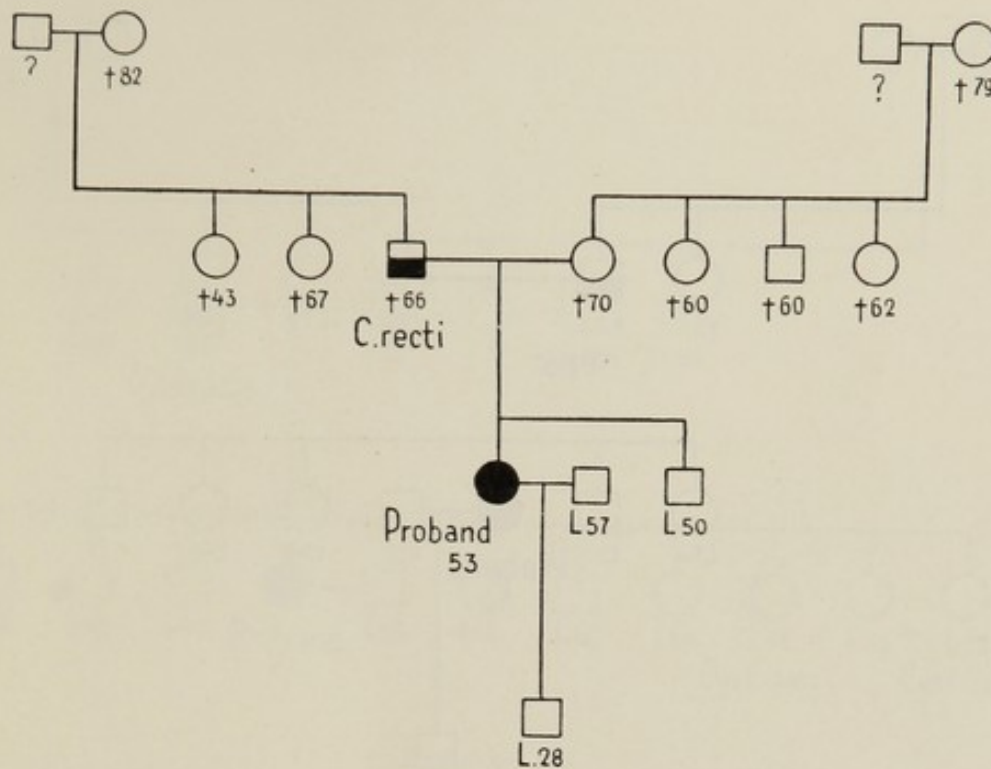


Pedigree 120.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 2203/43).—  
 ○, born in Houby by Fakse May 7th, 1873. Seamstress; single. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Never pregnant. Two years before admission she had hurt her left breast badly by falling against the edge of a table, but there had been neither swelling nor extravasation. The tumor in the left breast she had noticed a year before admission. May 27th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Fakse Oct. 19th, 1840. Workingman. Died in the Fakse Hospital Nov. 7th, 1908, of cancer of the stomach. The diagnosis verified by death certificate.

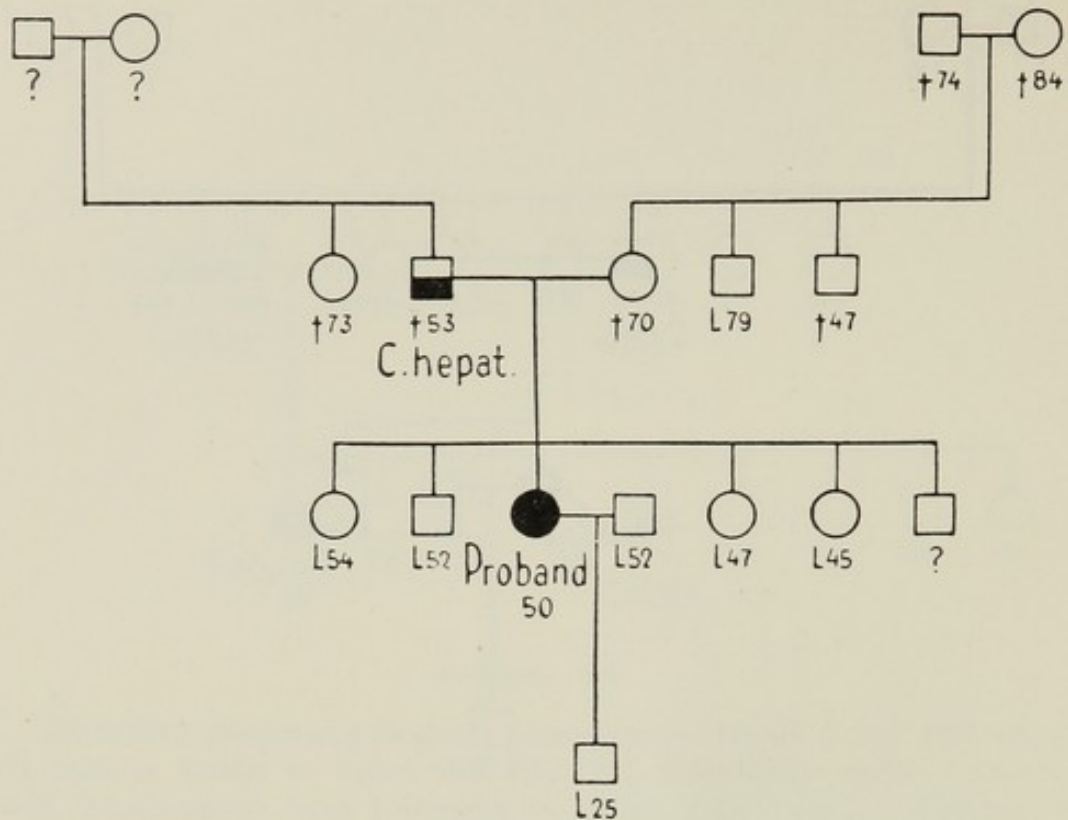
NEXT ELDEST BROTHER.—Born in Houby June 5th, 1880. Fundholder. Died in the Municipal Hospital, Copenhagen, May 7th, 1938, of cancer of the kidney. The diagnosis verified by death certificate.



Pedigree 121.

PROBAND (Bispebjerg Hospital, Copenhagen; service D, no. 3123/42).—  
 ○, born in Copenhagen Dec. 20th, 1889. ∞ blacksmith. Menstruation from  
 eighteenth to forty-eighth year, regular. Menopause normal. One child-  
 birth. Nursed about a year. The tumor in the left breast noticed eight  
 months before admission. Sep. 30th, 1942, ablation of the breast, with  
 evacuation of the axilla. Histologic diagnosis: solid carcinoma.

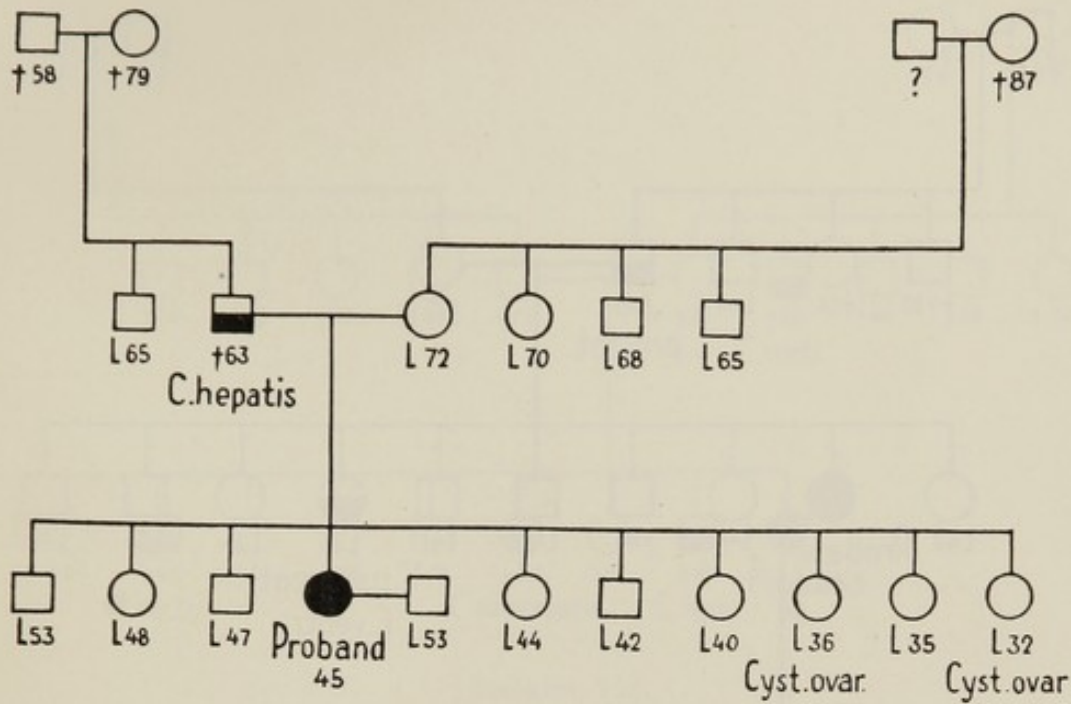
FATHER.—Born in Copenhagen Jan. 21st, 1867. Typographer. Died in  
 Copenhagen March 13th, 1934, of cancer of the rectum. The diagnosis  
 verified by death certificate.



Pedigree 122.

PROBAND (Bispebjerg Hospital, Copenhagen; service D, no. 2547/42).—  
 ○, born in Copenhagen July 1st, 1892. ∞ electrician. Menstruation from  
 fourteenth to fiftieth year, regular. One childbirth. Nursed barely three  
 months, owing to hypogalactia. The tumor in the right breast noticed a  
 week before admission. July 15th, 1942, ablation of the breast, with  
 evacuation of the axilla. Histologic diagnosis: solid carcinoma.

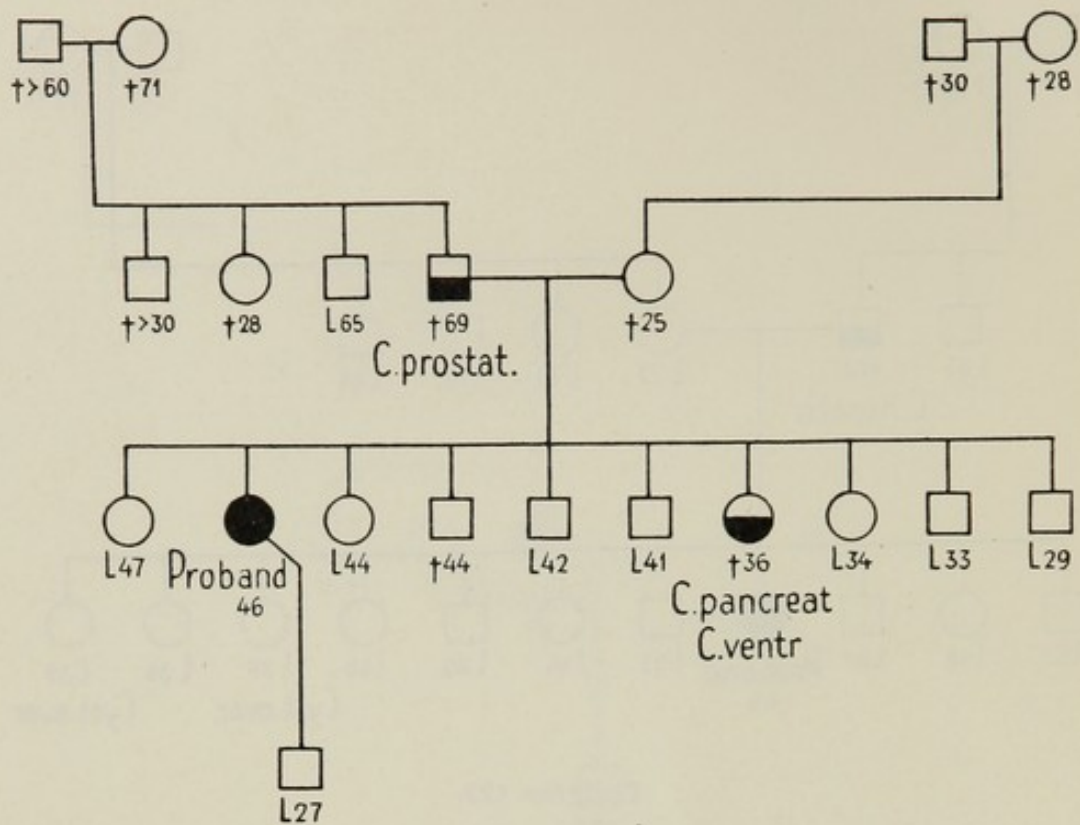
FATHER.—Born in Viksø May 19th, 1852. Watchman. Died in the  
 Municipal Hospital, Copenhagen, Feb. 17th, 1906, of cancer of the liver.  
 The diagnosis verified by the death register of the hospital.



Pedigree 123.

PROBAND (Radium Center, Copenhagen; no. 30363).—○, born in Esbjerg March 27th, 1898. ∞ commercial agent. Formerly well. Menstruation since fifteenth year, regular. Never pregnant. Had not herself noticed any tumor, but consulted physician owing to pricking pains in her left breast. Trephine biopsy. Histologic diagnosis: carcinoma.

FATHER.—Born in Vedersø Feb. 11th, 1863. Master carpenter. Died in the Haslev Hospital Jan. 26th, 1926, of cancer of the liver. The diagnosis verified by the hospital.



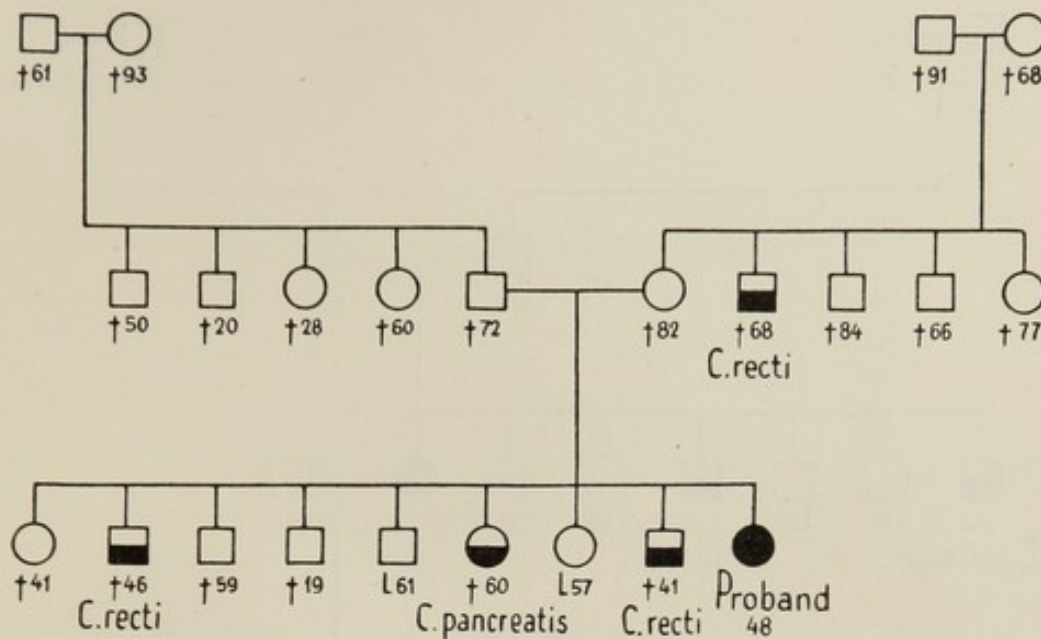
Pedigree 124.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 1453/43).—  
 ○, born in Snekkersten Jan. 4th, 1897. Single. As child well; now receiving  
 invalids' relief on account of nervous affection. Menstruation from thirteenth  
 to forty-fourth year, regular. Menopause normal. One childbirth. Nursed  
 only one month, for social reasons. Tumor in right breast noticed two  
 months before admission. Apr. 8th, 1943, ablation of the breast, with evacua-  
 tion of the axilla. Histologic diagnosis: solid carcinoma.

FATHER.—Born in Snekkersten March 4th, 1873. Fisherman. Died in  
 the Hillerød Hospital Nov. 5th, 1942, of cancer of the prostate. (Previously  
 treated at the Radium Center, Copenhagen; journal no. 27782).

NEXT YOUNGEST SISTER.—Born 1907 in Snekkersten. Waitress; single.  
 Died June 7th, 1943, in the Municipal Hospital, Copenhagen, of cancer of the  
 stomach. The diagnosis verified by the hospital.





Pedigree 125.

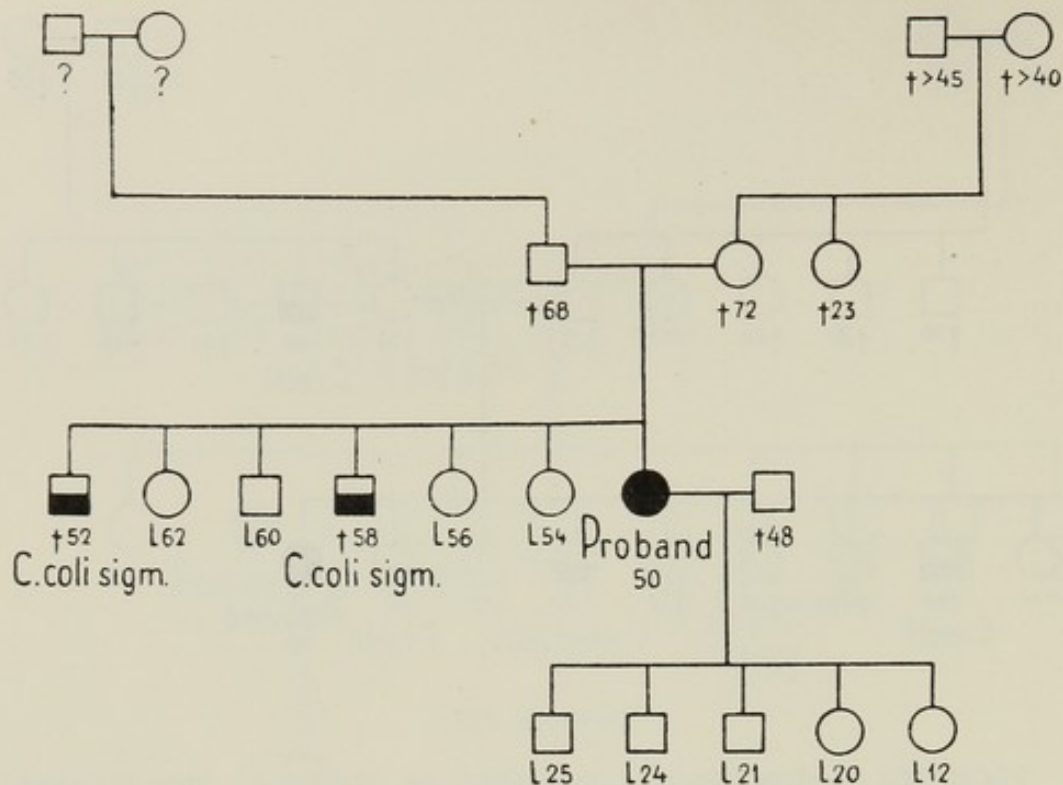
PROBAND (Radium Center, Copenhagen; no. 22487).—○, born in Viborg June 4th, 1892. Housekeeper; single. As child pleurisy, at twenty operated on for inflammation of the coccyx; otherwise formerly well. Menstruation since thirteenth year, regular. Never pregnant. The tumor in the left breast noticed a week before admission. July 29th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus carcinoma.

MOTHER'S ELDEST BROTHER.—Born 1854 in Viborg. Tailor. Died in Viborg Hospital Apr. 3rd, 1923, of cancer of the rectum. The diagnosis verified by the hospital.

ELDEST BROTHER.—Born in Viborg Feb. 8th, 1875. Cigar manufacturer. Died in Viborg Sep. 24th, 1921, of cancer of the rectum. The diagnosis verified by death certificate.

NEXT YOUNGEST SISTER.—Born in Viborg July 17th, 1883. ∞ sea-captain. Died in Aalborg Apr. 14th, 1944, of cancer of the pancreas. The diagnosis verified by death certificate.

YOUNGEST BROTHER.—Born in Viborg Feb. 12th, 1888. Lawyer. Died in Viborg Dec. 14th, 1929, of cancer of the rectum. The diagnosis verified by death certificate.

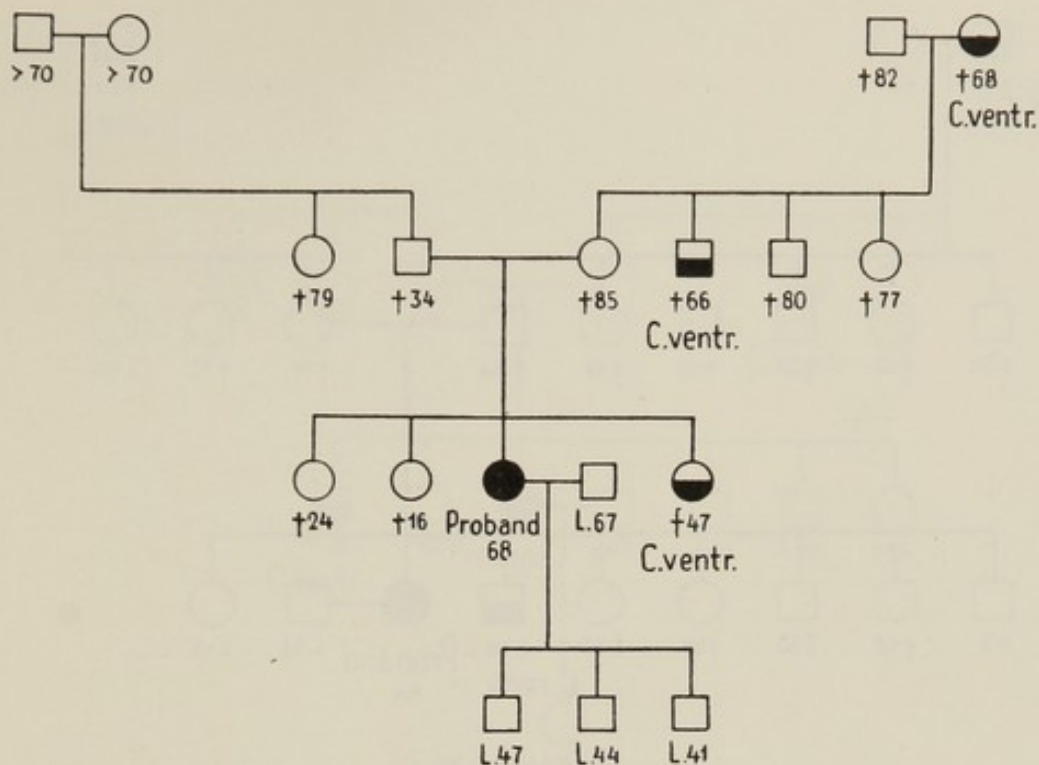


Pedigree 126.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 401/41).—  
 ○, born in Copenhagen Sep. 26th, 1891. Workingman's widow. Formerly  
 well. Menstruation from twelfth to fiftieth year, regular. Menopause normal.  
 Five childbirths. Nursed all the children. During the first lactation, twenty-  
 four years ago, galactophoritis of left breast, treated at home with warm  
 compresses. Tumor in the breast noticed five months before admission. Oct.  
 16th, 1941, ablation of the breast, with evacuation of the axilla. Histologic  
 diagnosis: solid carcinoma.

ELDEST BROTHER.—Born in Copenhagen Aug. 28th, 1880. Shopkeeper.  
 Died in the Bispebjerg Hospital, Copenhagen, March 1st, 1932, of cancer  
 of the sigmoid. The diagnosis verified by the hospital, service D.

YOUNGEST BROTHER.—Born in Copenhagen Jan. 8th, 1884. Working-  
 man. Died June 6th, 1942, of cancer of the sigmoid. The diagnosis verified  
 by death certificate.

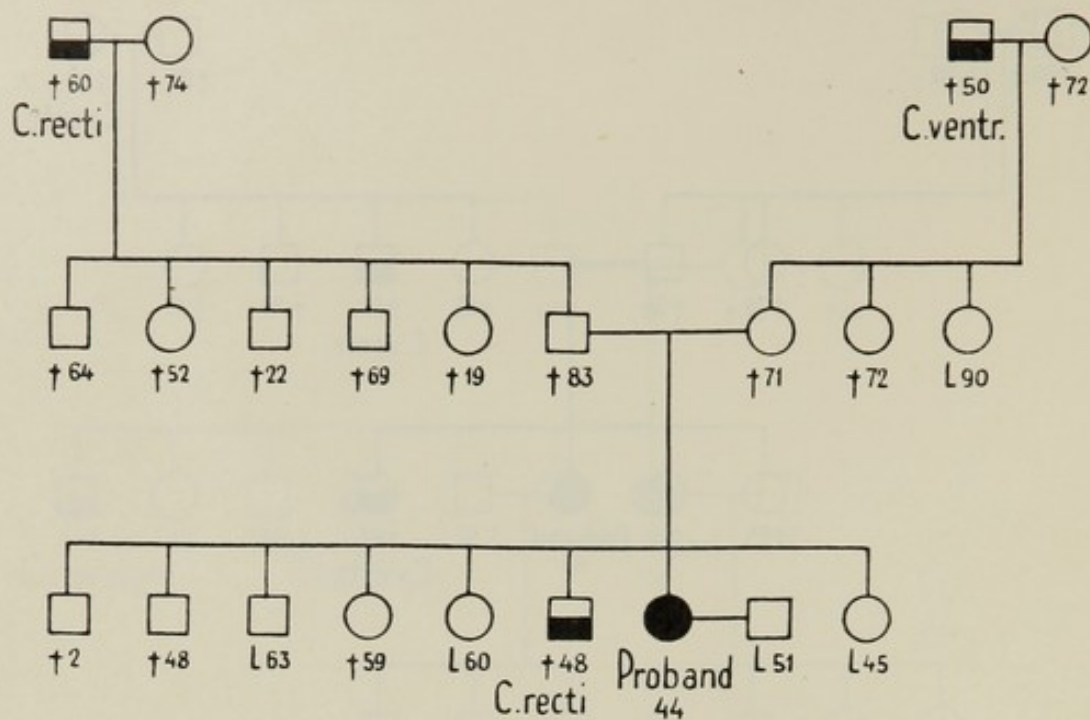


Pedigree 127.

PROBAND (Radium Center, Copenhagen; no. 31762).—○, born in Copenhagen Jan. 14th, 1875. ∞ old age pensioner. Menstruation from fifteenth to fifty-first year, regular. Menopause normal. Three normal pregnancies and childbirths. Did not nurse, owing to agalactia. Tumor in right breast noticed a week before she addressed herself to the Radium Center. Trephine biopsy. Histologic diagnosis: solid medullary carcinoma.

YOUNGEST SISTER.—Born March 6th, 1878. Died in Dr. Maaloe's clinic, Copenhagen, Jan. 23rd, 1926, of cancer of the stomach. The diagnosis verified by death certificate.

MOTHER'S MOTHER.—Born 1822 in Copenhagen. ∞ master mason, Brøndbyvester. Died Aug. 9th, 1890, after being ill for about a year with attacks of stenosis, increasing emaciation and icterus. According to the statement of the treating physician, it had been a case of stomach cancer with dissemination in the liver.



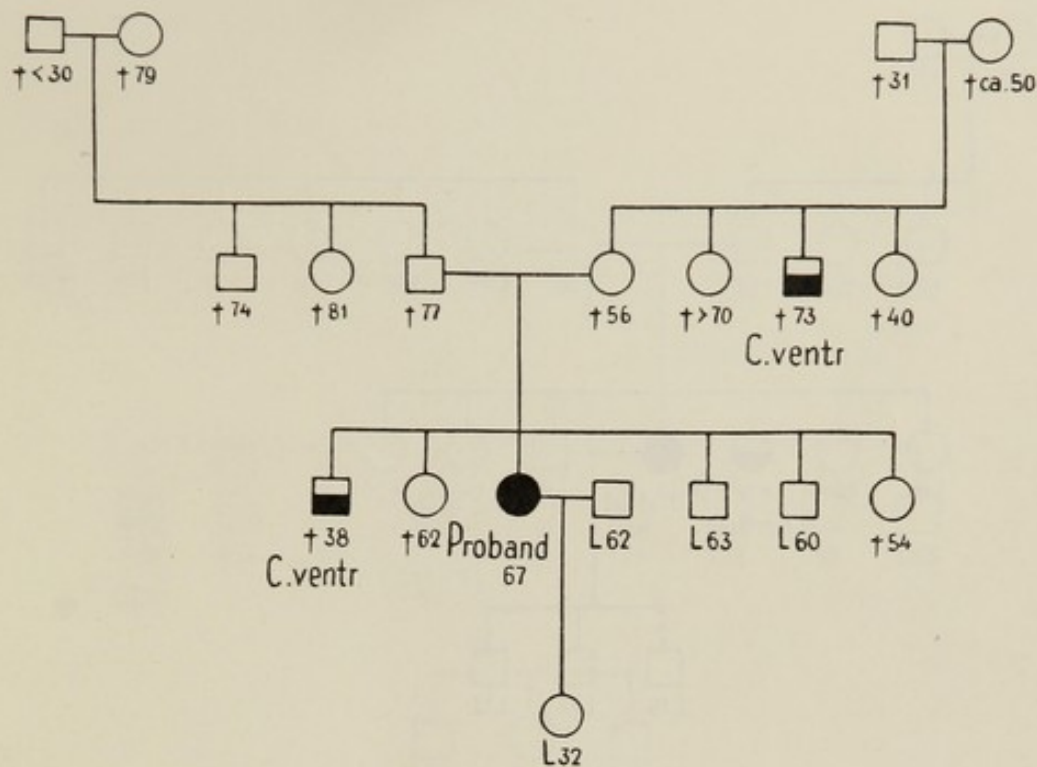
Pedigree 128.

PROBAND (Radium Center, Copenhagen; no. 20280).—○, born in Copenhagen Nov. 19th, 1895. ∞ bookkeeper. Formerly well. Menstruation from fourteenth to forty-fourth year, regular. Never pregnant. Tumor in left breast noticed about a month before admission. Nov. 13th, 1939, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous carcinoma.

FATHER'S FATHER.—Born Apr. 22nd, 1793. Clergyman. Died in Vivild Aug. 12th, 1853, of cancer of the rectum. The treating physician stated to the proband's father that death was due to cancer of the rectum.

MOTHER'S FATHER.—Born 1820 in Sweden. Innkeeper. Died 1870 in Vrigsted, Sweden, after about two years' illness beginning with dyspeptic symptoms, to which were later added signs of stenosis with frequent vomitings, several times with partly digested blood. In the last stage, icterus. Diagnosis: cancer of the stomach.

YOUNGEST BROTHER.—Born in Copenhagen Aug. 25th, 1885. Department manager. Died in Copenhagen June 4th, 1934, of cancer of the rectum. The diagnosis verified by death certificate.

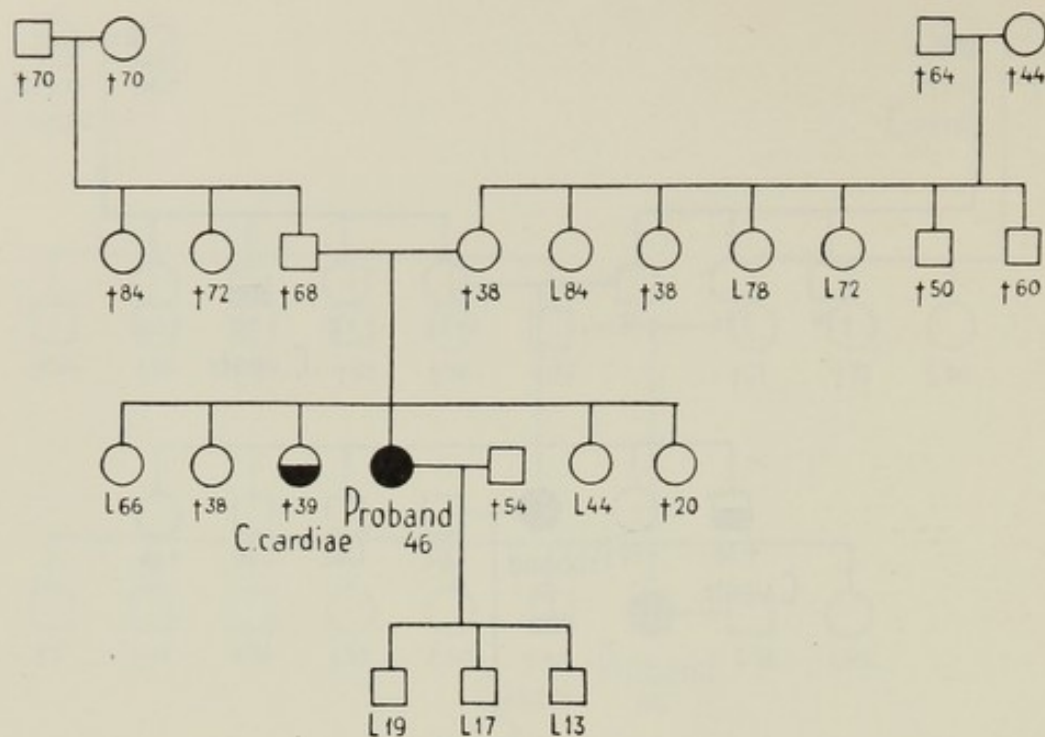


Pedigree 129.

PROBAND (Radium Center, Copenhagen; no. 23246).—○, born in Copenhagen Jan. 22nd, 1873. ∞ petrol-filling station man. Menstruation from fourteenth to forty-seventh year, regular. Menopause normal. One child-birth. Nursed fourteen months. At forty-eight diabetes mellitus, treated with insulin retard, 5 + 5 units. In 1939 admitted to the Bispebjerg Hospital, Copenhagen, for cholelithiasis; no surgical intervention. Six weeks before admission to the Radium Center she had noticed a hard lump in her right breast. Dec. 6th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus carcinoma.

ELDEST BROTHER.—Born in Copenhagen March 13th, 1872. Commercial agent. Died in the Municipal Hospital, Copenhagen, Apr. 20th, 1910, of cancer of the stomach. The diagnosis verified by the hospital.

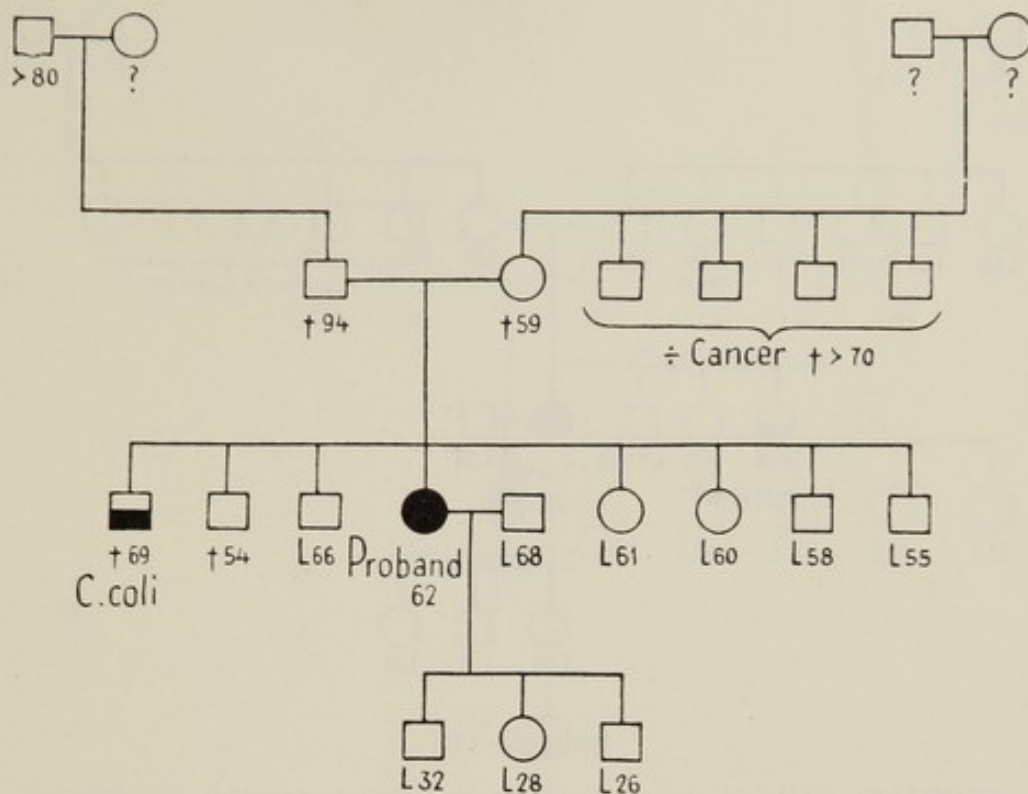
MOTHER'S BROTHER.—Born in Højslev Jan. 4th, 1852. Brickworks' laborer. Died in Skive Nov. 11th, 1925, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 130.

PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 946/42).—  
 ○, born in Copenhagen (Frederiksberg) May 20th, 1896. Civil engineer's  
 widow. Formerly well. Menstruation since fifteenth year, regular. Three  
 childbirths. Lactation normal. Tumor in right breast noticed six months  
 before admission. Nov. 9th, 1942, ablation of the breast, with evacuation  
 of the axilla. Histologic diagnosis: adenocarcinoma.

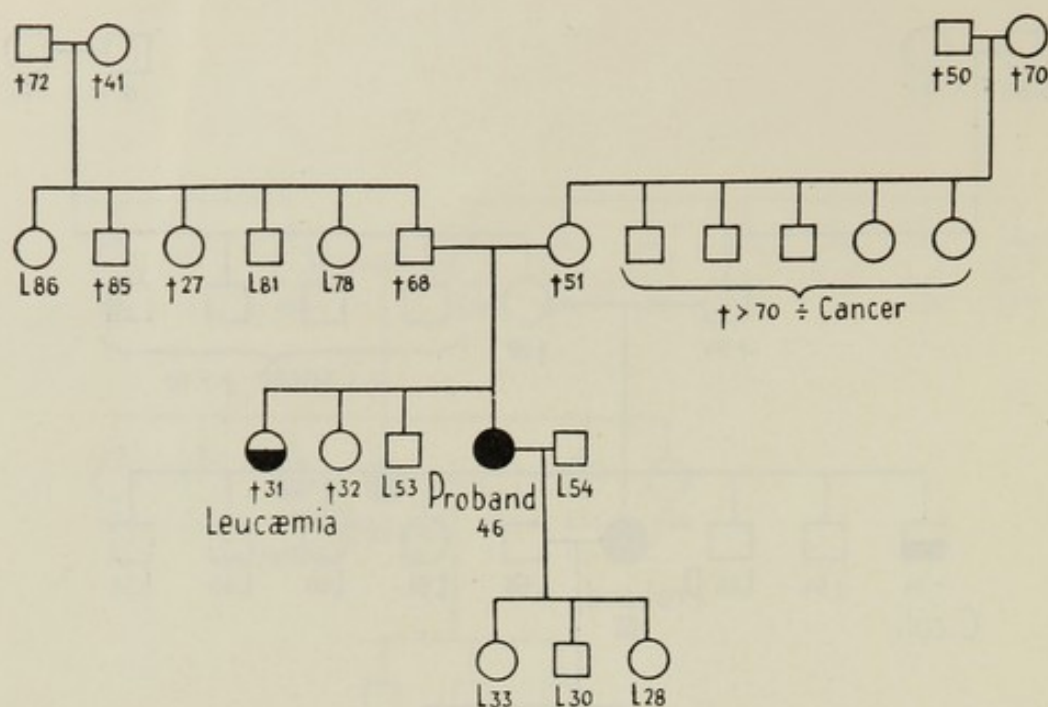
SISTER.—Born in Copenhagen Apr. 21st, 1889. ∞ provision merchant.  
 Died in the Frederiksberg Hospital, Copenhagen, Aug. 6th, 1928, of cancer  
 of the stomach. The diagnosis verified by death certificate.



Pedigree 131.

PROBAND (Municipal Hospital, Copenhagen; service 5).—○, born in Aalborg Jan. 12th, 1880. ∞ sea captain. Menstruation from fiteenth to fifty-eighth year, regular. Menopause normal. In 1931, operated on in the Municipal Hospital, service 5, for appendicitis. Three childbirths. Nursed all the children for over six months. Tumor in left breast noticed nine days before admission. Oct. 1st, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: primarily adenomatous carcinoma.

BROTHER.—Born in Aalborg Jan. 17th, 1873. Merchant. Died in Börnsen Bergdorff, Hamburg, Dec. 6th, 1942, presumably of cancer of the colon. It has not been possible to get the diagnosis verified by inquiry to the hospital, but according to statement of the proband's sister, who is a trained nurse, death was due to a malignant tumor which on operation was found to be inoperable.

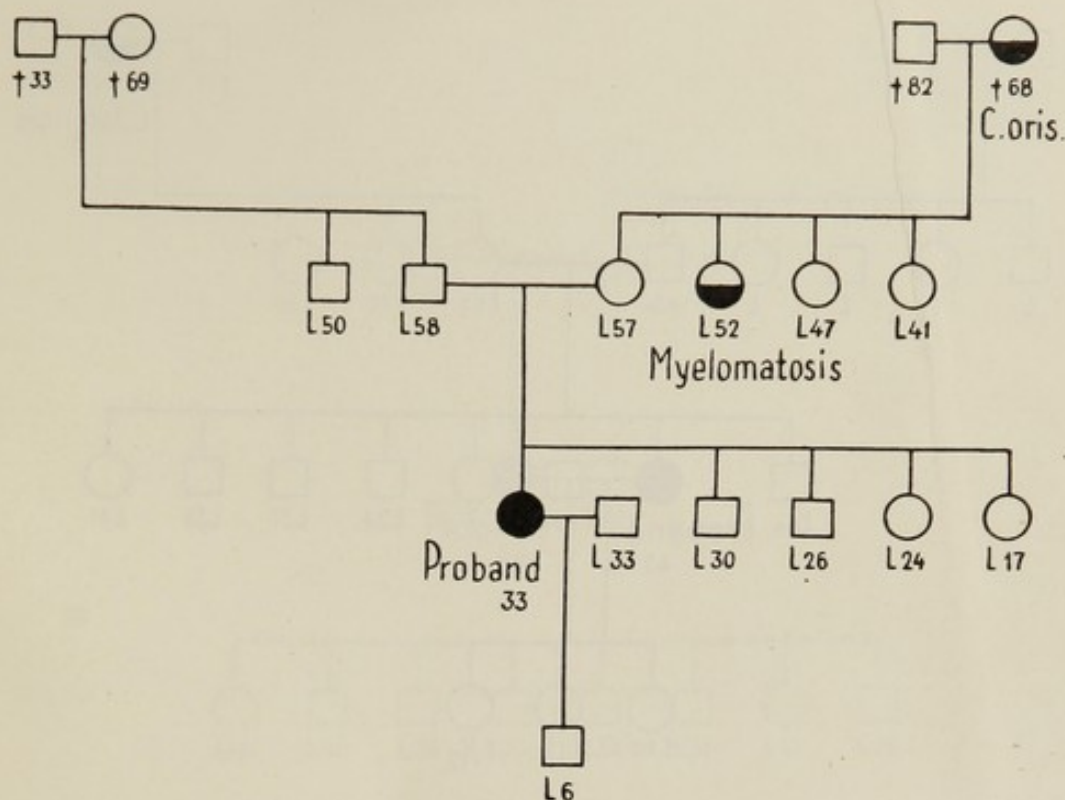


Pedigree 132.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 366/38).—  
 ○, born in Copenhagen Jan. 16th, 1892. Head laundress; divorced. Formerly well. Menstruation from sixteenth to forty-sixth year, regular. Menopause normal. Three childbirths. Nursed all the children for over six months. In 1927, she fell when riding her bicycle, and hurt her right breast against the handlebar. The tumor in the breast noticed about a month before admission. Sep. 23rd, 1938, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: carcinoma; fibrous mastitis. Aug. 4th, 1942, taken under treatment for metastases to bones.

ELDEST SISTER.—Born in Lemvig June 2nd, 1885. ∞ fisherman. Died in hospital in Vordinborg Dec. 23rd, 1916, of leukemia. The diagnosis verified by the hospital.



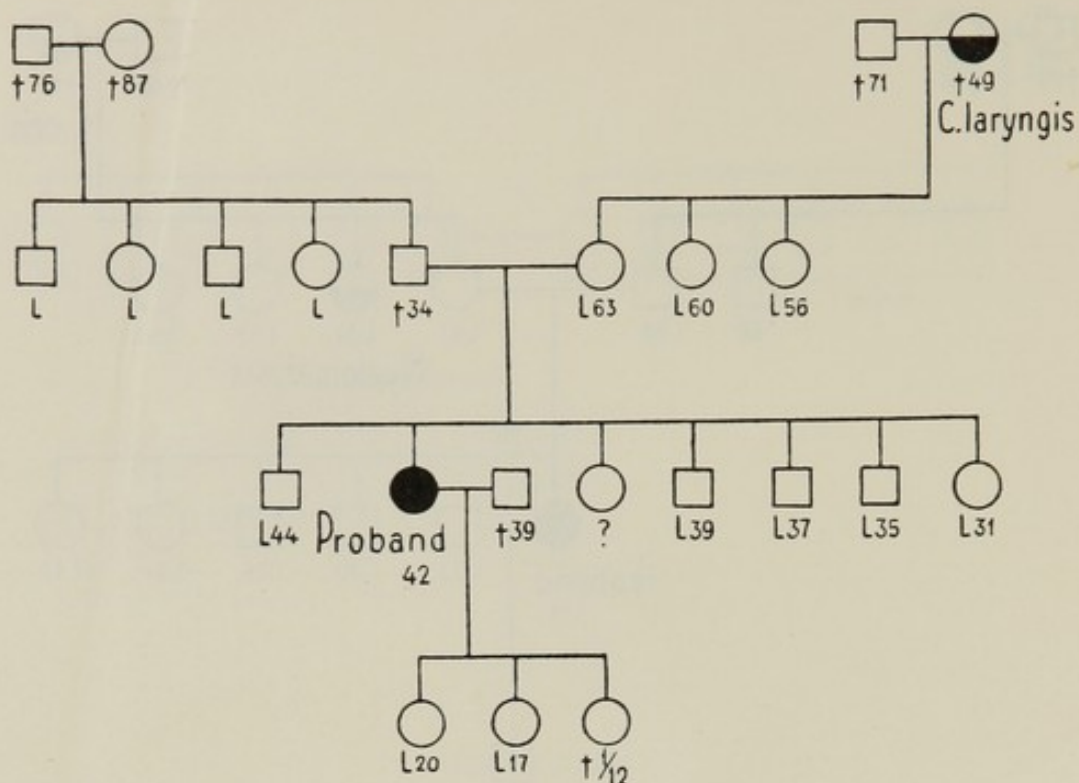


Pedigree 133.

PROBAND (Municipal Hospital, Copenhagen; service I, no. 56/43).—  
 ○, born Apr. 4th, 1909. ∞ commercial agent. Formerly well. Menstruation  
 since fifteenth year, regular. One childbirth. Nursed only a few weeks,  
 owing to hypogalactia. Tumor in left breast noticed about two months be-  
 fore admission. Dec. 19th, 1942, ablation of the breast, with evacuation of  
 the axilla. Histologic diagnosis: primarily solid, adenomatous carcinoma.

MOTHER'S MOTHER.—Born in Dragør Aug. 11th, 1859. ∞ seaman. Died  
 in Dragør Nov. 28th, 1928, of cancer of the mouth. The diagnosis verified  
 by death certificate.

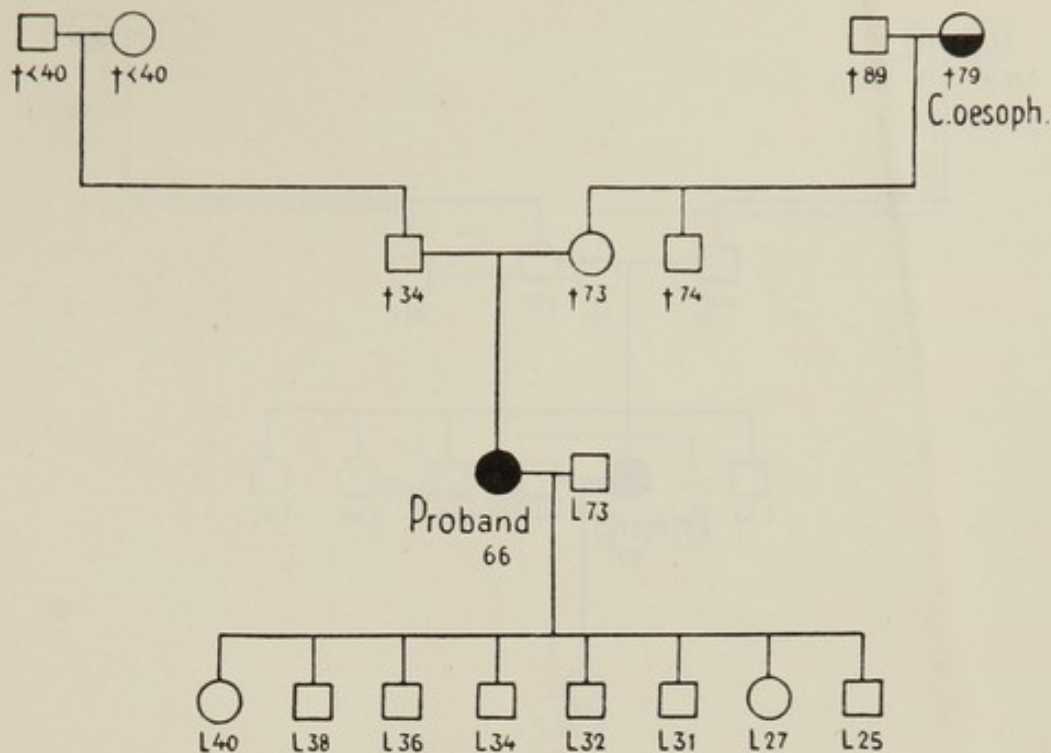
MOTHER'S ELDEST SISTER.—Born in Dragør June 11th, 1890. ∞ farm  
 overseer. Died in her home Oct. 10th, 1942, of myelomatosis, after being  
 treated in the Municipal Hospital, Copenhagen, (service 2 and roentgen  
 clinic). The diagnosis verified by the hospital journal.



Pedigree 134.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 485/42).—  
 ○, born in Copenhagen June 10th, 1900. Cabinetmaker's widow. Formerly  
 well. Menstruation since fifteenth year, regular. Two childbirths. Nursed  
 about a year each time. Tumor in left breast noticed about four months  
 before admission. June 12th, 1942, ablation of the breast, with evacuation  
 of the axilla. Histologic diagnosis: solid carcinoma; fibroadenomatosis.

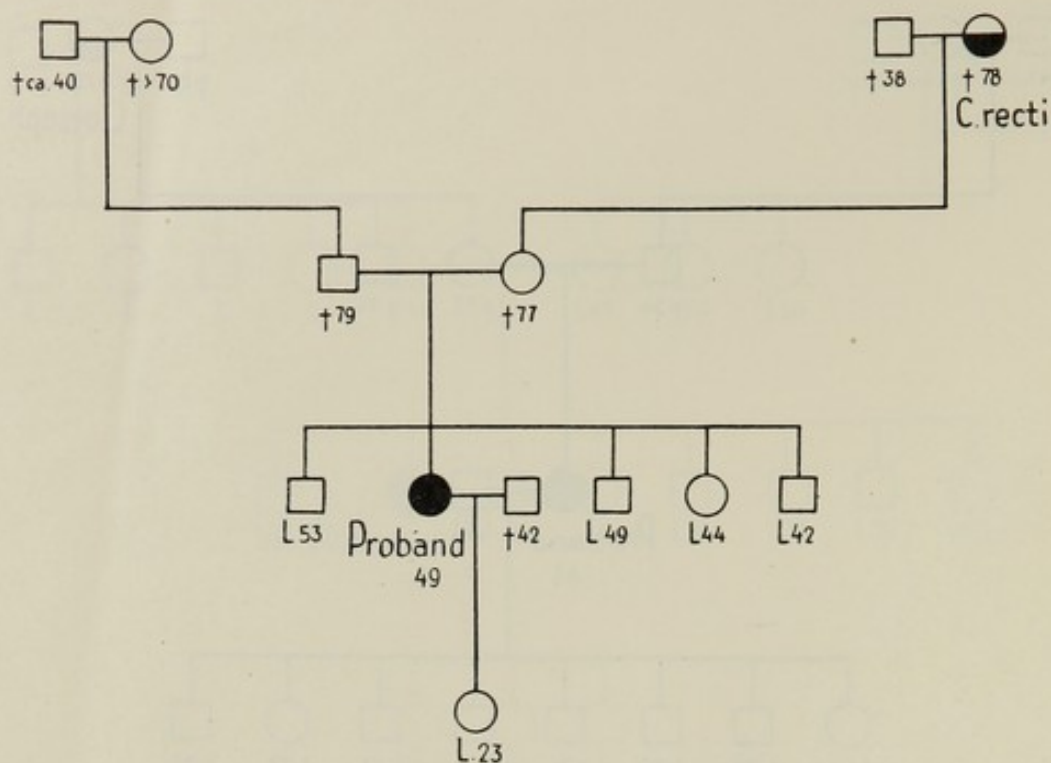
MOTHER'S MOTHER.—Born 1850 in Copenhagen. ~ workingman. Died  
 in the Municipal Hospital, Copenhagen, Aug. 11th, 1889, of cancer of the  
 larynx. The diagnosis verified by the hospital.



Pedigree 135.

PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 808/42).—  
 ○, born in Buttrup Apr. 9th, 1876. ∞ farmer. Formerly well. Menstruation  
 from fifteenth to fifty-third year, regular. Menopause normal. Eight child-  
 births. During the first lactation suppurating mastitis of left breast, treated  
 with many incisions. During subsequent nursings secretion only from right  
 breast; nevertheless all children nursed for over six months. In 1934,  
 operation for gallstone. Tumor in the right breast noticed over six months  
 before admission. Oct. 8th, 1942, ablation of the breast, with evacuation of  
 the axilla. Histologic diagnosis: solid adenomatous carcinoma.

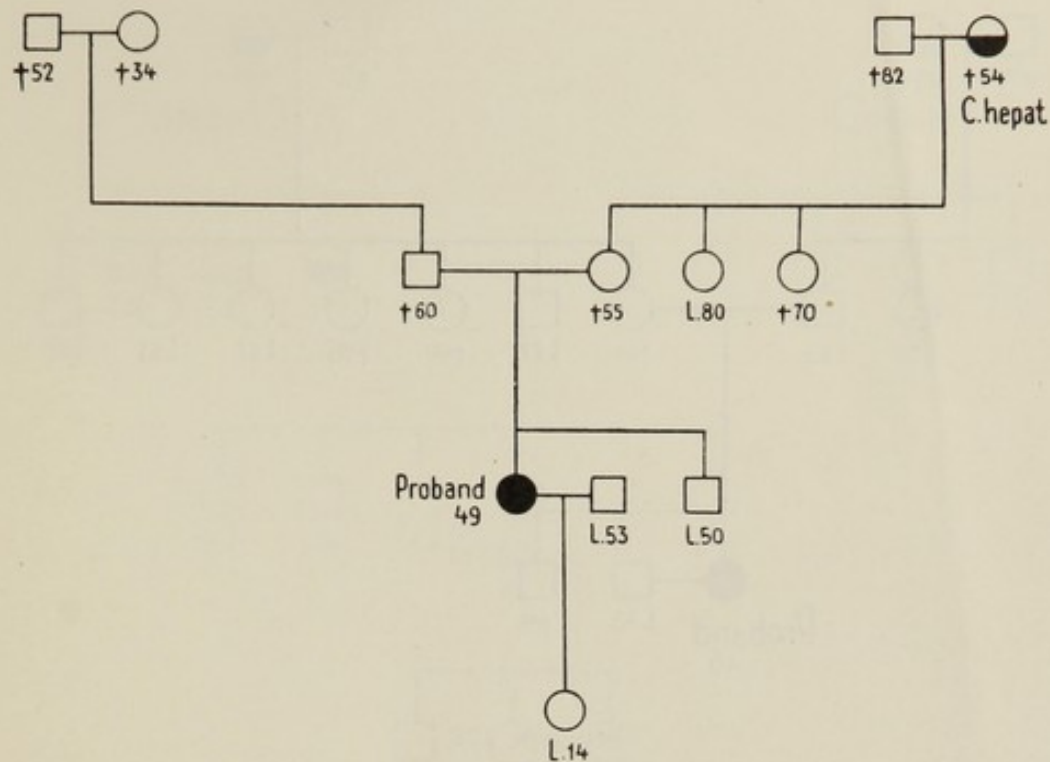
MOTHER'S MOTHER.—Born 1808 in Buttrup. ∞ cowman. Died in But-  
 trup in June 1888, of cancer of the esophagus. The disease had been  
 developing for about six months, with increasing stenosis of the organ. At  
 the time of death, the patient was extremely emaciated (died of innutrition).  
 No hospitalisation.



Pedigree 136.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 206/40).—  
 ○, born in Otterup March 23rd, 1891. Typewriter; divorced. Formerly well.  
 Menstruation from fifteenth year, regular. Menopause normal. One child-  
 birth. Nursed a year. Knew for two years before she consulted a physician  
 that she had a slowly growing tumor in the left breast. July 4th, 1940,  
 ablation of the breast, with evacuation of the axilla. Histologic diagnosis:  
 adenocarcinoma in fibroadenoma.

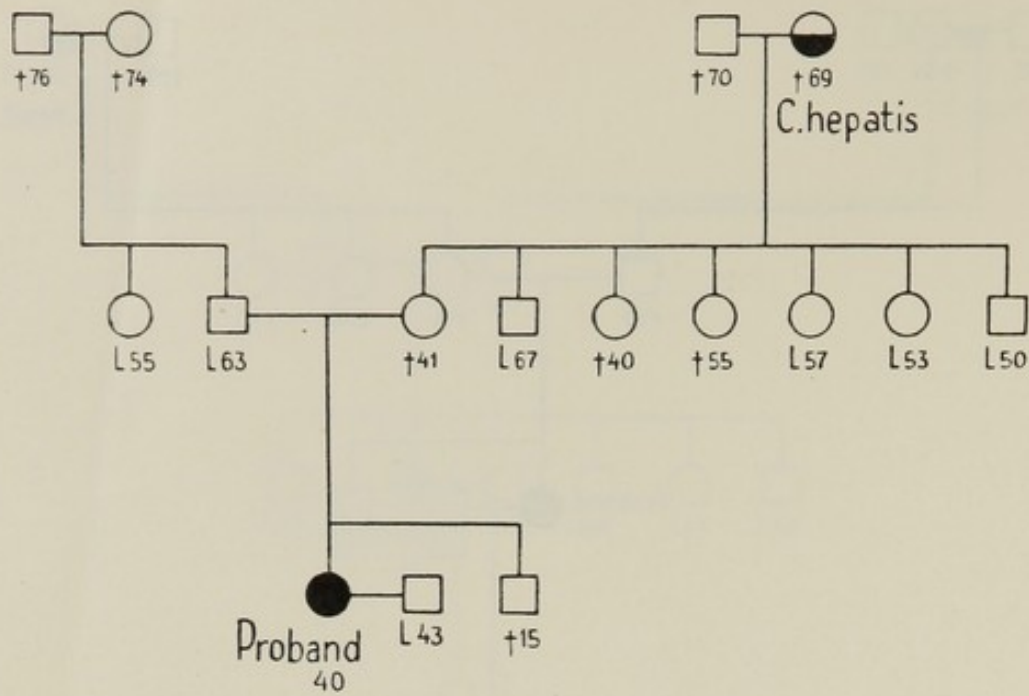
MOTHER'S MOTHER.—Born Aug. 31st, 1844. ∞ farmer. Died 1922 in  
 Marslev, of cancer of the rectum. The diagnosis verified by St. Joseph's  
 Hospital, Odense.



Pedigree 137.

PROBAND (Radium Center, Copenhagen; no. 24433).—○, born in Jebjerg June 19th, 1891. ∞ confidential clerk. As child recurring otitis media, in 1924 otogenic meningitis. Menstruation since fifteenth year, regular until 1940, when she was treated with roentgen for metrorrhagia and fibroma of the uterus. After that time no essential disorder. One normal pregnancy and delivery. Nursed the child only two months, owing to hypogalactia. The tumor in the right breast noticed a week before admission. June 26th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

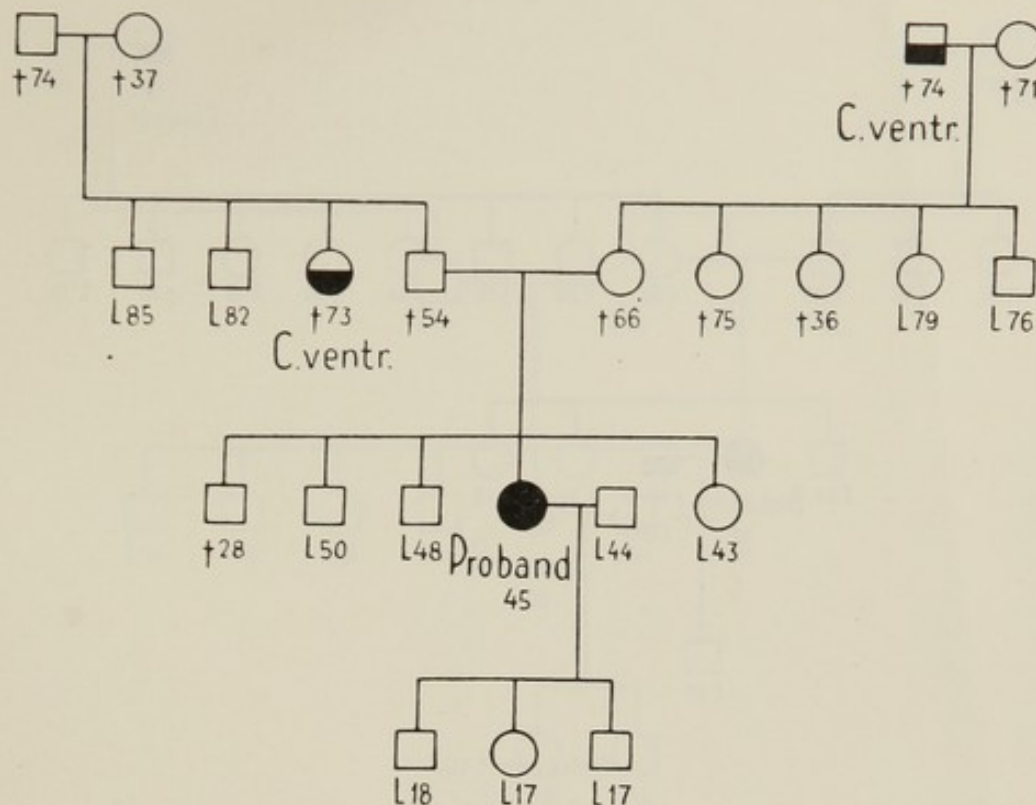
MOTHER'S MOTHER.—Born 1834 in Jebjerg. Died in 1888 after two years' illness, beginning with slight symptoms from the stomach and intestine, followed by increasing emaciation and protracted icterus. According to the statement of the treating physician to the mother of the proband, death was due to cancer of the liver.



Pedigree 138.

PROBAND (Radium Center, Copenhagen; no. 24385).—○, born in Copenhagen Jan. 29th, 1901. ∞ mechanic. Three times hospitalised for gastric ulcer, last time in 1942. Menstruation since thirteenth year, regular. Never pregnant. In 1936, operated on in the surgical policlinic of the State Hospital, Copenhagen, for tumor of the left breast. Histologic examination showed fibroadenomatosis and papilliferous cystadenoma. In 1941, two months before present admission, slight sanguinolent secretion from the slightly retracted nipple. Underneath the cicatrix, a small tumor was found. July 4th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: papilliferous adenocarcinoma.

MOTHER'S MOTHER.—Born in Bukkerup Aug. 13th, 1837. ∞ workingman. Died 1906, after about a year's illness marked throughout by massive icterus. According to the treating physician's statement to the family, the case was one of malignant tumor of the liver.

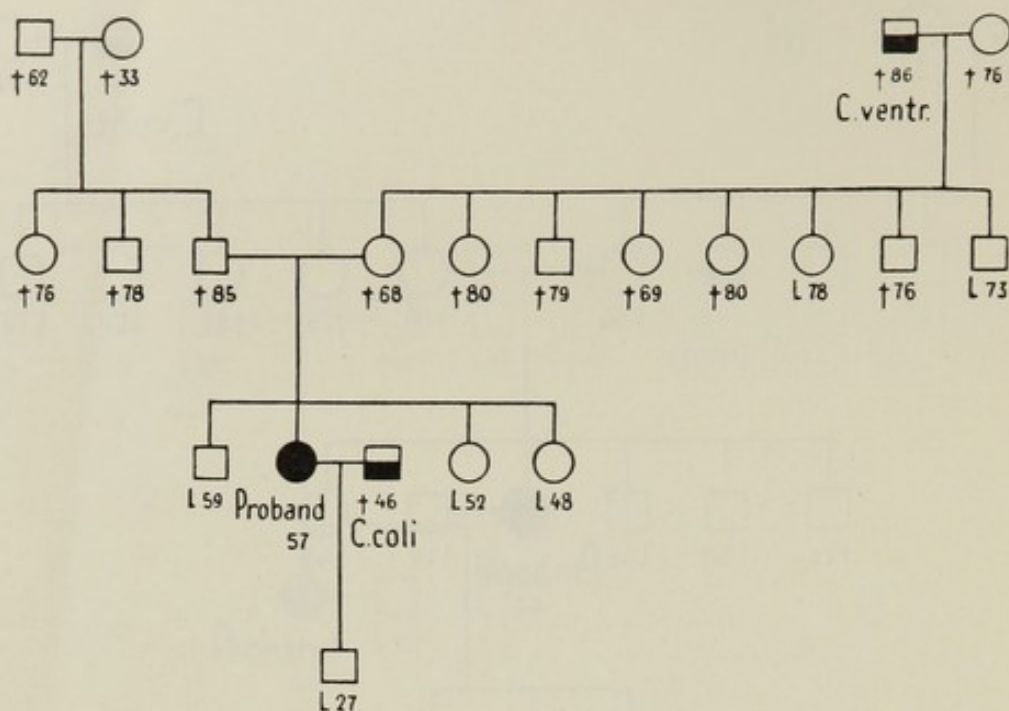


Pedigree 139.

PROBAND (Radium Center, Copenhagen; no. 31310).—○, born in Copenhagen Nov. 11th, 1897. ∞ brewery workman. Formerly well. Menstruation since fourteenth year, regular. Three childbirths. Nursed fully six months each time. Tumor in left breast noticed a month before admission. July 26th, 1942, ablation of the breast. Histologic diagnosis: adenomatous, solid carcinoma.

MOTHER'S FATHER.—Born 1821. Riding master. Died 1895 in Bredtved by Holbæk, after fully two years' illness, during which there for a long time were no other symptoms than fatigue and loss of flesh, but later frequent vomitings, oftenest immediately after meals, occasional obstipation and often entirely black stools. To the patient's children, the treating physician stated that it was a case of cancer of the stomach. The description of the symptoms seems to confirm this diagnosis.

FATHER'S SISTER.—Born 1866 in Copenhagen. ∞ cabinetmaker. Died in the Municipal Hospital, Copenhagen, Jan. 1939, of cancer of the stomach. The diagnosis verified by death certificate.

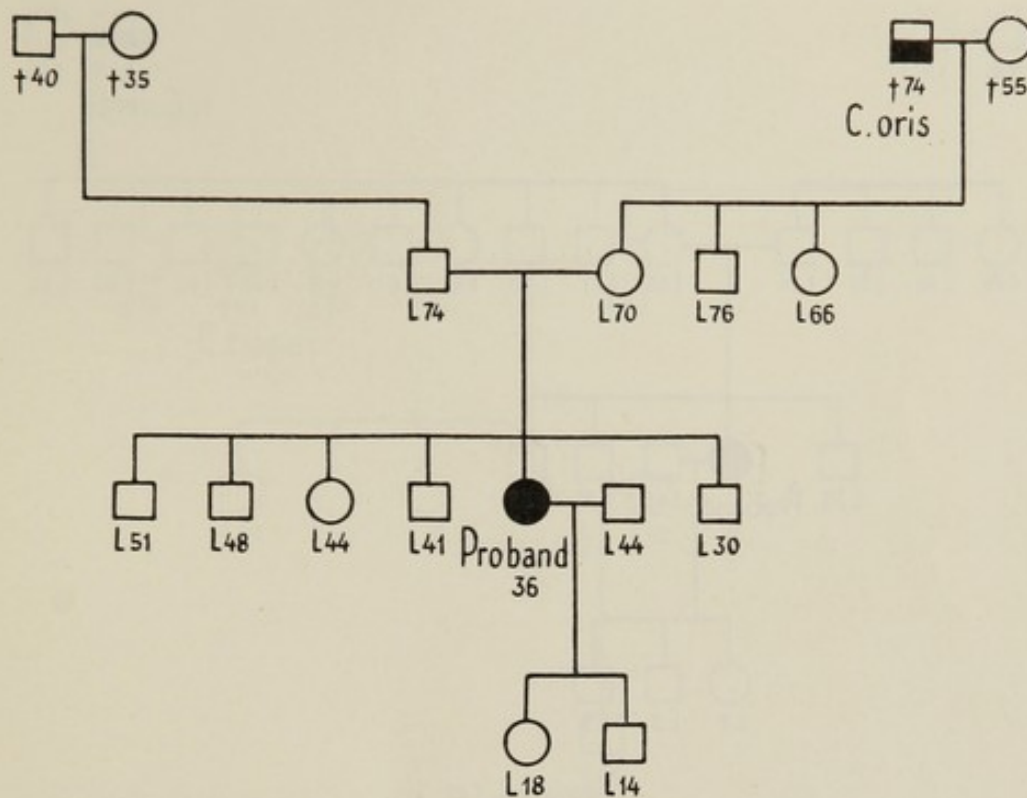


Pedigree 140.

PROBAND (Radium Center, Copenhagen; no. 30339).—○, born in Tikøb Jan. 8th, 1886. Haulage contractor's widow. Formerly well. Menstruation from twelfth to fifty-sixth year, always irregular. From Aug. 1942, menorrhagia; treated for two months with estibilin tablets (0.1 mg. each, twice daily) and injections of estibilin, 16 in all. One childbirth. Did not nurse, owing to agalactia. Tumor in left breast noticed three days before admission to Radium Center Apr. 13th, 1943. Trephine biopsy. Histologic diagnosis: solid carcinoma.

MOTHER'S FATHER.—Born 1823 in Tikøb. Thatcher. Died in Tikøb Jan. 2nd, 1911, after twenty-one months' illness. The anamnesis points to cancer of the stomach, which also according to the treating physician's statement to the family was the cause of death.

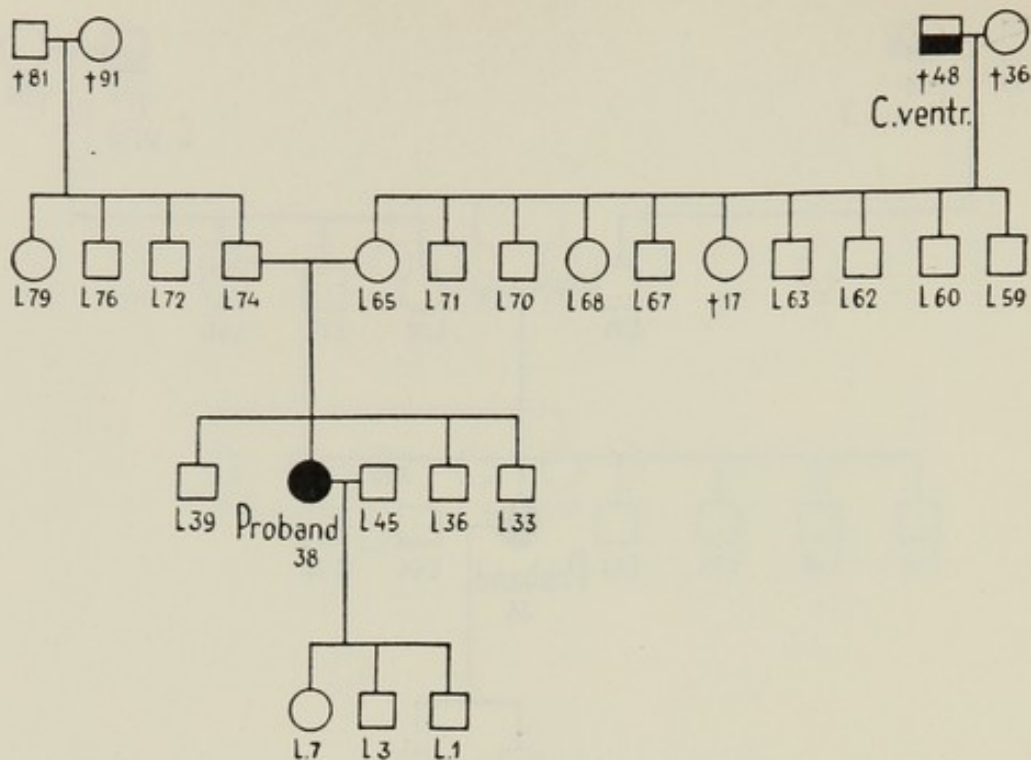




Pedigree 141.

PROBAND (Sundby Hospital, Copenhagen; surg. service, no. 747/42).—  
 ○, born in Copenhagen July 23rd, 1905. ∞ cabinetmaker. Formerly well.  
 Menstruation since fourteenth year, regular. Two childbirths. Nursed a little  
 less than a year each time. Tumor in right breast noticed a week before  
 admission. March 20th, 1942, ablation of the breast, with evacuation of the  
 axilla. Histologic diagnosis: solid carcinoma.

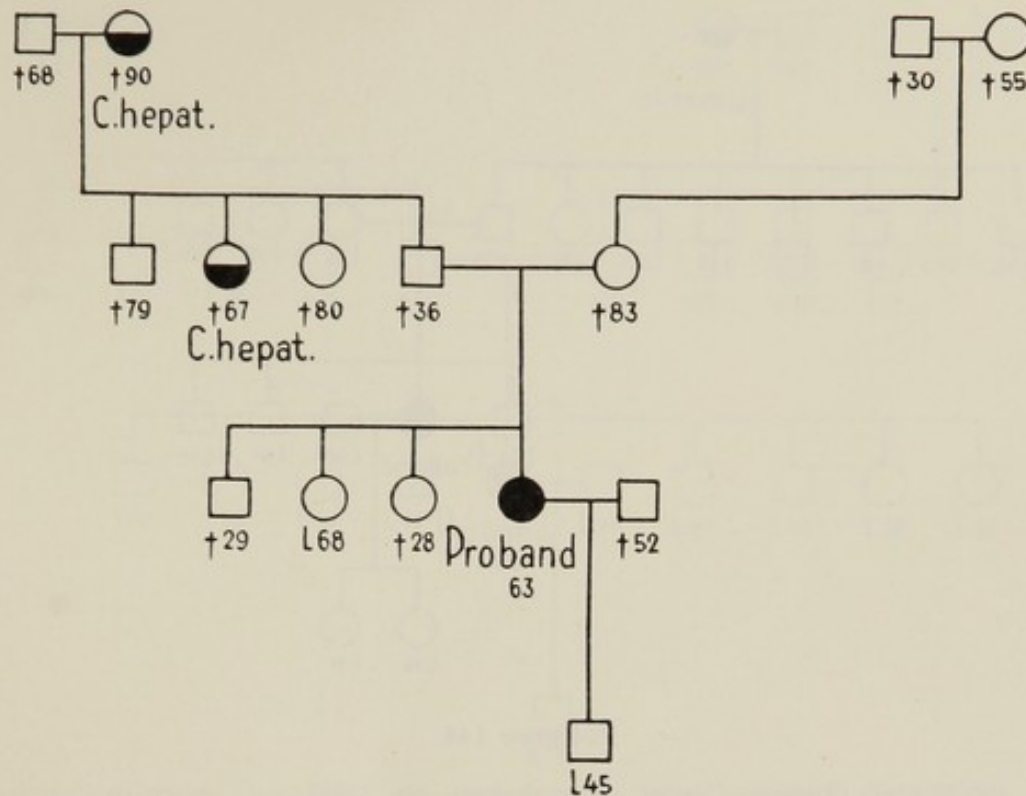
MOTHER'S FATHER.—Born 1837 in Copenhagen. Workingman. Died  
 March 1912 in an Old People's Home, of old age and cancer of the mouth.  
 The diagnosis verified by death certificate.



Pedigree 142.

PROBAND (Radium Center, Copenhagen; no. 30416).—○, born in Dronninglund June 29th, 1905. ∞ housepainter. Formerly well. Menstruation since fourteenth year, regular. Three childbirths. Did not nurse the first child, but the two others for about six months. During the last lactation galactophoritis of left breast, for which she was admitted to the Municipal Hospital, Copenhagen, and treated with warm compresses. Tumor in the breast noticed a month before admission to the Radium Center. Trephine biopsy. Histologic diagnosis: solid adenomatous carcinoma.

MOTHER'S FATHER.—Born in Jetsmark Feb. 18th, 1847. Farmer. Died in Skovgaard March 15th, 1895. The proband's mother states that he had been ill for about a year. Especially towards the end there had been vomitings nearly after all meals, extreme emaciation and icterus. According to the treating physician it had been a hopeless case of stomach cancer. In my opinion there can be no doubt about the correctness of this diagnosis.

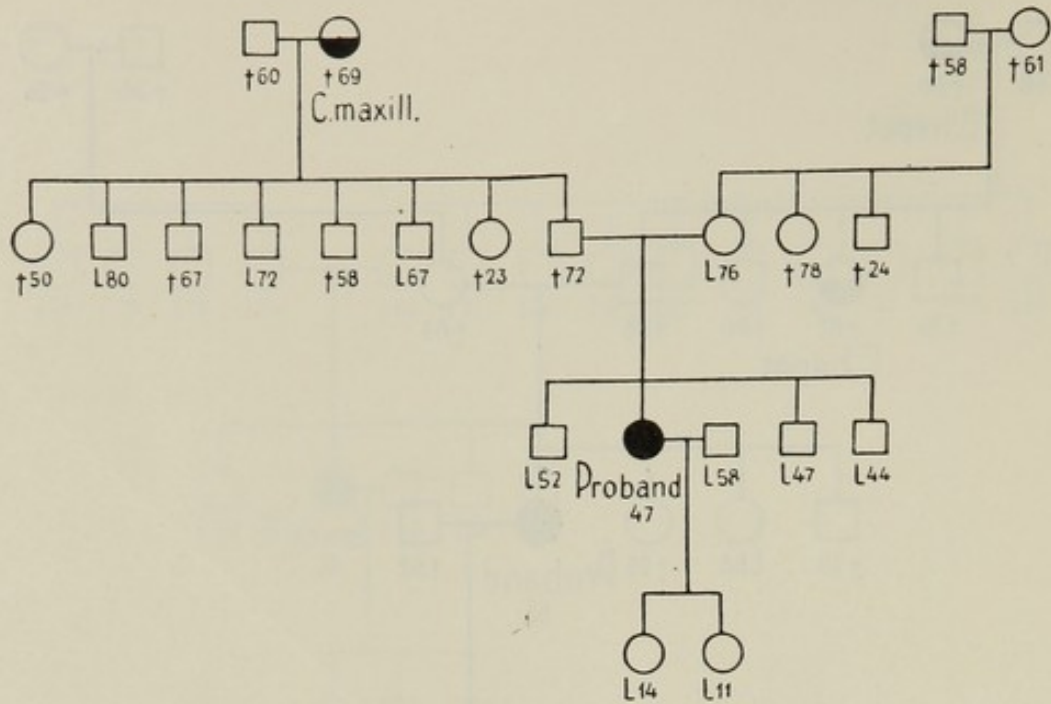


Pedigree 143.

PROBAND (Radium Center, Copenhagen; no. 30452).—○, born in Copenhagen May 16th, 1879. ∞ stockbroker. As child and young well. Menstruation from eleventh to thirty-eighth year, when she was given roentgen treatment for menorrhagias and fibroma of the uterus. Since then no bleeding from the vagina. One childbirth. Nursed only two months, owing to hypogalactia. Nineteen years ago she had fallen and hurt her right breast, resulting in slight extravasations. The tumor in the breast not noticed until a few days before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.

FATHER'S MOTHER.—Born in Magleby Aug. 13th, 1816. ∞ farmer. Died in Storehedinge March 10th, 1907, of cancer of the liver. The diagnosis verified by death certificate.

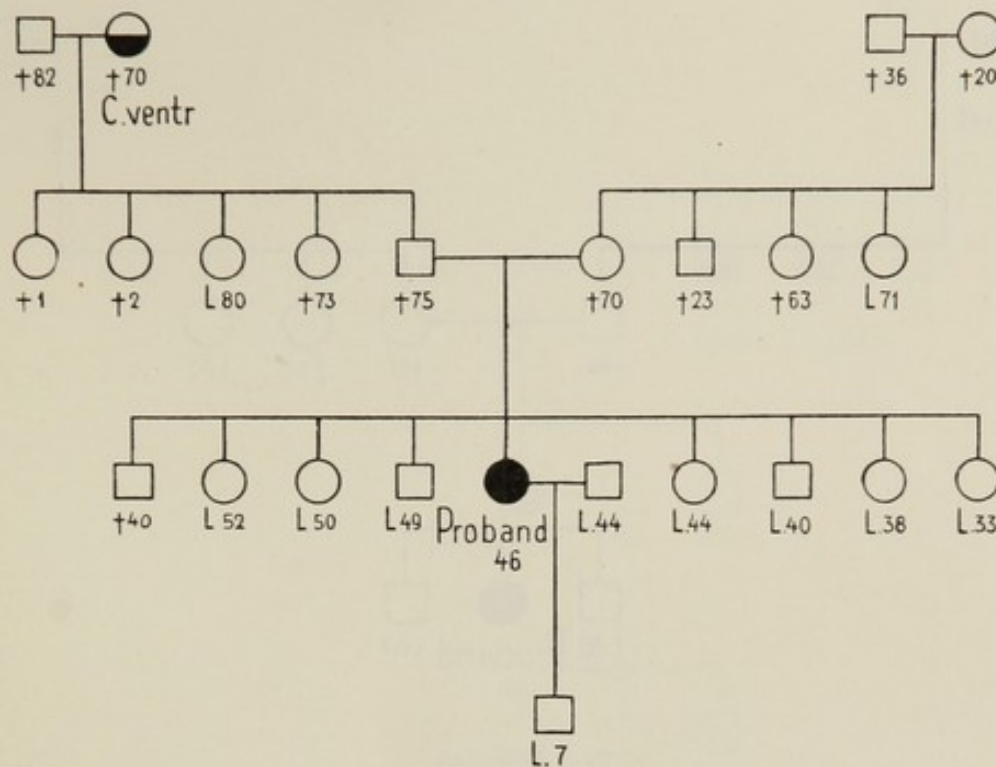
FATHER'S ELDEST SISTER.—Born 1856 in Storehedinge. Midwife; married. Died in Storehedinge Aug. 4th, 1923, of cancer of the liver. The diagnosis verified by death certificate.



Pedigree 144.

PROBAND (Radium Center, Copenhagen; no. 23857).—○, born in Copenhagen Nov. 4th, 1893. ∞ town-hall messenger. Formerly well. Menstruation from fifteenth to forty-fifth year, regular. Menopause normal. Two child-births. Nursed respectively eight and ten months. Tumor in left breast noticed eight months before admission. May 6th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma and solid carcinoma.

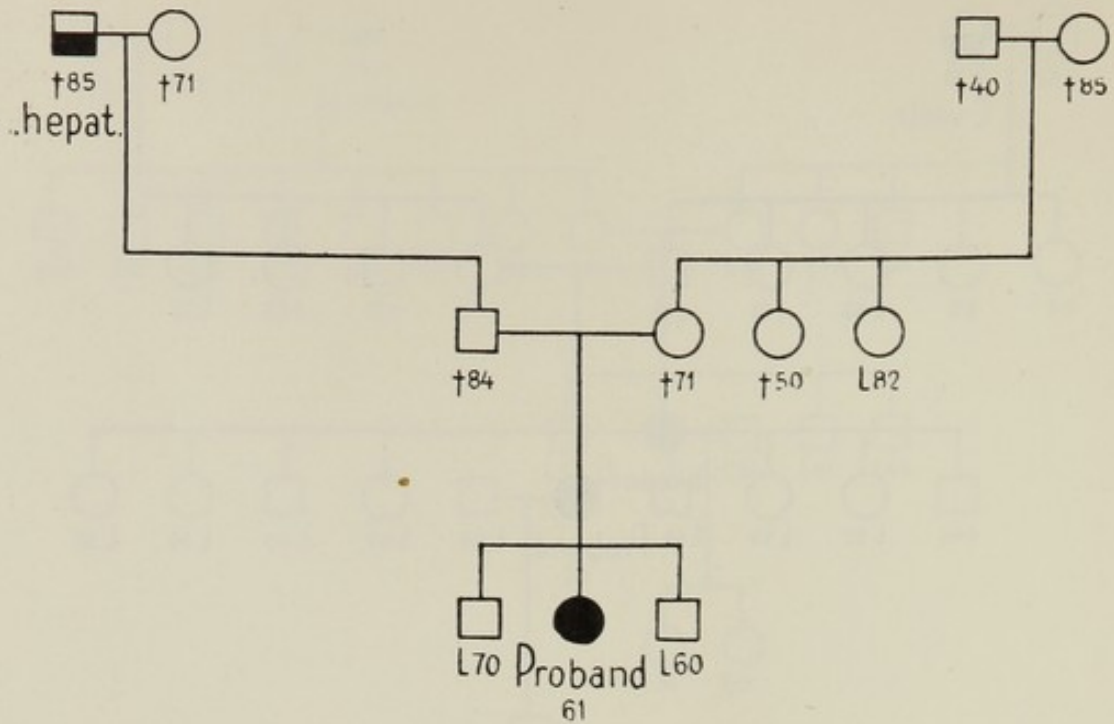
FATHER'S MOTHER.—Born in Copenhagen Sep. 3rd, 1837. ∞ weaver. Died in Copenhagen Apr. 3rd, 1907, of cancer of the maxilla. The diagnosis verified by death certificate.



Pedigree 145.

PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 947/42).—  
 ○, born on Ærø March 2nd, 1896. ∞ schoolmaster. Formerly well. Menstruation since fourteenth year, regular. No climacteric symptoms. One childbirth. Nursed fully eight months. In 1936 treated with ovex for sterility (100 tablets, 1000 units each, distributed over some months). Small lump in left breast noticed a week before admission. Oct. 10th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenomatous and solid carcinoma.

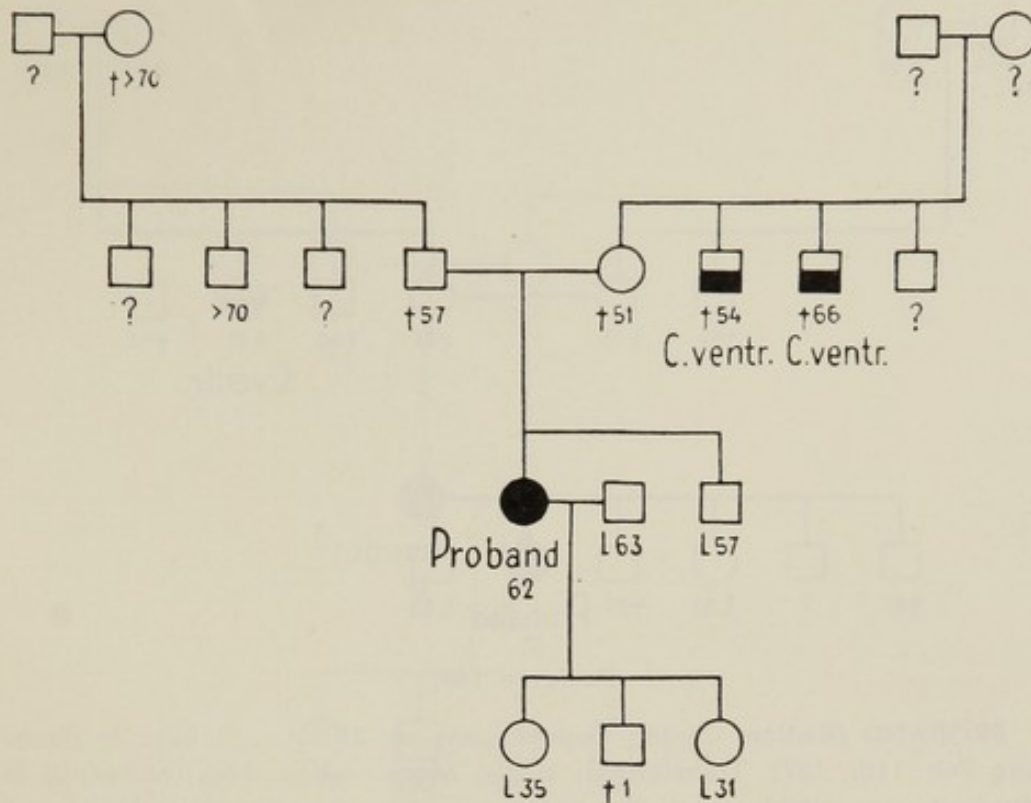
FATHER'S MOTHER.—Born on Ærø Aug. 2nd, 1839. ∞ barrister. Died on Ærø Febr. 13th, 1910, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 146.

PROBAND (Radium Center, Copenhagen; no. 26356).—○, born in Copenhagen March 31st, 1875. Old age pensioner; single. Formerly well. Menstruation from eleventh to forty-fifth year, regular. Never pregnant. For three years before admission aware of the presence of a slowly growing tumor in her left breast. Oct. 26th, 1936, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma. In 1941 treated at the Radium Center, Copenhagen, for pain localised to the pelvis. Roentgenographs of the latter did not show any signs of metastases to the bone.

FATHER'S FATHER.—Born in Odense Jan. 6th, 1819. Merchant tailor. Died in Storehedinge Jan. 23rd, 1904, of cancer of the liver. The diagnosis verified death certificate.

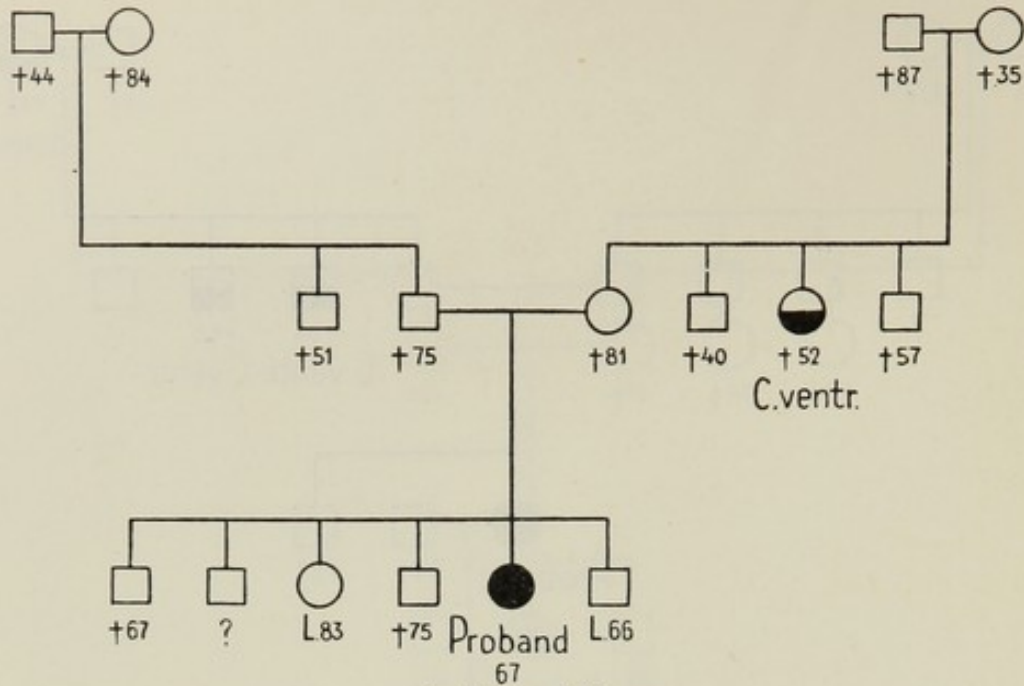


Pedigree 147.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 90/40).—  
 ○, born in Holstebro Apr. 4th, 1877. ∞ wholesale merchant. Formerly well.  
 Menstruation from fifteenth to forty-eighth year, regular. Menopause normal.  
 Three childbirths. Nursed about a year on each occasion. Two years before  
 admission she had fallen and hurt her left breast badly against the sharp  
 edge of a table, resulting in rather large extravasations. The tumor in the  
 breast first noticed ten days before admission. May 6th, 1940, ablation of  
 the breast, with evacuation of the axilla. Histologic diagnosis: solid car-  
 cinoma.

MOTHER'S ELDEST BROTHER.—Born 1852 in Vinding, Farmer. Died in  
 Vinding March 14th, 1905, of cancer of the stomach. The anamnesis typical;  
 the diagnosis verified by the treating physician.

MOTHER'S NEXT ELDEST BROTHER.—Born in Vinding June 2nd, 1860.  
 Schoolmaster. Died in the Aarhus County Hospital Jan. 14th, 1927, of cancer  
 of the stomach. The diagnosis verified by death certificate.

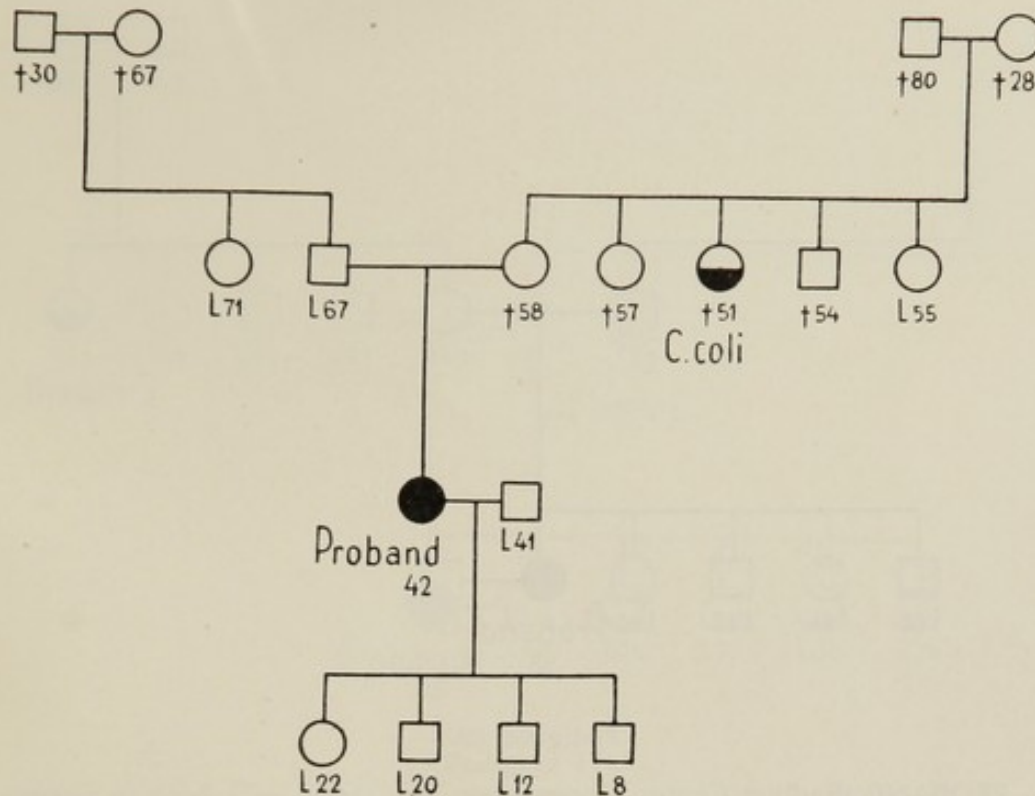


Pedigree 148.

PROBAND (Radium Center, Copenhagen; no. 21051).—○, born in Flensborg Feb. 11th, 1872. Translatress; single. Menstruation from fourteenth to fifty-first year; regular until the last year, when she got menorrhagia and was admitted to the State Hospital, Copenhagen, service D, where she was given roentgen treatment. Since then no bleeding. A month before admission to the Radium Center she had noticed that the nipple of her right breast was retracting, and at the same time she had felt a hazelnut-sized lump in the breast. Nov. 4th, 1939, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma and solid carcinoma.

MOTHER'S SISTER.—Born 1829 in Flensborg. ∞ general merchant. Died 1881 after about two years' illness marked by increasing stenosis, repeated hematemeses and, toward the end, icterus. The diagnosis given to the proband by the patient's physician was cancer of the stomach.

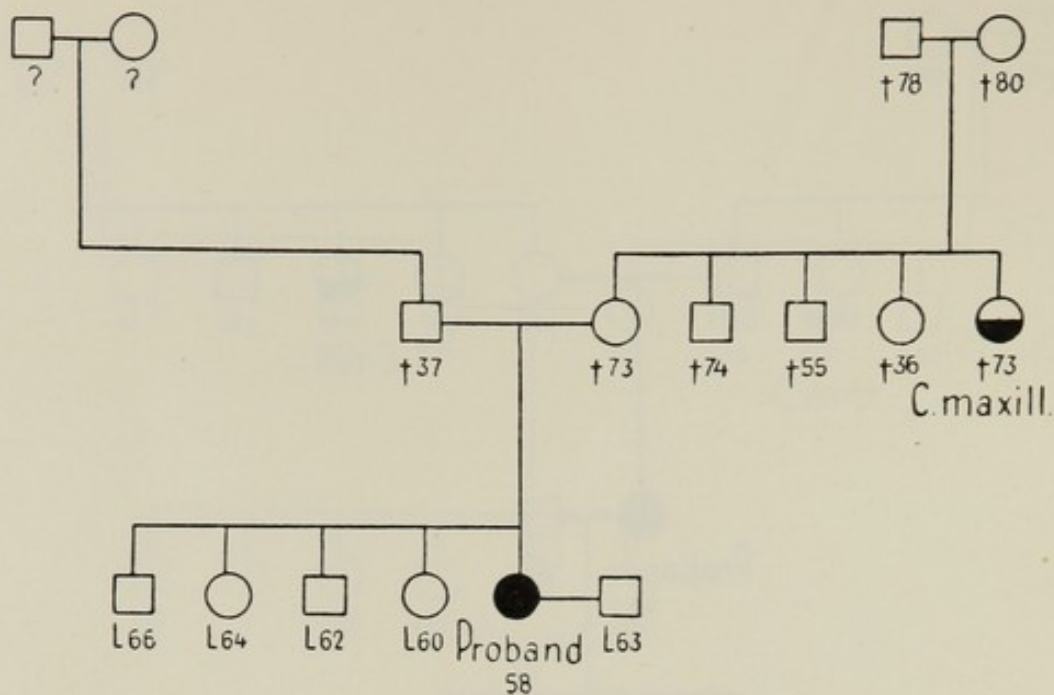




Pedigree 149.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 2839/42).—  
 ○, born in Copenhagen (Frederiksberg) Feb. 16th, 1900. Divorced. Formerly  
 well. Menstruation since thirteenth year, regular. In the last months more  
 profuse bleeding, some headache and vertigo. Four childbirths. Lactation  
 each time normal, of about eight months' duration. Tumor in the left breast  
 noticed about two months before admission. July 9th, 1942, ablation of the  
 breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

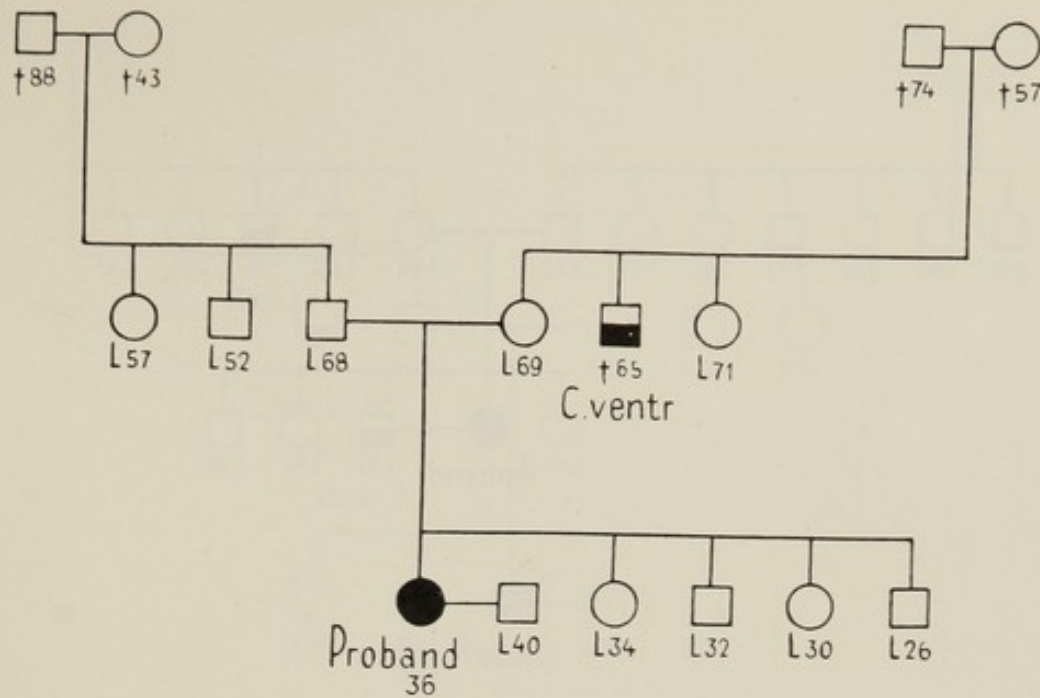
MOTHER'S SISTER.—Born 1881 in Copenhagen. Died in the Haslev Hos-  
 pital May 2nd, 1932, of cancer of the colon. The diagnosis verified by death  
 certificate.



Pedigree 150.

PROBAND (Radium Center, Copenhagen; no. 31469).—○, born in Copenhagen Jan. 23rd, 1885. ∞ coffee roaster. Formerly well. Menstruation from thirteenth to forty-eighth year, regular. Menopause normal. In 1922 treated in the Municipal Hospital, Copenhagen, for extrauterine pregnancy. Never born any children. Tumor in left breast noticed a week before admission. Trepine biopsy. Histologic diagnosis: solid carcinoma.

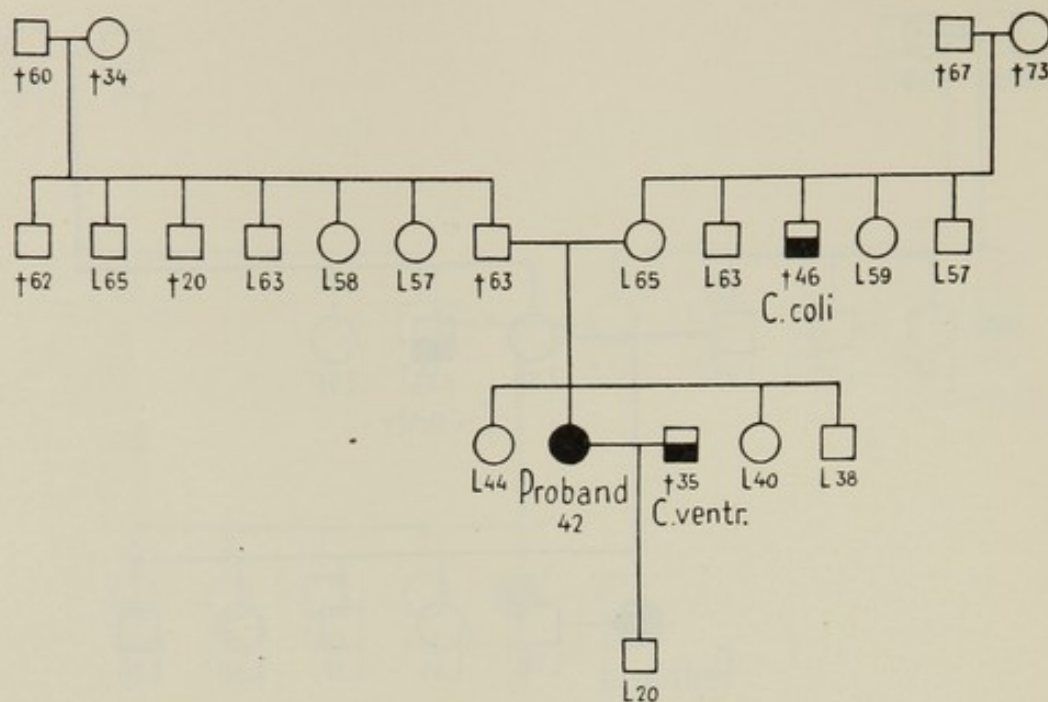
MOTHER'S YOUNGEST SISTER.—Born 1868 in Copenhagen. Bricklayer's widow. Died in the Sundby Hospital, Copenhagen, Sep. 27th, 1941, of cancer of the maxilla. The diagnosis verified by the hospital.



Pedigree 151.

PROBAND (Bispebjerg Hospital, Copenhagen; service D; no. 3268/42).—  
 ○, born in Copenhagen Nov. 14th, 1905. ∞ chief railway-assistant. Formerly  
 well. Menstruation since fourteenth year, regular. Never pregnant. A month  
 before admission she had noticed a lump in her left breast and consulted  
 a physician, who according to her statement declared it for a "gland" and  
 treated her for two weeks with glucovex tablets, six tablets daily. (Each  
 tablet contains 0.1 mg. of estrone-tetra-acetyl-glucoside). In the following  
 two weeks, the tumor rapidly grew larger, and she was admitted to the  
 hospital. Aug. 8th, 1942, extirpation of the tumor. Histologic diagnosis:  
 scirrhous carcinoma.

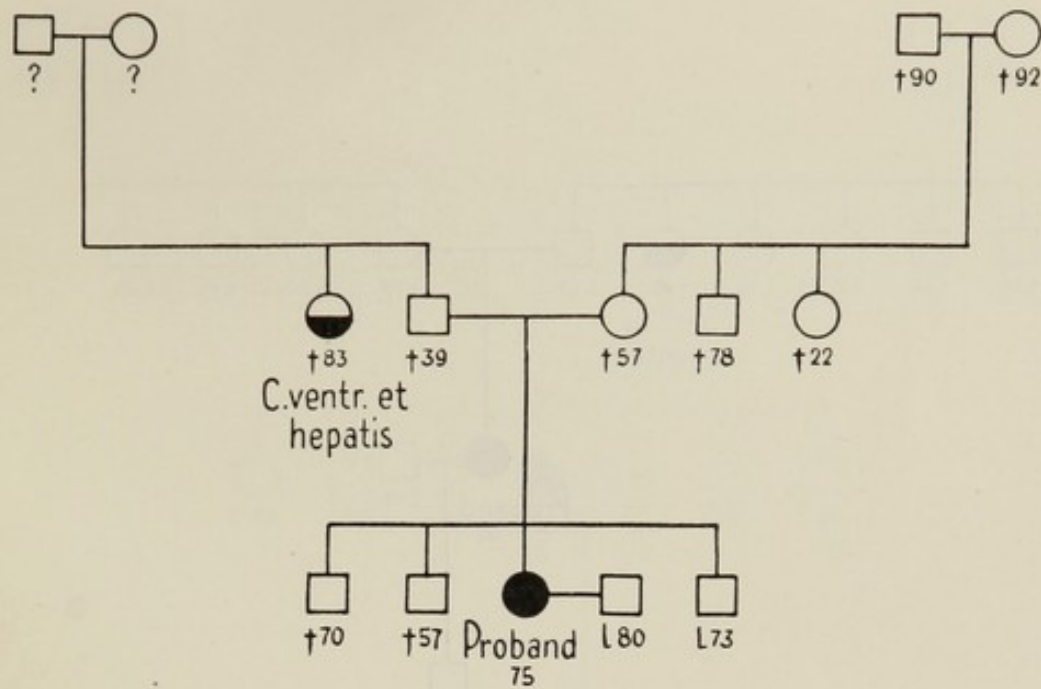
MOTHER'S BROTHER.—Born in Tikøb Apr. 21st, 1868. Died in Elsinore  
 Apr. 3rd, 1934, of cancer of the stomach. The diagnosis verified by death  
 certificate.



Pedigree 152.

PROBAND (Bispebjerg Hospital, Copenhagen; service D, no. 3208/42).—  
 ○, born in Ikast July 16th, 1900. Widow. Formerly well. Menstruation since  
 fourteenth year, regular. One childbirth. Nursed only two months, owing  
 to hypogalactia. Had for more than a year noticed increasing retraction of  
 left nipple, but only four days before admission discovered the presence of  
 a tumor. Oct. 12th, 1942, ablation of the breast, with evacuation of the axilla.  
 Histologic diagnosis: adenomatous and solid carcinoma.

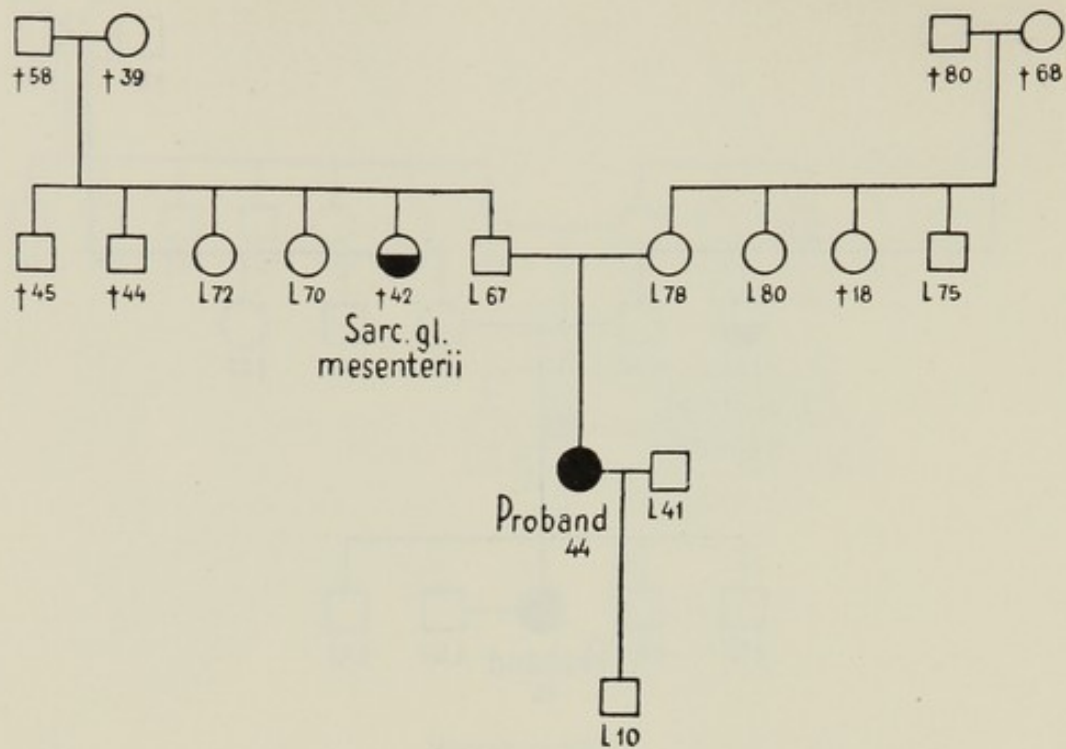
MOTHER'S BROTHER.—Born in Herning Nov. 15th, 1881. Shoemaker.  
 Died in the Municipal Hospital, Copenhagen, Apr. 22nd, 1928, of cancer of  
 the colon. The diagnosis verified by the death register of the hospital.



Pedigree 153.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 1601/43).—  
 ○, born in Copenhagen March 16th, 1868. ∞ naval ordnance officer. Formerly well. Menstruation from sixteenth to forty-eighth year, regular. Never pregnant. Tumor in right breast noticed about six months before admission. April 7th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.

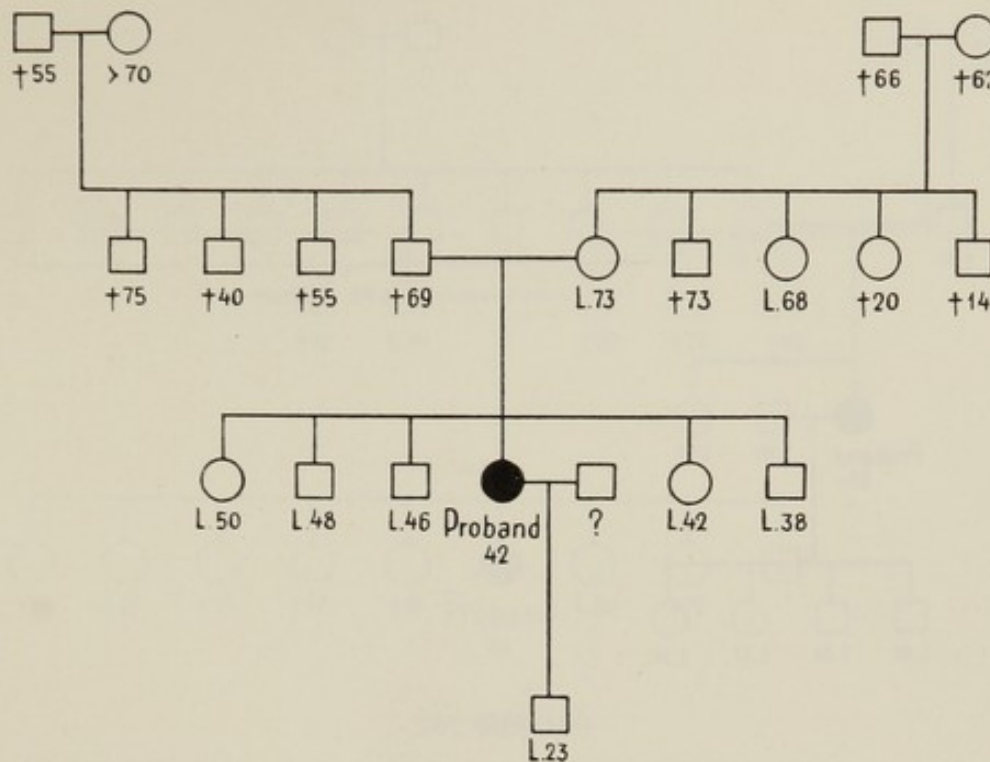
FATHER'S SISTER.—Born in Copenhagen Aug. 31st, 1842. Matron; single. Died in Copenhagen July 20th, 1925, of cancer of the stomach. The diagnosis verified by death certificate.



Pedigree 154.

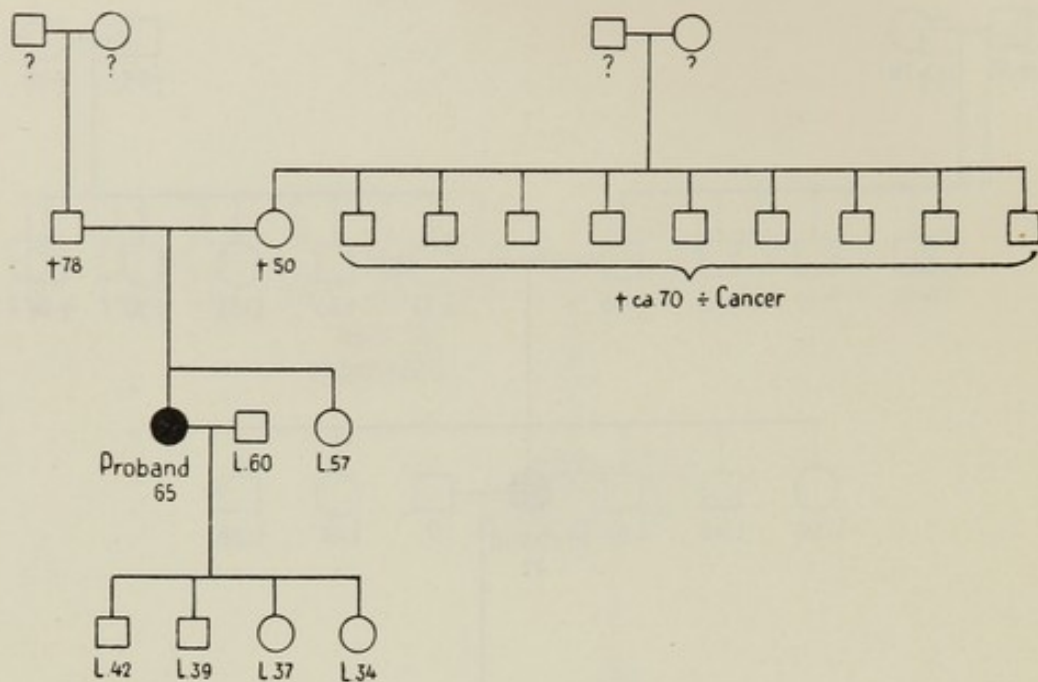
PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 1841/42). —○, born in Copenhagen Sep. 17th, 1898. ∞ inspector. Formerly well. Menstruation since eleventh year, regular. One childbirth. Nursed six months. Tumor in right breast noticed about two months before admission. Sep. 21st, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: adenocarcinoma.

FATHER'S YOUNGEST SISTER.—Born i Avedøre June 26th, 1878. ∞ workingman. Died in the Copenhagen County Hospital, Gjentofte, in Oct. 1920, of sarcoma of the mesenteric gland. The diagnosis verified by death certificate.



Pedigree 155.

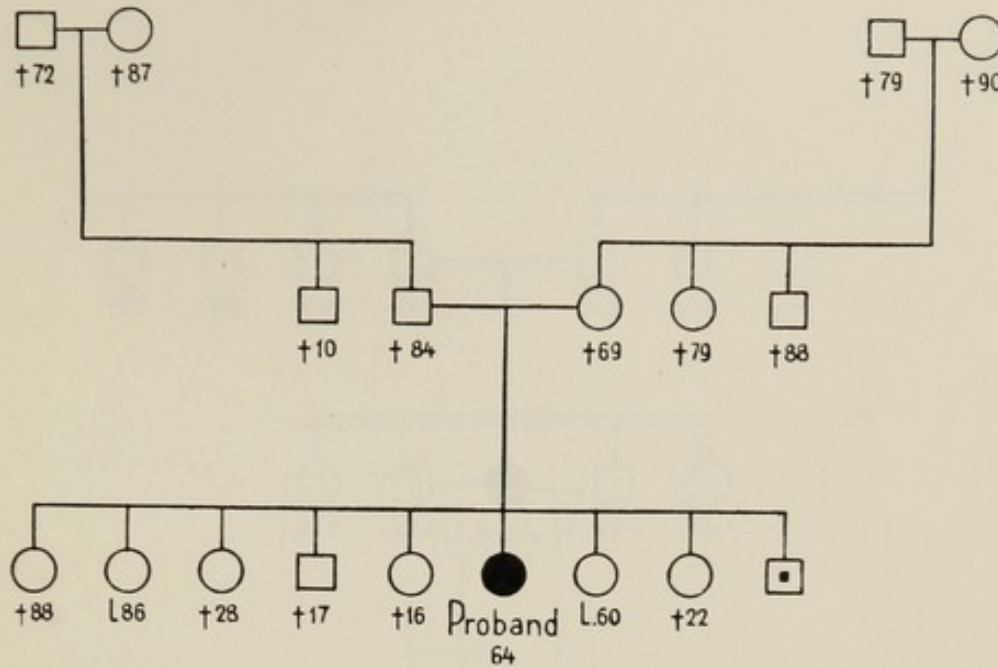
PROBAND (Radium Center, Copenhagen; no. 24455).—○, born in Hillerød March 5th, 1899. Brewery worker; divorced. Menstruation since seventeenth year, of late somewhat irregular. Climacteric troubles, with headaches and hot flushes. One childbirth. Nursed a month, but then had to give it up on account of her work. Frequent slight injuries to both breasts in the course of her occupation with lifting and carrying cases of beer. Two weeks before admission she noticed first an indolent, enlarged lymph node in her left axilla, thereafter a tumor in the left breast. Trepine biopsy. Histologic diagnosis solid carcinoma. June 24th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid medullary carcinoma.



Pedigree 156.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 373/40).—  
 ○, born in Middelfart July 2nd, 1877. ∞ tramway employee. Menstruation from twelfth to fiftieth year, regular. Menopause normal. Four childbirths. Nursed each time for about a year. In 1927, operation for gallstone. Six weeks before admission she noticed a slowly growing tumor in her left breast. Oct. 2nd, 1942, ablation of the breast, with evacuation of the axilla (State Hospital, surgical policlinic). Histologic diagnosis: solid carcinoma.

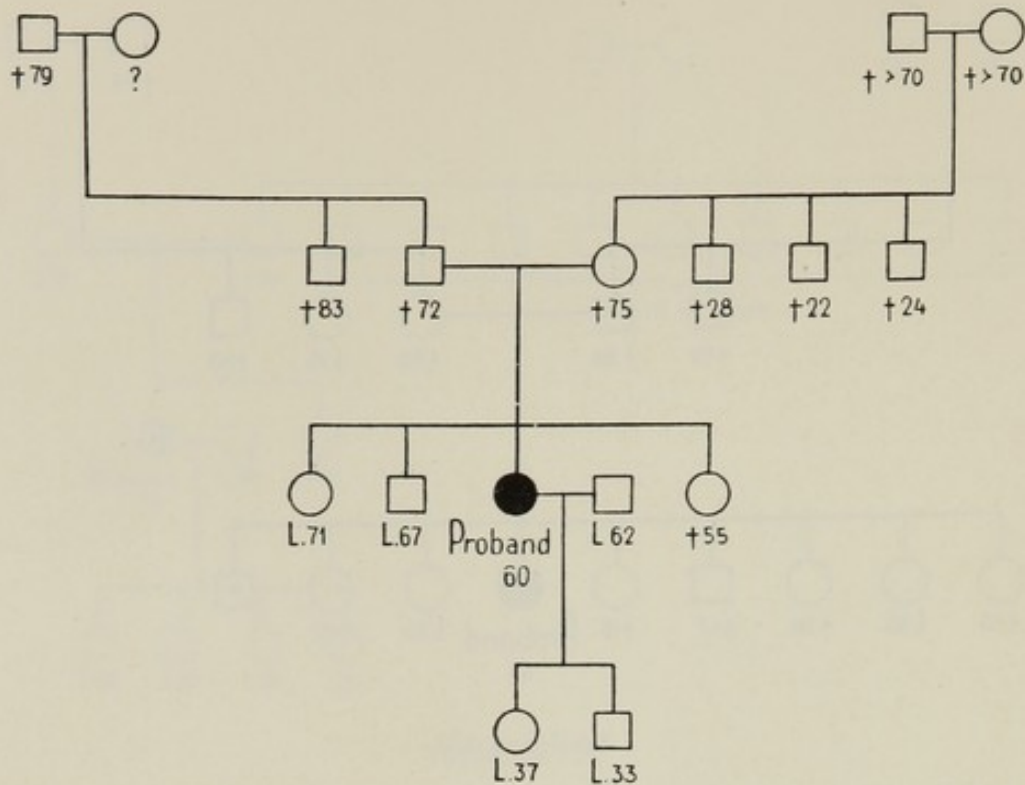




Pedigree 157.

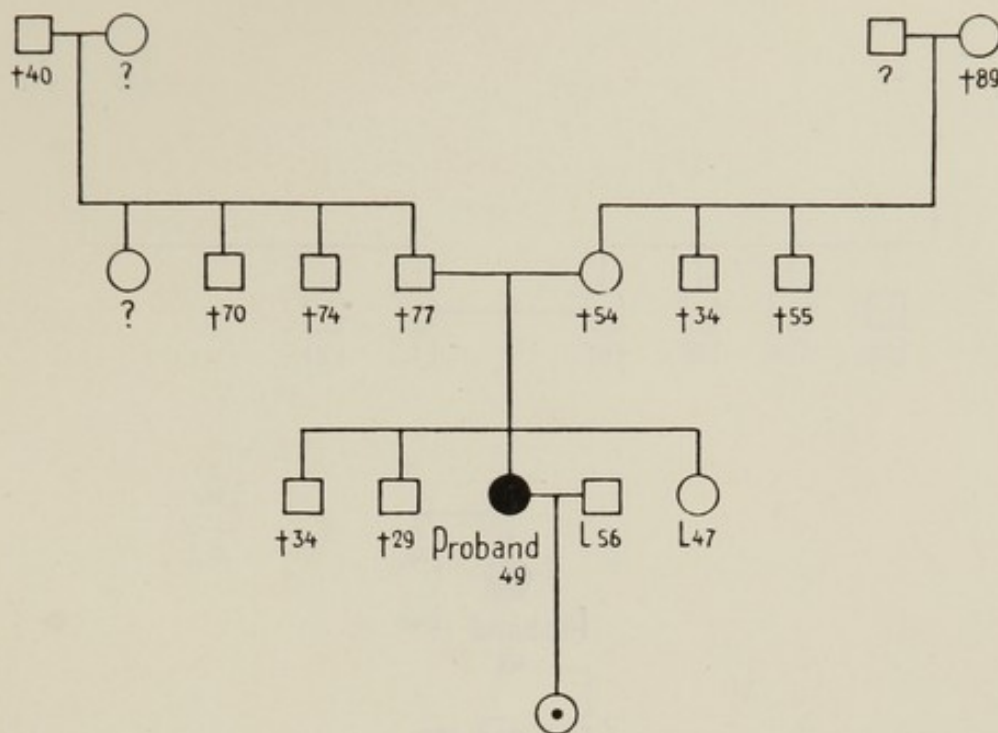
PROBAND (Radium Center, Copenhagen; no. 28143).—○, born on Hanstholm Aug. 25th, 1879. Trained nurse; single. Menstruation from nineteenth to forty-ninth year, regular. Menopause normal. Never pregnant. It seems that for a long time a whalebone in her corset had been giving her trouble by pressing on her left breast. When she after a year got a pain in the breast and consulted a physician, no tumor could be found, however. Gradually, ezcema developed around the areola, and underneath it a small, hard nodule. Trepine biopsy. Histologic diagnosis: solid carcinoma; Paget's disease.

MOTHER.—Born on Hanstholm Sep. 27th, 1852. ∞ coastguard. Died on Hanstholm Nov. 22nd, 1901. It seems that four years before she died she had been operated on for a tumor in the abdomen, after which time she never became quite well, but gradually declined; but there was no later hospitalisation. It may have been a case of malignant tumor, but as there is no death certificate, I consider the case as too uncertain to be counted as positive.



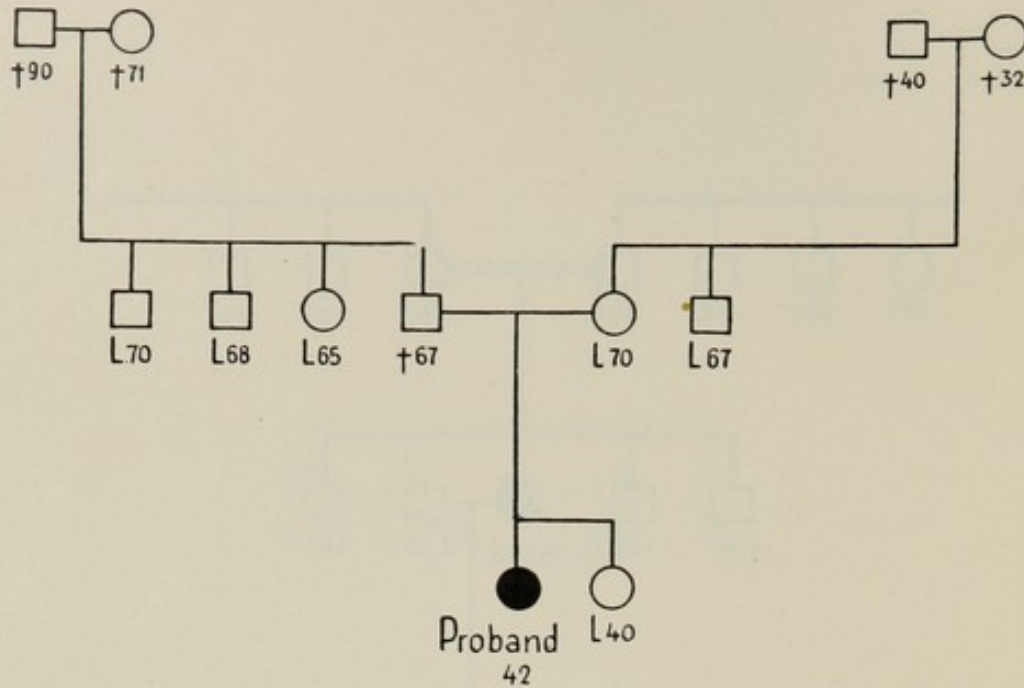
Pedigree 158.

PROBAND (Radium Center, Copenhagen; no. 31638).—○, born in Nakskov Oct. 18st, 1882. ∞ electrometer controller. Menstruation from sixteenth to fifty-second year, regular. Menopause normal. Two childbirths. For social reasons she did not nurse the first child, the second she nursed for over a year. The tumor in the right breast noticed four-five years before admission. Trephine biopsy. Histologic diagnosis: scirrhus carcinoma.



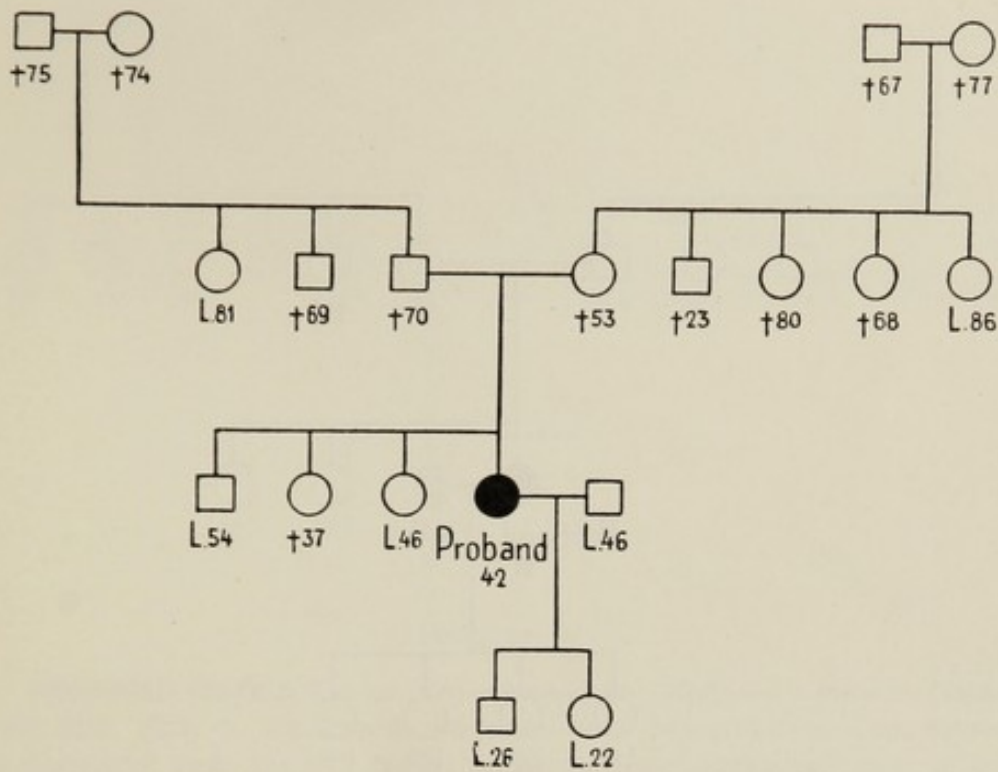
Pedigree 159.

PROBAND (Radium Center, Copenhagen; no. 32021).—○, born in Copenhagen May 5th, 1894. Actuary; single. Menstruation from thirteenth to forty-eighth year, regular. Menopause normal. One childbirth (still-birth). Tumor in left breast noticed four days before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.



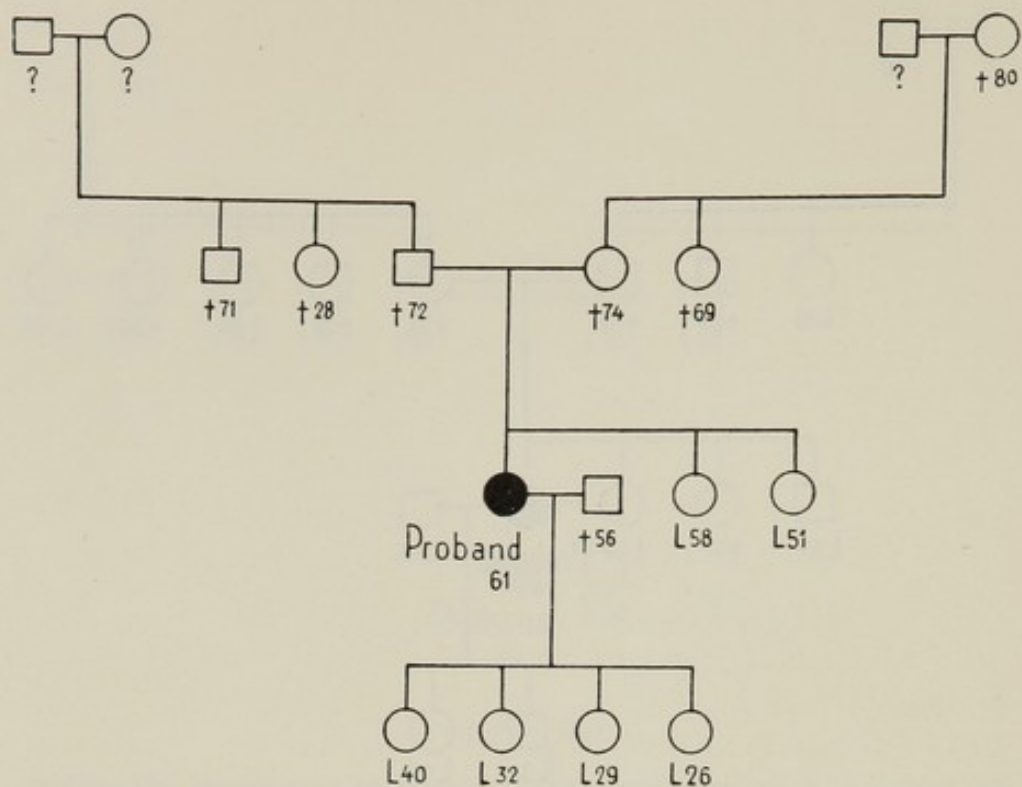
Pedigree 160.

PROBAND (Municipal Hospital, Copenhagen; service 5, no. 2001/42).—  
 ○, born in Aagerup by Roskilde Jan. 26th, 1900. ∞ mechanic. Formerly  
 well. Menstruation since fifteenth year, regular. Never pregnant. Four years  
 before admission she had fallen when riding her bicycle, and had hurt her  
 left breast against the handlebar. There had been pain for some days, but  
 no swelling or extravasation. When she discovered the lump in her breast,  
 she at once consulted a physician and was immediately admitted to the  
 hospital. Sept. 19th, 1942, ablation of the breast, with evacuation of the  
 axilla. Histologic diagnosis: primarily solid, adenomatous carcinoma.



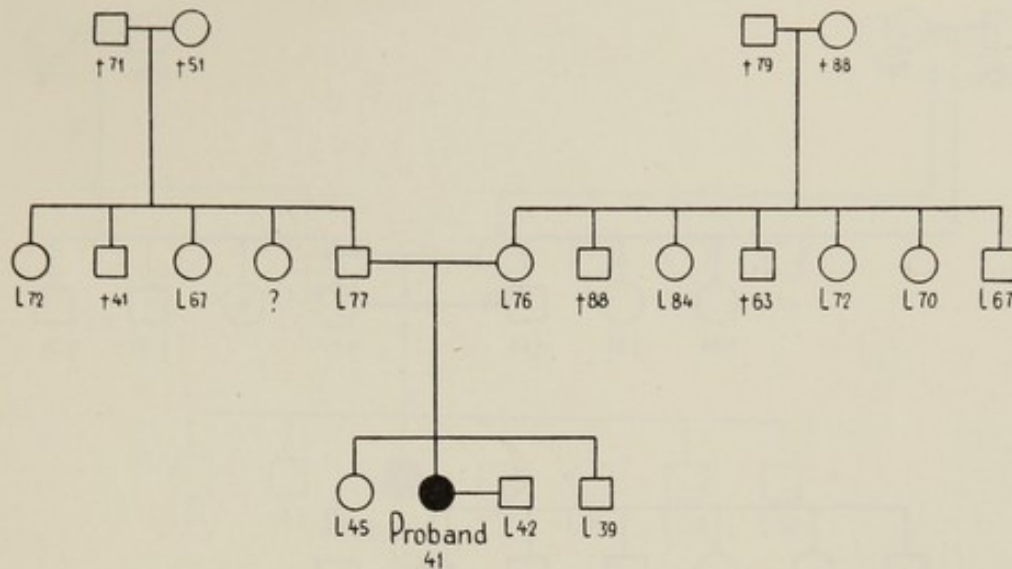
Pedigree 161.

PROBAND (State Hospital, Copenhagen; radiol. service).—○, born in Antwerpen, Belgium, Nov. 22nd, 1897. ∞ shipbuilder. Formerly well. Menstruation since fourteenth year, regular. Two childbirths. Nursed about a year each time. Tumor in right breast noticed six months before admission. Apr. 25th, 1939, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid scirrhus carcinoma.



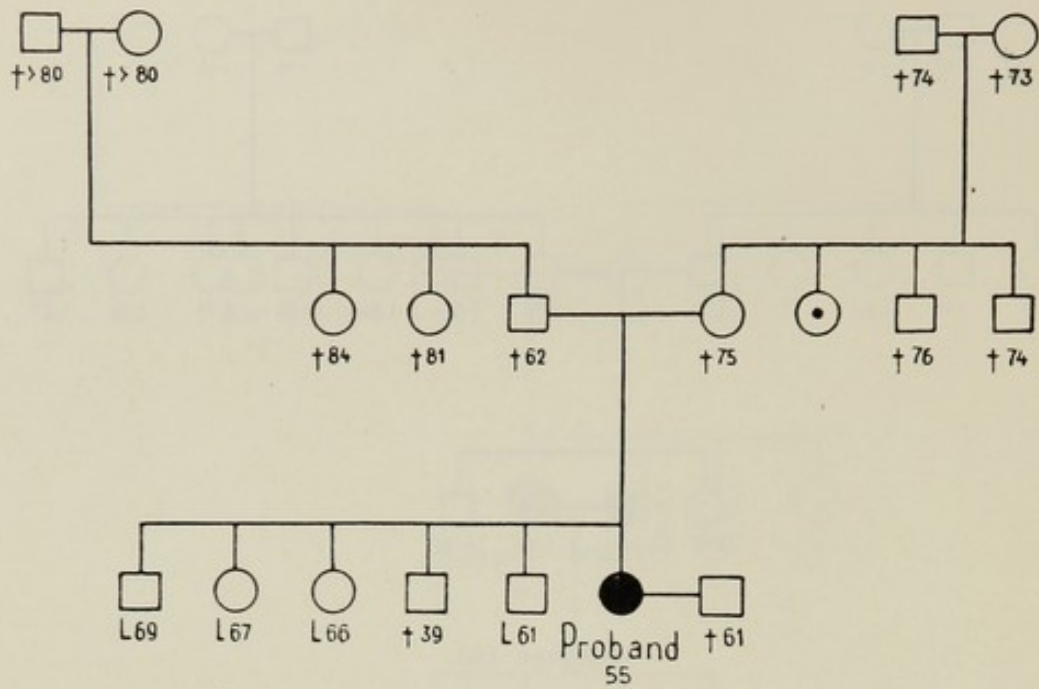
Pedigree 162.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1787/42).—  
 ○, born in Sweden Dec. 16th, 1881. Shoemaker's widow. Formerly well.  
 Menstruation from fourteenth to forty-fifth year, regular. Menopause normal.  
 Four childbirths. Nurse from seven to ten months. During the first lactation  
 bilateral suppurating mastitis, treated with incisions. Tumor in right breast  
 noticed a year before she consulted physician. Aug. 17th, 1942, ablation of  
 the breast. Histologic diagnosis: solid carcinoma.



Pedigree 163.

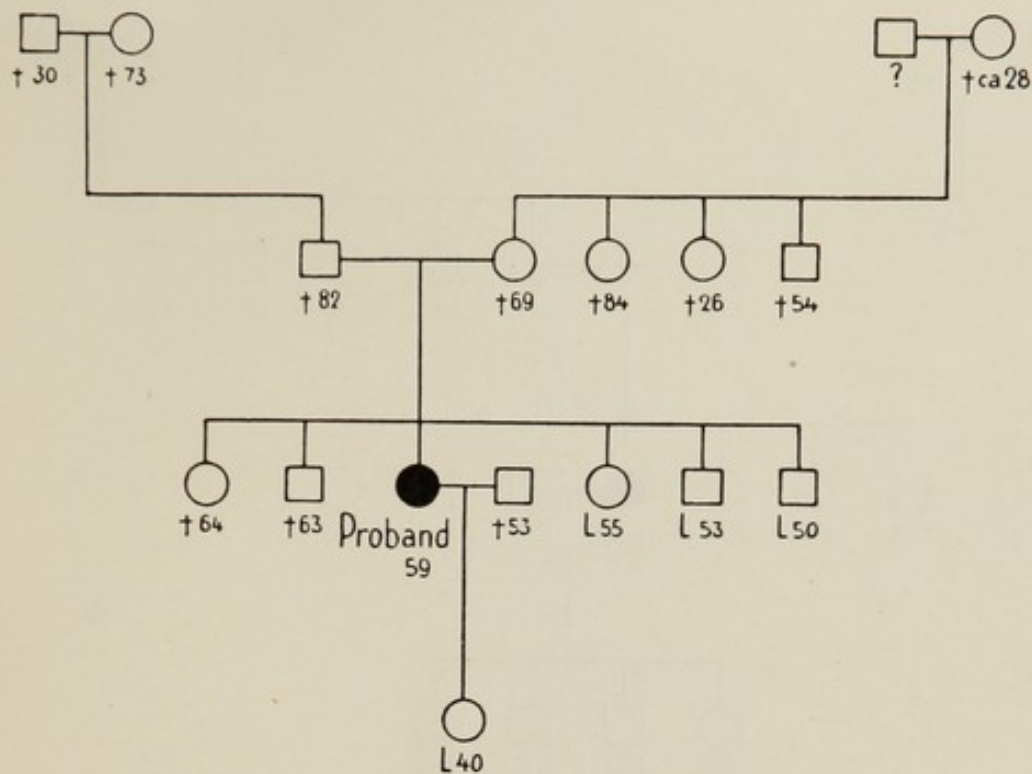
PROBAND (Radium Center, Copenhagen; no. 28749).—○, born in Elsinore July 31st, 1901. ∞ blacksmith. Formerly well. Menstruation from fifteenth to forty-first year, regular. Never pregnant. Slowly growing tumor in right breast noticed a year before she addressed herself to the Radium Center. After ten months a large ulceration had developed, which she treated herself for about two months before she sought medical advice. Oct. 6th, 1942, trephine biopsy. Histologic diagnosis: scirrhus carcinoma. Three months later, the tissue of the left breast felt hard, infiltrated. Trephine biopsy. Histologic diagnosis: solid carcinoma.



Pedigree 164.

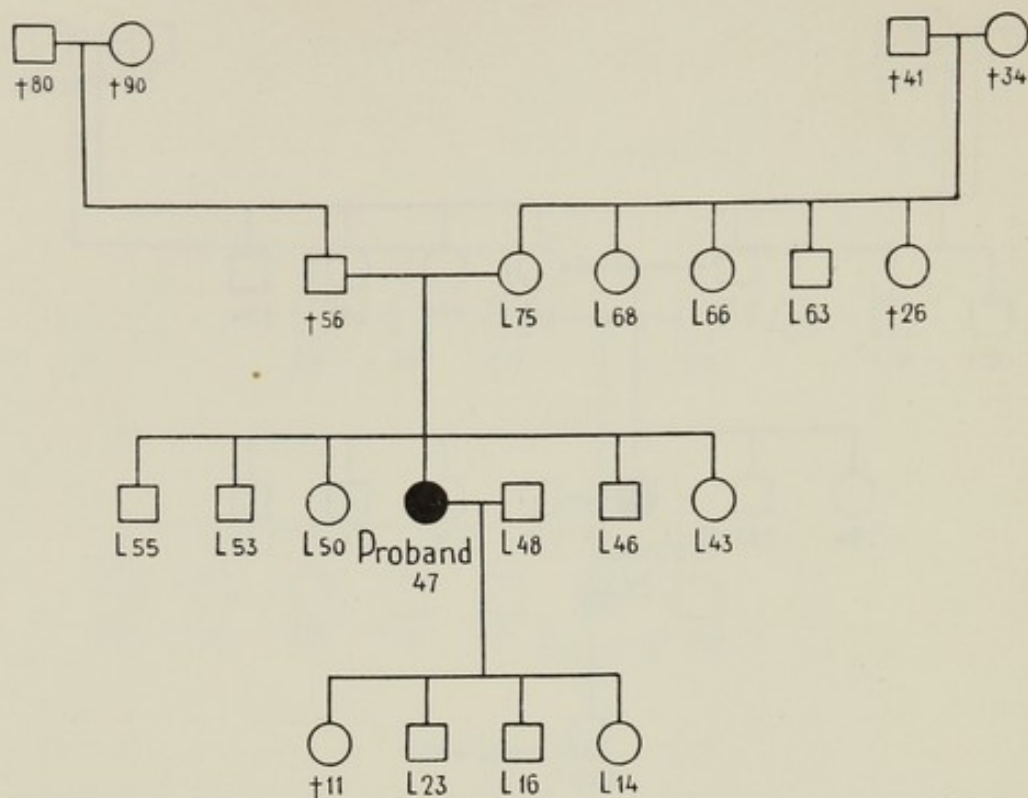
PROBAND (State Hospital, Copenhagen; service D, no. 1154/42).—  
 ○, born Apr. 7th, 1883. Tailor's widow. Formerly well. Menstruation from  
 fourteenth to forty-sixth year, regular. Menopause normal. Never pregnant.  
 Tumor in right breast noticed several years before admission, but as it did  
 not seem to grow larger, she had not sought medical advice. May 29th,  
 1942, trephine biopsy. Histologic diagnosis: solid and scirrhous carcinoma.





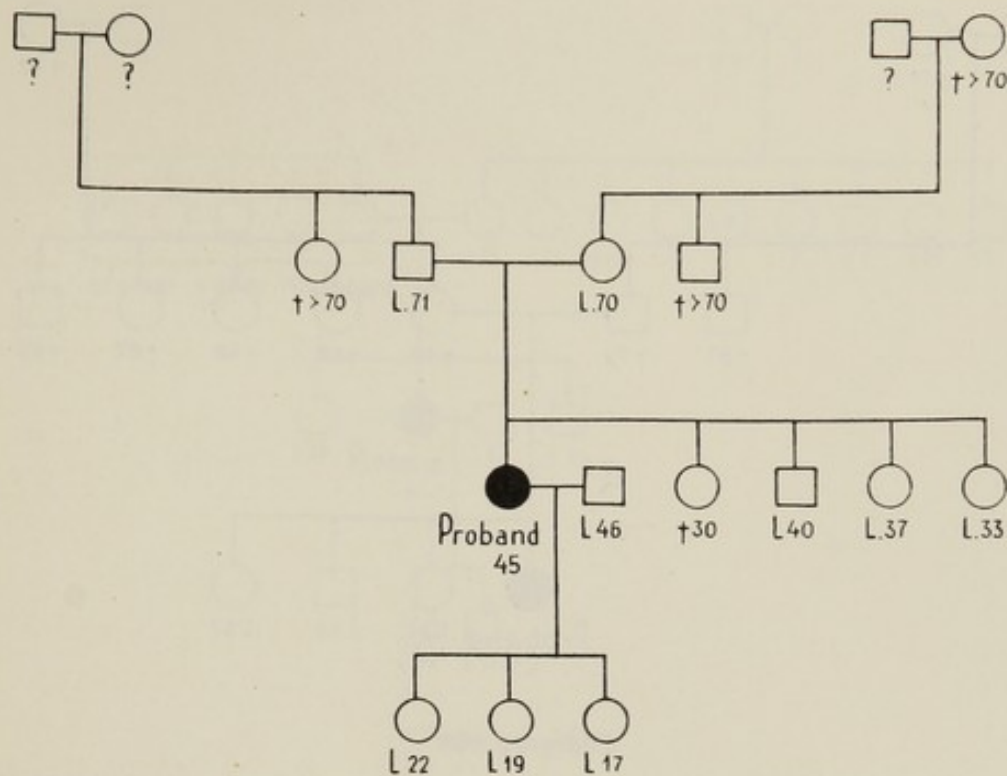
Pedigree 165.

PROBAND (Radium Center, Copenhagen; no. 21890).—○, born in Grenaa Aug. 29th, 1880. Restaurantkeeper's widow. Formerly well. Menstruation from fourteenth to fifty-first year, when she was operated on for fibroma of the uterus. Since then no bleeding. One childbirth. Did not nurse, owing to hypogalactia. Tumor in right breast noticed three months before admission. Apr. 24th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.



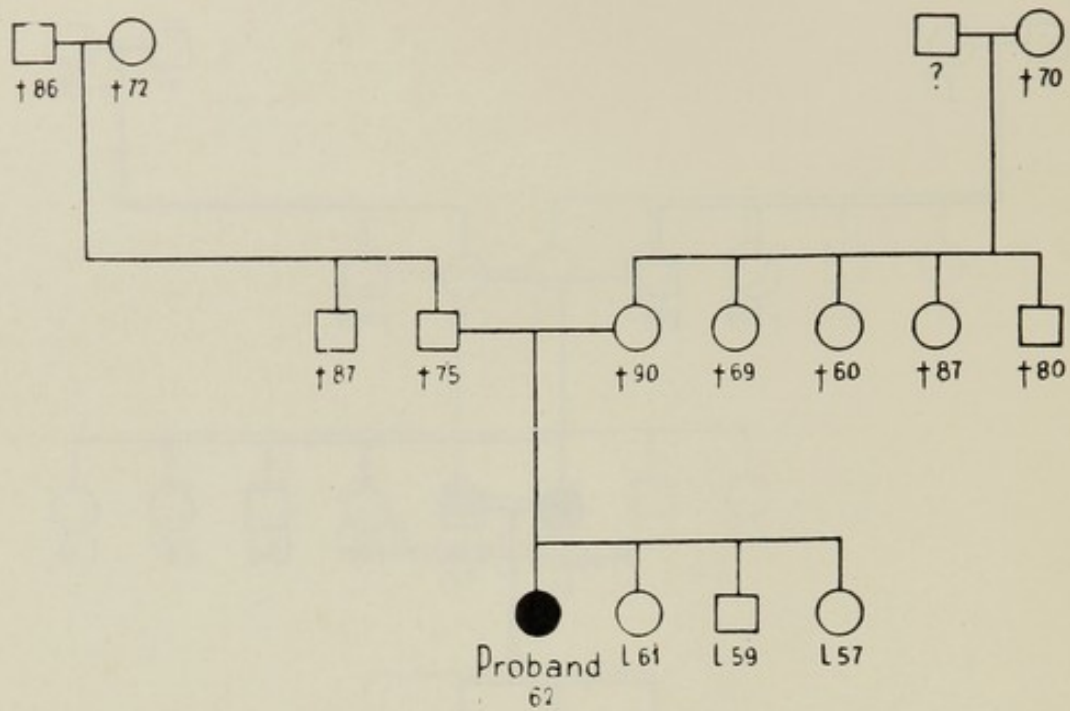
Pedigree 166.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 843/43).—  
 ○, born in Copenhagen Nov. 19th, 1895. ∞ coachman. Formerly well. Menstruation from fourteenth to thirty-ninth year, when she was admitted to the Bispebjerg Hospital, service A, for menorrhagia. Diagnosis: fibroma of the uterus; thence laparotomy and amputation of the supravaginal part of the cervix. Four childbirths. Had to give up nursing, owing to hypogalactia. In 1938, she sustained an injury of her right breast, but there was no swelling or extravasation. The tumor in the breast noticed six months before admission. May 12th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: carcinoma.



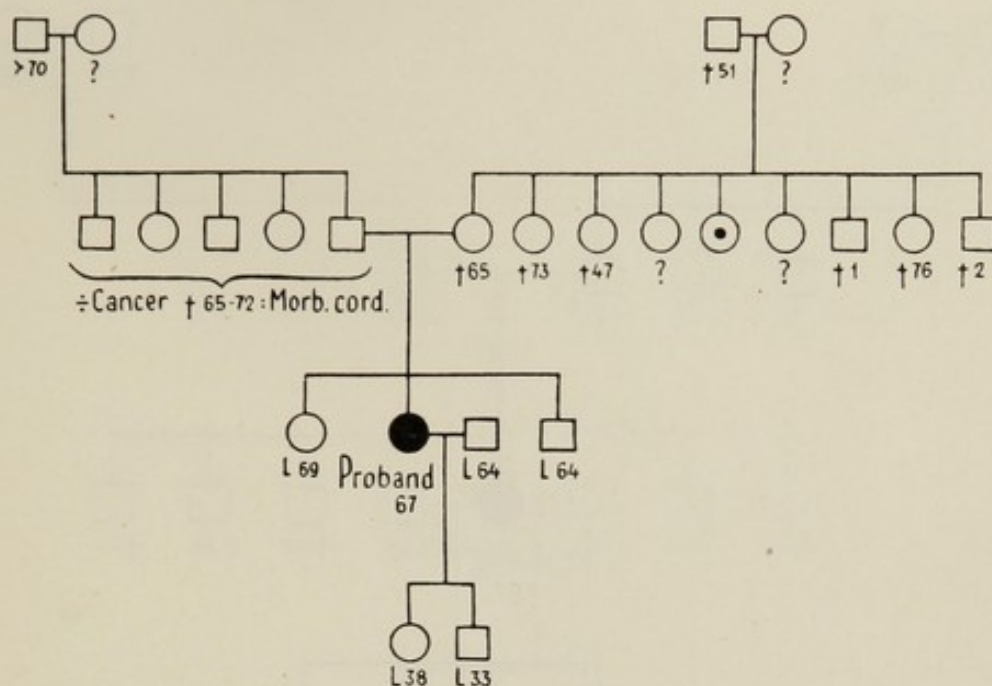
Pedigree 167.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 490/42).—  
 ○, born in Fakse Apr. 13th, 1892. ∞ warehouse workman. Formerly well.  
 Menstruation since fifteenth year, regular. Four childbirths. Nursed all the  
 children for over six months. A year before she noticed the tumor in her  
 left breast, she had hurt the breast badly against a door handle, but did  
 not seek medical advice until a month after the discovery. June 16th, 1937,  
 ablation of the breast, with evacuation of the axilla. Histologic diagnosis:  
 alveolar carcinoma. In 1942, ulcerating metastasis in left axilla.



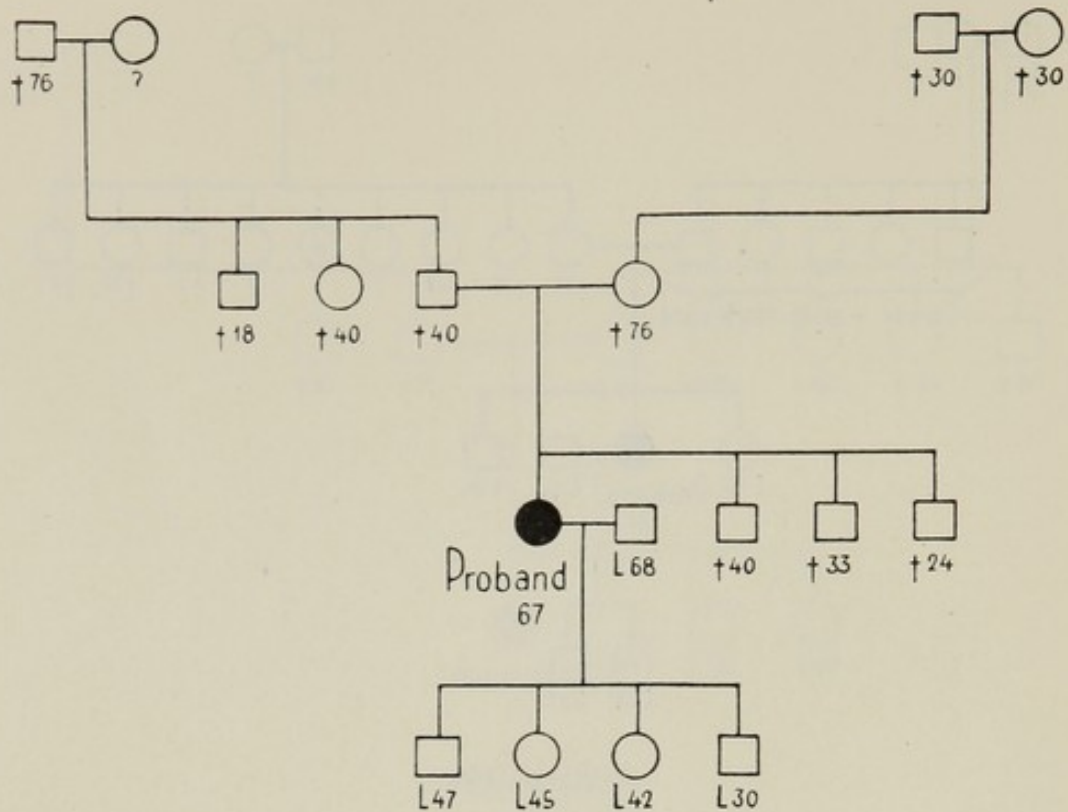
Pedigree 168.

PROBAND (Radium Center, Copenhagen; no. 30822).—○, born in U.S.A. Dec. 25th, 1880. Houseowner; single. Formerly well. Menstruation from fourteenth to forty-fifth year, regular. Menopause normal. Never pregnant. A month before she addressed herself to the Radium Center, she has got a suppurating eruption below the left breast, and at the same time she noticed that this breast was harder than the right. On examination, both breasts were found to be of more than usually firm consistence, and bilateral trephine biopsy was done. Histologic diagnosis: right breast, solid carcinoma; left breast, scirrhous carcinoma.



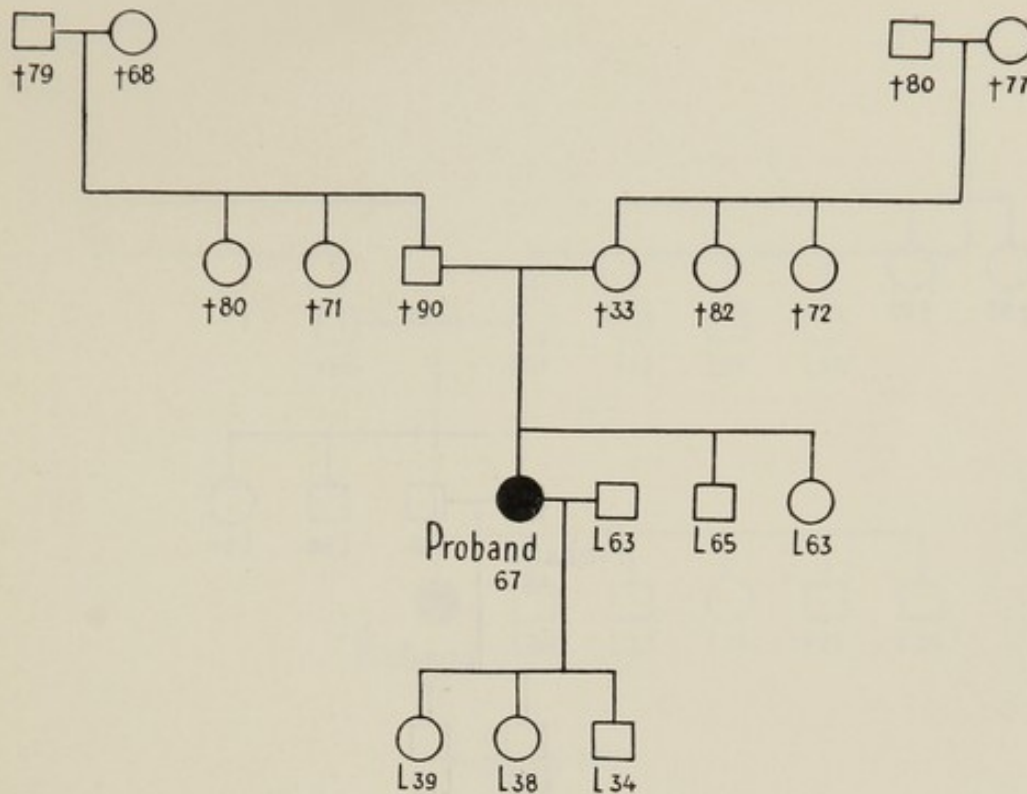
Pedigree 169.

PROBAND (Municipal Hospital, Copenhagen; service 1, no. 1539/42).—  
 ○, born in Copenhagen May 13th, 1875. ∞ trade union president. Formerly  
 well. Menstruation from thirteenth to forty-eighth year, regular. Menopause  
 normal. Two childbirths. Nursed both times only a few weeks, owing to  
 hypogalactia. Tumor in right breast noticed five months before admission.  
 June 29th, 1942, ablation of the breast, with evacuation of the axilla. His-  
 tologic diagnosis: adenomatous and solid scirrhous carcinoma.



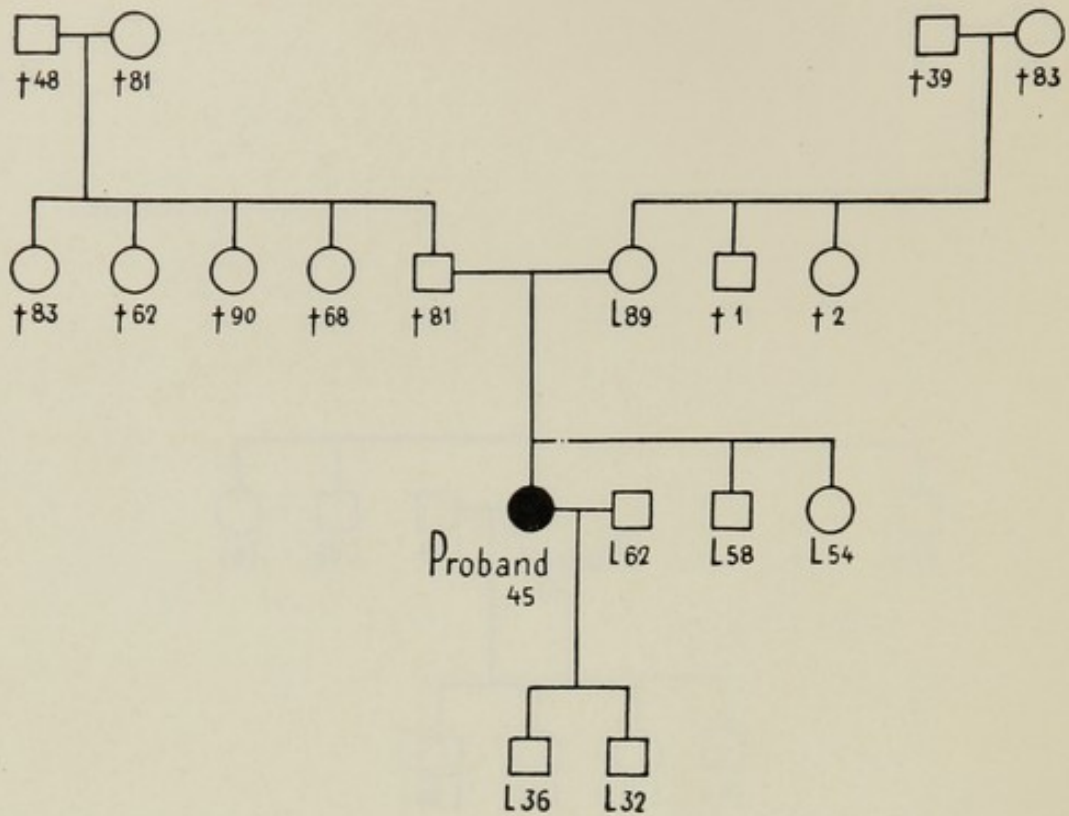
Pedigree 170.

PROBAND (Radium Center, Copenhagen; no. 29608).—○, born in Nakskov July 26th, 1875. ∞ blacksmith. Formerly well. Menstruation from fourteenth to forty-fifth year, regular. Menopause normal. Four childbirths. Nursed all the children for over six months. Tumor in right breast noticed two months before admission. March 26th, 1943, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous adenocarcinoma.



Pedigree 171.

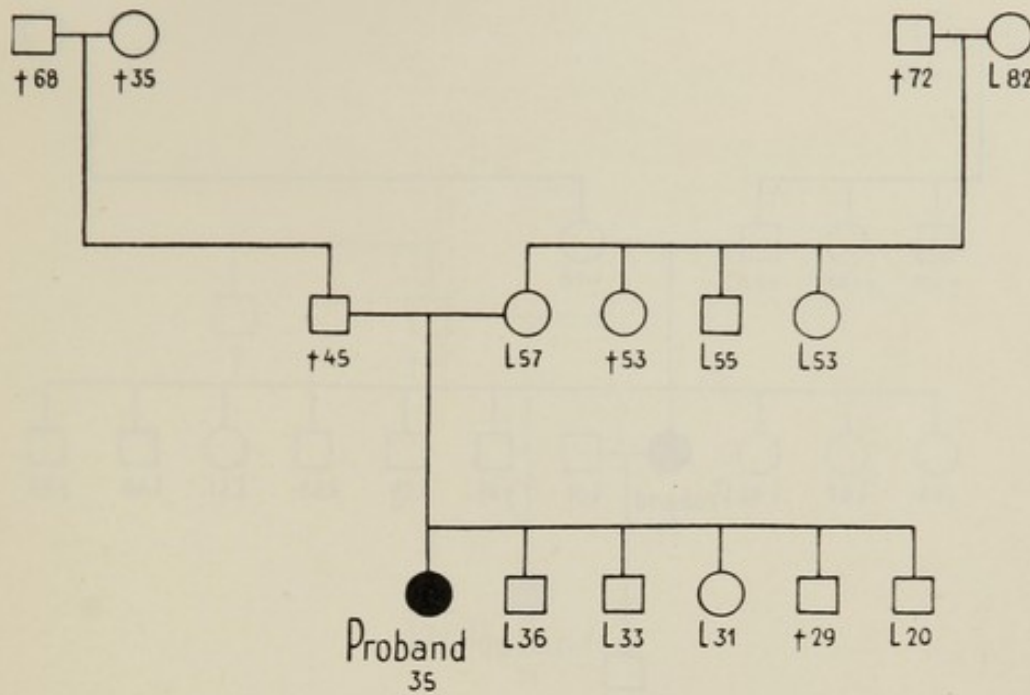
PROBAND (Radium Center, Copenhagen; no. 29884).—○, born in Sweden Jan. 1st, 1876. ∞ workingman. Formerly well. Menstruation from fourteenth to forty-eighth year, regular. Menopause normal. Three childbirths. Nursed a year each time. Tumor in left breast noticed four years before admission, but medical advice not sought, because it did not grow larger and did no cause her any discomfort. When she finally was hospitalised, a large tumor was found also in the right breast. Bilateral biopsy. Histologic diagnosis: scirrhus carcinoma.



Pedigree 172.

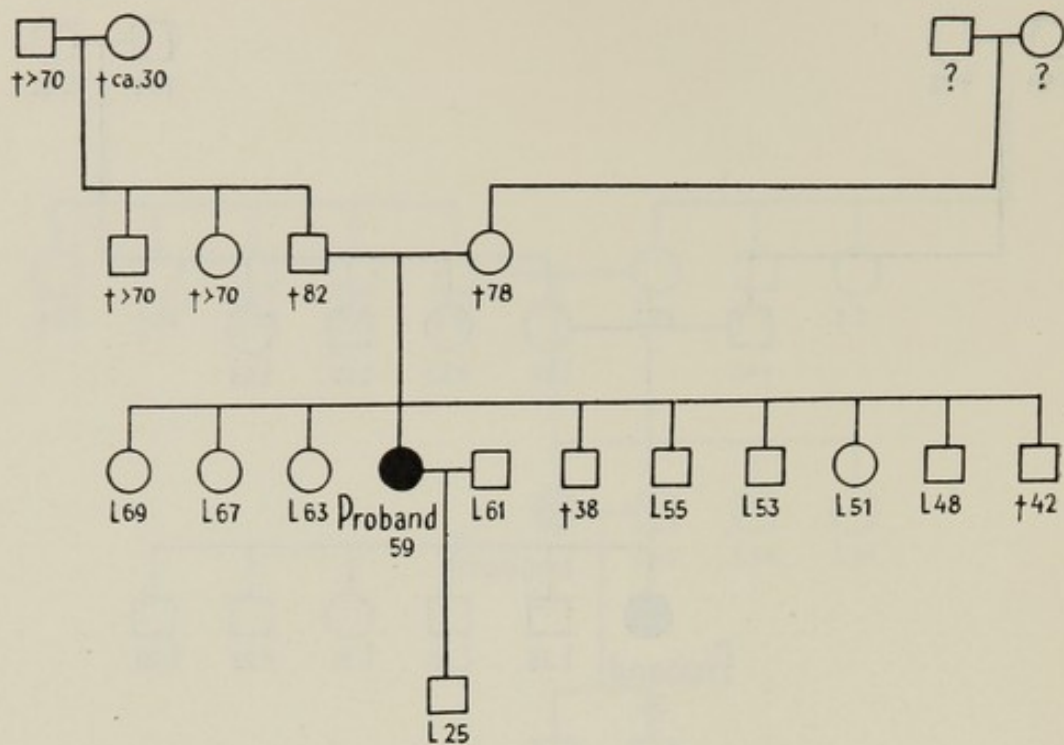
PROBAND (Radium Center, Copenhagen; no. 26232).—○. born in Assens March 26th, 1881. ∞ cabinetmaker. Formerly well. Menstruation from fifteenth to forty-third year, regular. Menopause normal. Two childbirths. Nursed only a few weeks both times, owing to hypogalactia. In 1925, she fell and hurt her right breast badly against the edge of a bed. About a year afterwards she noticed a tumor in the breast. June 8th, 1926, ablation of the breast in St. Joseph's Hospital, Copenhagen. Histologic diagnosis: carcinoma. In 1941 treated at the Radium Center, for recurrence. Biopsy. Histologic diagnosis: adenocarcinoma and solid carcinoma.





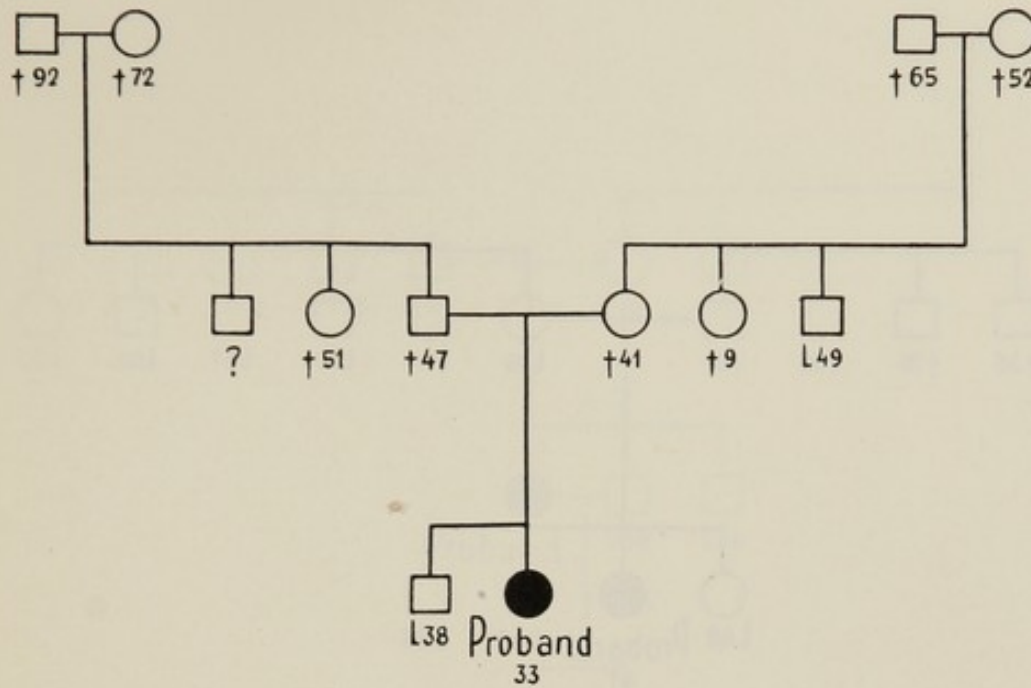
Pedigree 173.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 1/41).—○, born in Randers Dec. 17th, 1905. ∞ shop assistant. Formerly well. Menstruation since eighteenth year, regular. Never pregnant. Tumor only discovered when she consulted a physician for pain in the right breast. It had by then attained the size of a hen's egg. Dec. 17th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.



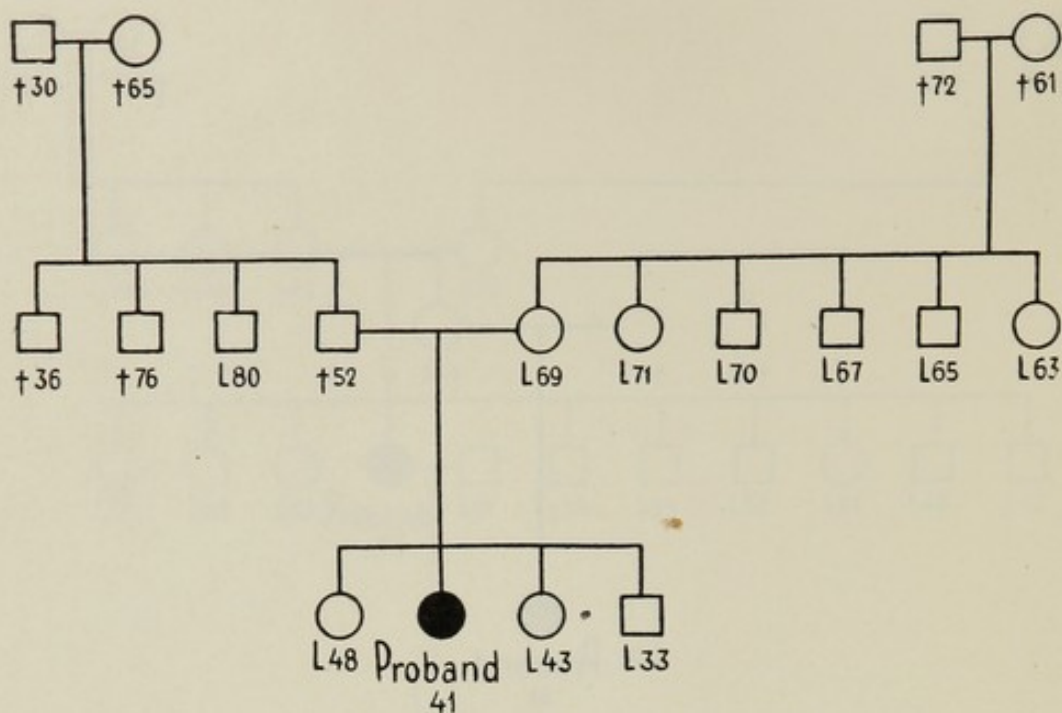
Pedigree 174.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 234/40).—  
 ○, born in Nørre Omme May 10th, 1881. ∞ machine worker. Formerly well.  
 Menstruation from fourteenth to forty-ninth year, regular. Menopause  
 normal. One childbirth. Nursed nine months. Tumor in left breast noticed  
 about a year before admission. Aug. 26th, 1940, ablation of the breast, with  
 evacuation of the axilla. Histologic diagnosis: solid scirrhous carcinoma.



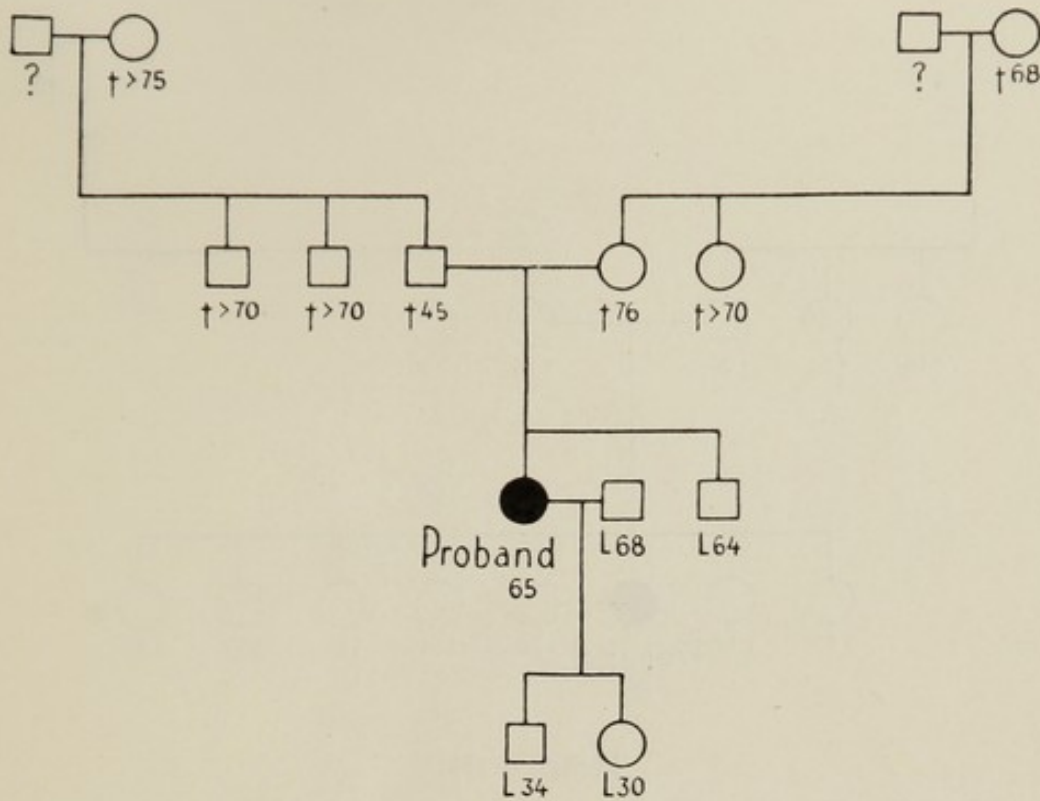
Pedigree 175.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 433/41).—  
 ○, born in Fredericia Apr. 28th, 1908. Domestic science teacher; single.  
 Menstruation since fourteenth year, regular. Never pregnant. Tumor in left  
 breast noticed three months before admission. Oct. 16th, 1941, ablation of  
 the breast, with evacuation of the axilla. Histologic diagnosis: solid scir-  
 rous carcinoma.



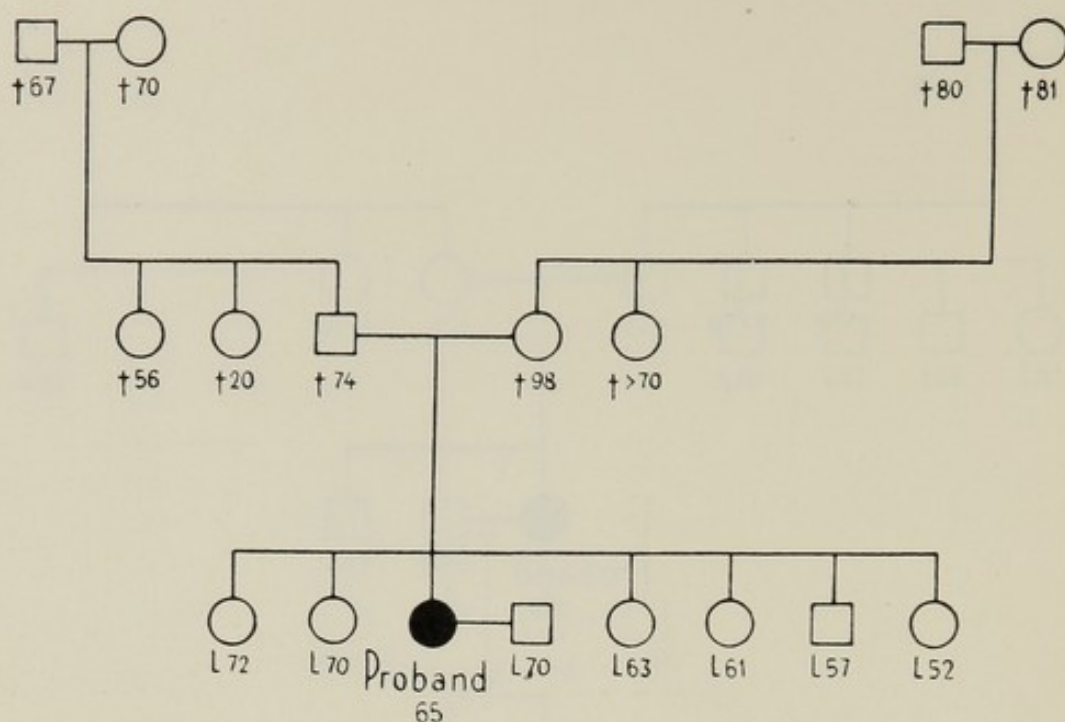
Pedigree 176.

PROBAND (State Hospital, Copenhagen; service C, no. 2283/42).—○, born in Copenhagen Aug. 20th, 1897. Dressmaker; single. Formerly well. Menstruation from fourteenth to forty-fourth year, regular. Menopause normal, except for some very troublesome hot flushes, for which she since Oct. 1942 has been treated with neurovex tablets. Never pregnant. Two years before admission to the State Hospital, service C, in 1938, she had noticed a slowly growing tumor in her left breast. Nov. 24th, 1938, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous carcinoma. Since Oct. 1942 treated at the Radium Center, Copenhagen, for metastases to the spinal column.



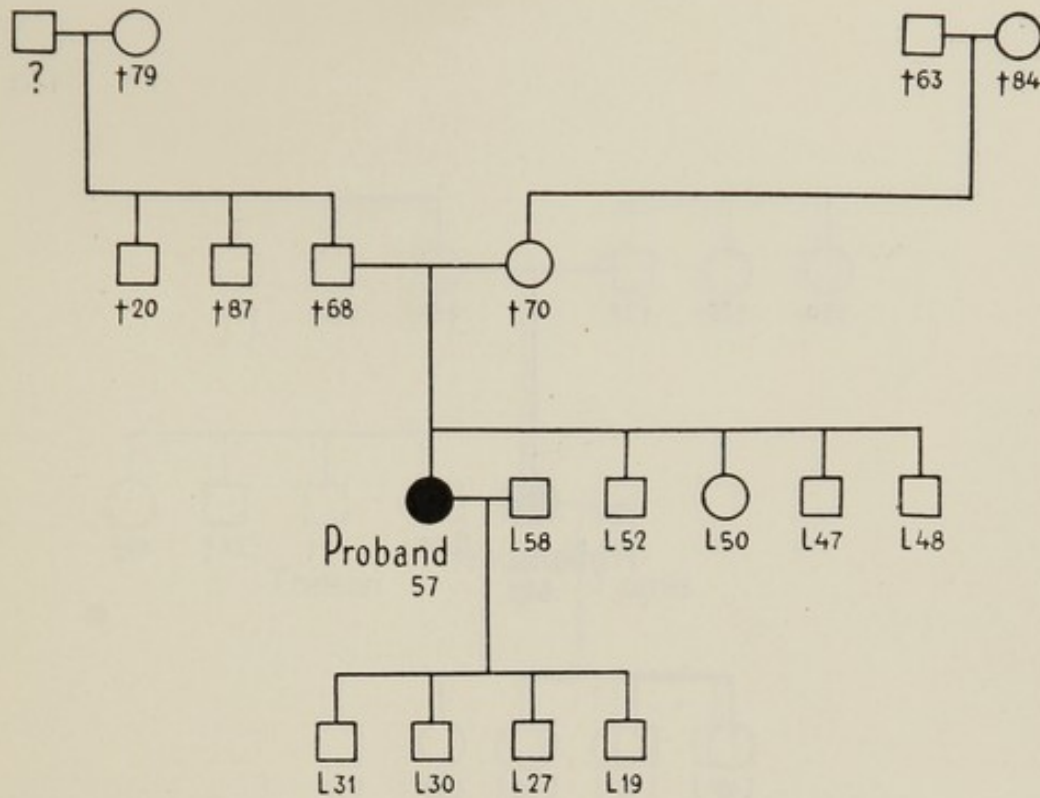
Pedigree 177.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 287/40).—  
 ○, born in Copenhagen June 18th, 1874. ∞ provision dealer. Formerly well.  
 Menstruation from fifteenth to forty-sixth year, regular. Menopause normal.  
 Two childbirths. Nursed only a couple of months each time, owing to hypo-  
 galactia. Tumor in the left breast noticed about two months before admis-  
 sion. Aug. 6th, 1940, ablation of the breast, with evacuation of the axilla.  
 Histologic diagnosis: solid carcinoma.



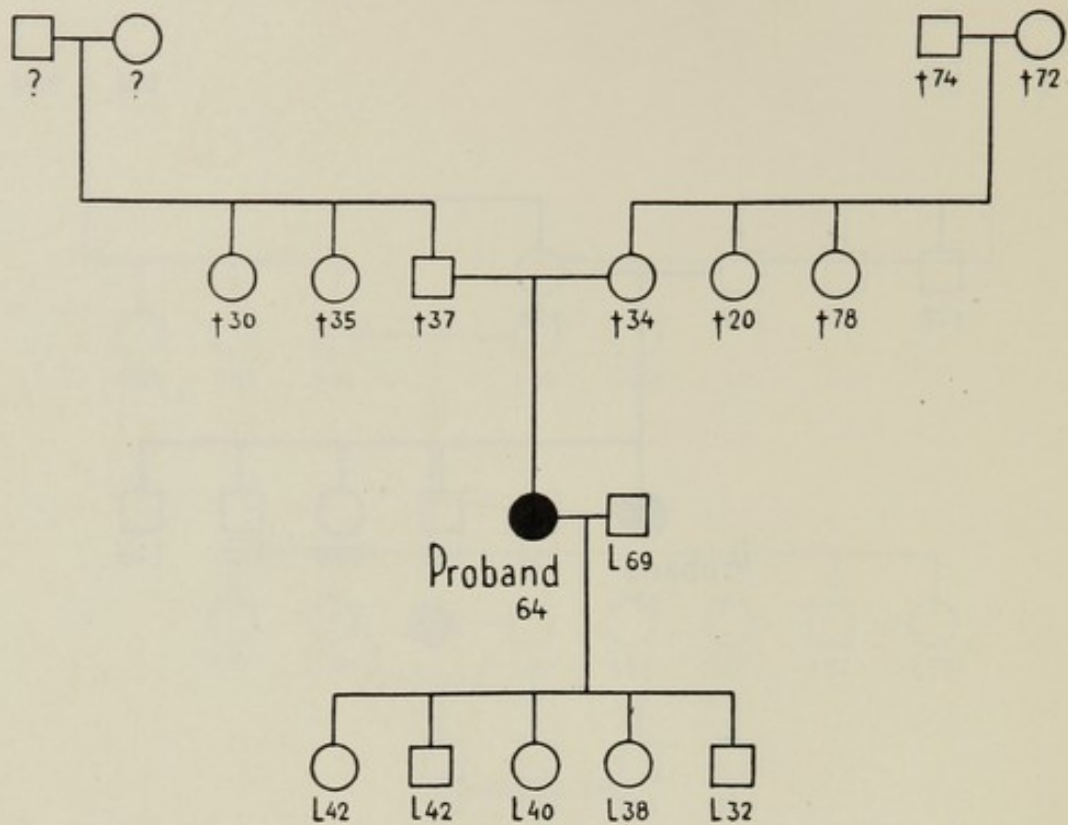
Pedigree 178.

PROBAND (Sundby Hospital, Copenhagen; surg. service, no. 301/42).—  
 ○, born in Tversted Sep. 22nd, 1878. ∞ shoemaker. Formerly well. Menstruation from fourteenth to forty-eighth year, regular. Menopause normal. Never pregnant. Tumor in right breast noticed two weeks before admission. Jan. 7th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous carcinoma.



Pedigree 179.

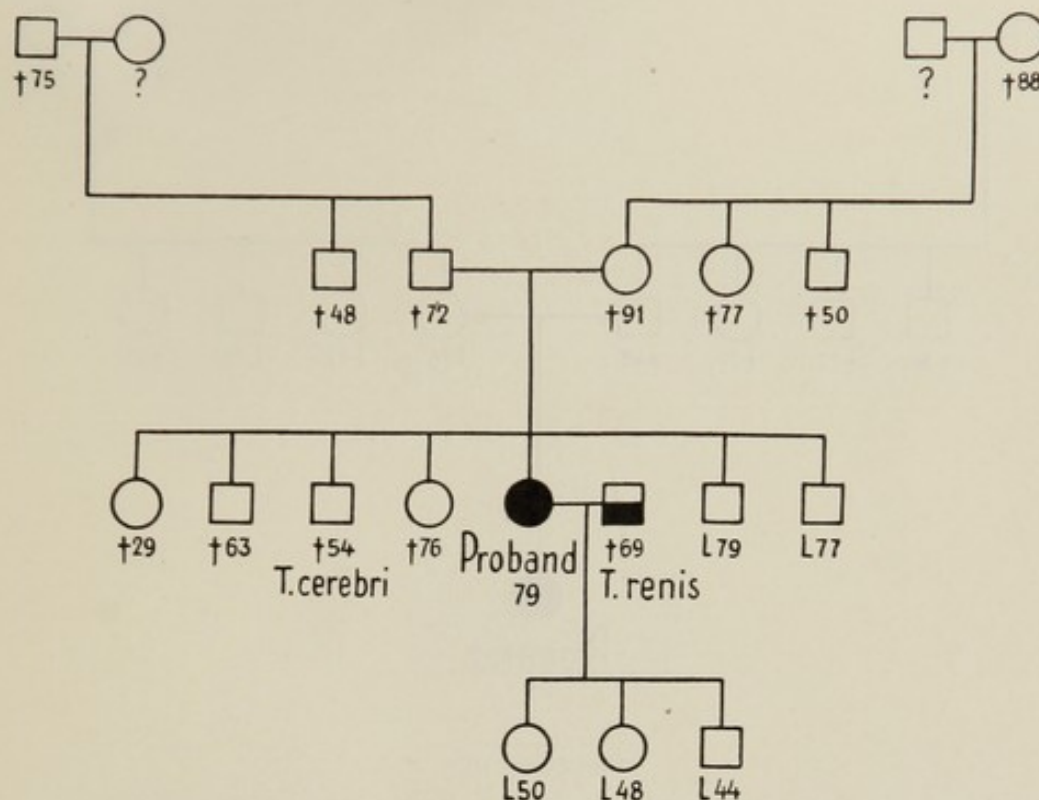
PROBAND (Radium Center, Copenhagen; no. 31033).—○, born in Copenhagen March 9th, 1886. ∞ old age pensioner. Formerly well. Menstruation from fourteenth to fifty-fourth year, regular. Menopause normal. Four child-births. Nursed about eight months each time; no complications. Tumor in right breast noticed six months before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.



Pedigree 180.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 804/42). —○, born in Hjørring May 6th, 1878. ∞ restaurant keeper. Formerly well. Menstruation from fourteenth to fiftieth year, regular. Menopause normal. Five childbirths. Nursed only about two months each time, owing to hypogalactia. Tumor in left breast noticed a year before admission. March 28th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid and adenomatous carcinoma.

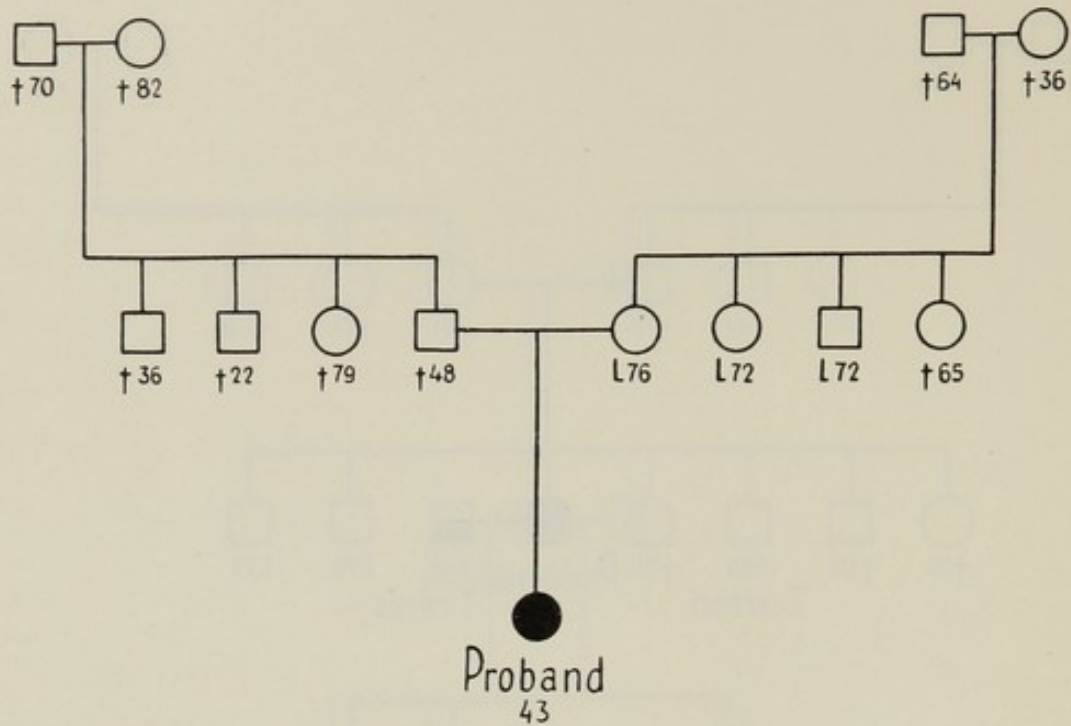




Pedigree 181.

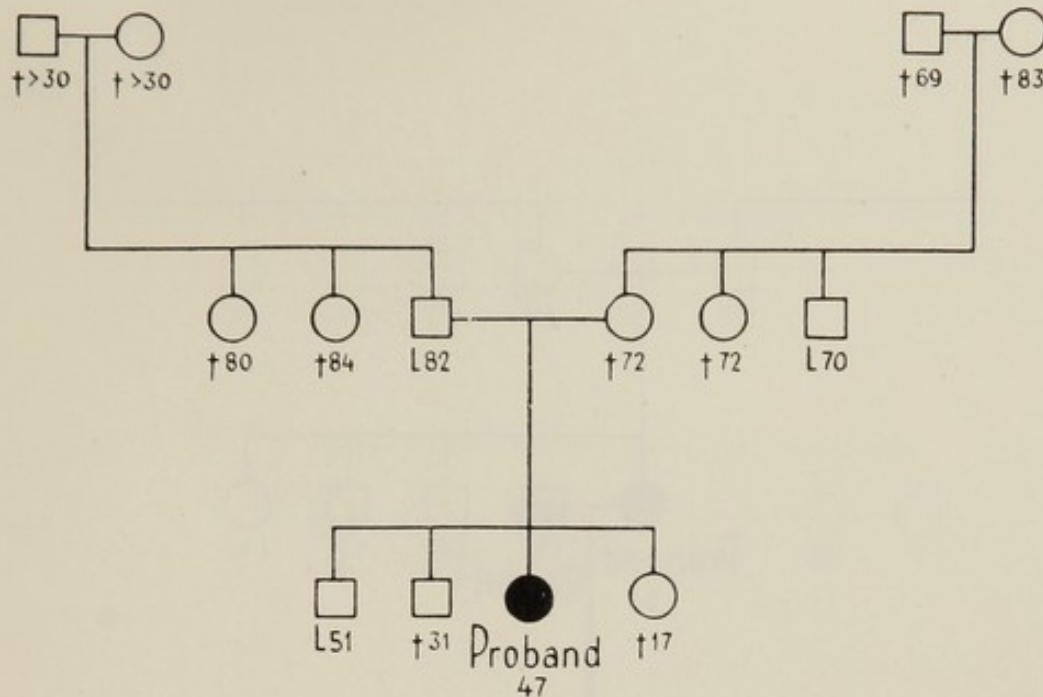
PROBAND (Radium Center, Copenhagen; no. 23297).—○, born in Ondløse Oct. 4th, 1861. Widow. Formerly well. Menstruation from thirteenth to fifty-third year, regular. Menopause normal. Three childbirths. Nursed from eight to ten months. Six months before admission she had fallen and hurt her right breast against a ladder. No swelling or extravasation. Five months later she noticed a lump in the breast and treated herself by painting with iodine. Trephine biopsy. Histologic diagnosis: solid carcinoma.

NEXT ELDEST BROTHER.—Born 1853 in Ondløse. Engine driver. Died May 1st, 1907, in the Municipal Hospital, Copenhagen, service C, of tumor of the brain. Diagnosis (according to the hospital journal): hemorrhagic cerebral tumor. Necropsy being refused, no histologic examination could be made; it is therefore impossible to say if the tumor was malignant.



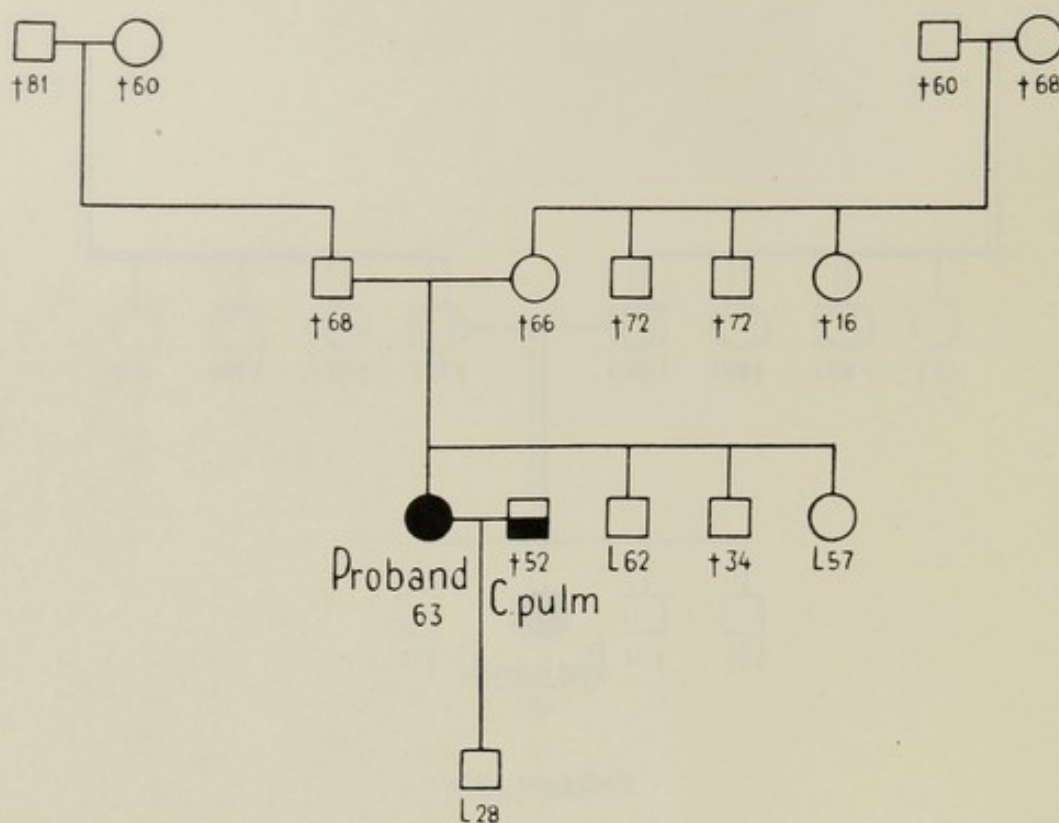
Pedigree 182.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 298/42).—  
 ○, born in Copenhagen Oct. 2nd, 1897. Clerk; single. As child and young well. Menstruation since fourteenth year, regular until a year ago, when the intervals became longer and the bleeding very profuse. Jan. 1942, curettage of uterine mucosa. Histologic diagnosis on basis of specimen removed: climacteric changes of irregular hyperplastic character. Never pregnant. Tumor in left breast noticed four months before admission. Jan. 28th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid, partly scirrhous carcinoma.



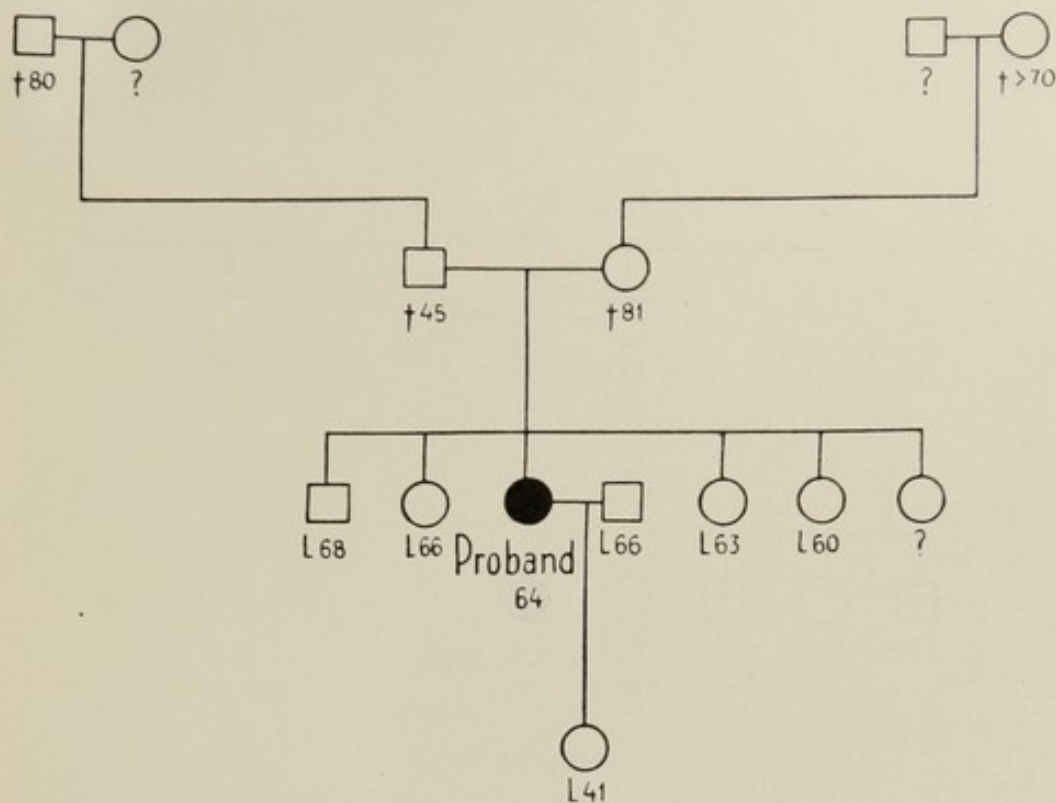
Pedigree 183.

PROBAND (Radium Center, Copenhagen; no. 31633).—○, born in Vordingborg July 31st, 1896. Housekeeper; single. Formerly well. Menstruation since fifteenth year, regular until a year before admission, when the intervals became longer and the bleeding more profuse. At the same time headaches and troublesome heat flashes, for which she was during seven months treated with estibilin, 2 tablets, each of 0.1 mg., daily. Never pregnant. Tumor in left breast noticed a week before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.



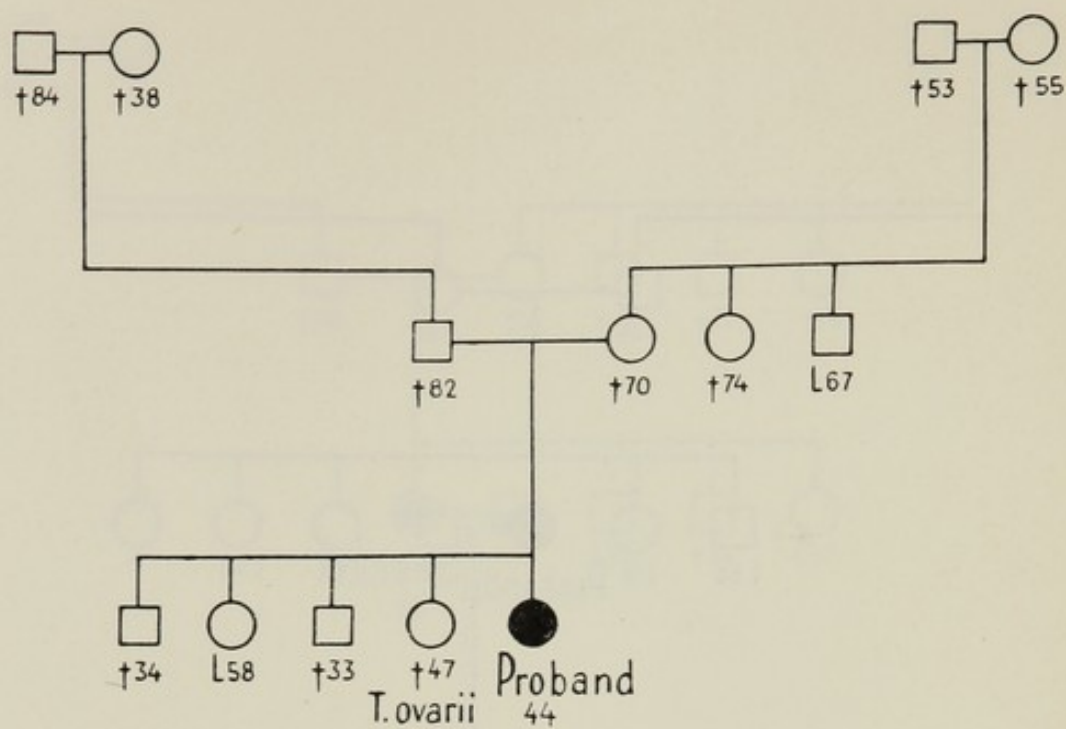
Pedigree 184.

PROBAND (Radium Center, Copenhagen; no. 26000).—○, born in Skuderløse Aug. 11th, 1878. Tailor's widow. Formerly well. Menstruation from seventeenth to fifty-second year. Menopause normal. One childbirth. Nursed only about three months, owing to work outside the home. Tumor in right breast noticed a month before admission. Jan. 15th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus carcinoma.



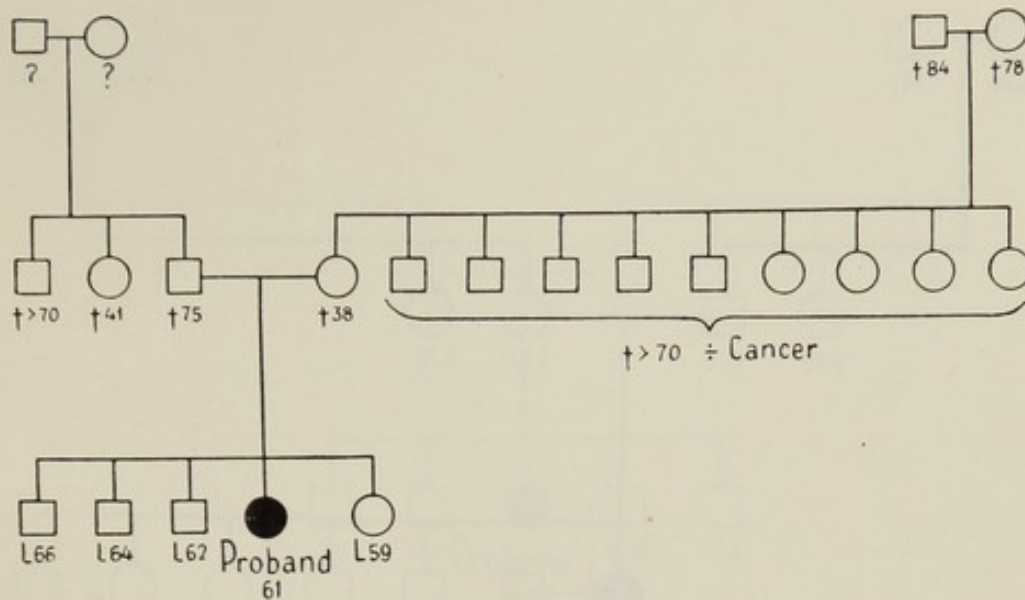
Pedigree 185.

PROBAND (State Hospital 1, Copenhagen; radiol. service, no. 701/42).—  
 ○, born in Løvel parish May 17th, 1877. ∞ goldsmith. Formerly well. Menstruation from fifteenth to fortieth year, regular. Menopause normal. One childbirth. Nursed only two months, owing to hypogalactia. Thinks she remembers having fallen and hurt her left breast about fifteen years ago. Has been aware of a slowly growing tumor in the breast for over a year before admission. Nov. 26th, 1941, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid, partly colloid carcinoma.



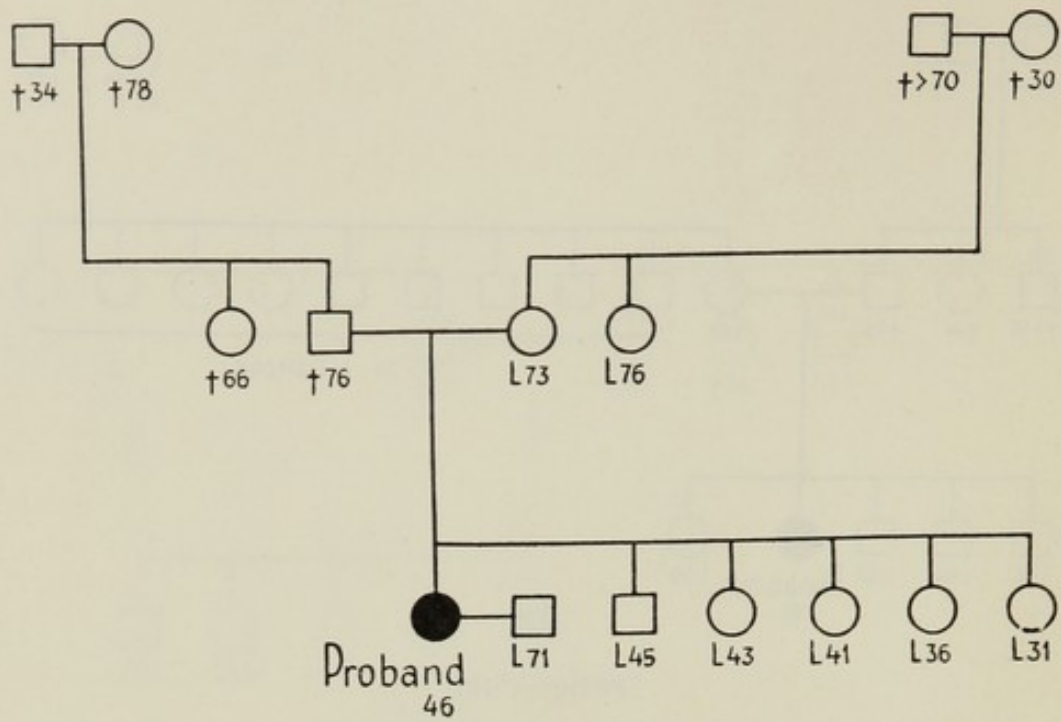
Pedigree 186.

PROBAND (Radium Center, Copenhagen; no. 25433).—○. born in Nykøbing, Falster, May 6th, 1897. Housekeeper; single. Formerly well. Menstruation since fifteenth year, regular; the bleeding of late less profuse than before. Never pregnant. Tumor in left breast noticed three months before admission. Trephine biopsy. Histologic diagnosis: adenocarcinoma.



Pedigree 187.

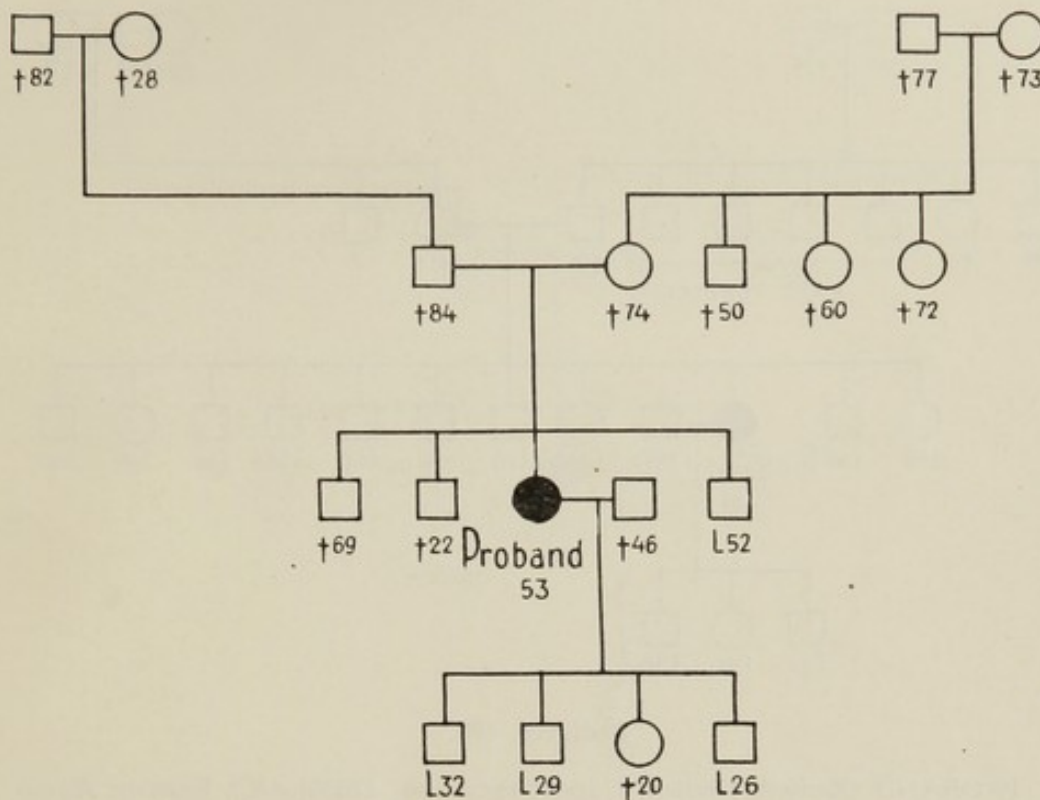
PROBAND (State Hospital, Copenhagen; radiol. service, no. 441/40).—  
 ○, born Nov. 30th, 1879. Domestic servant; single. Formerly well. Menstruation from nineteenth to forty-fourth year, regular. Menopause normal. Never pregnant. Tumor in left breast noticed three months before admission. Aug. 17th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.



Pedigree 188.

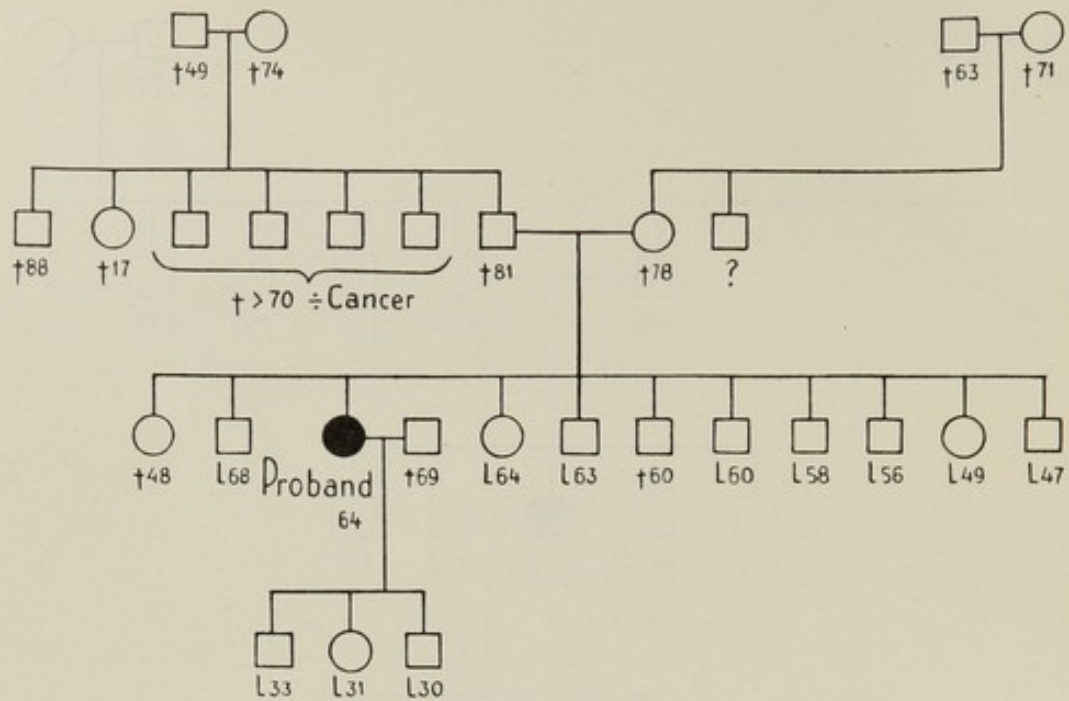
PROBAND (Radium Center, Copenhagen; no. 26836).—○, born in Haderslev Febr. 5th, 1896. ∞ engineer. Formerly well. Menstruation since fifteenth year, regular. Never pregnant. Walnut-sized tumor in right breast noticed six months before admission. March 26th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid medullary carcinoma.





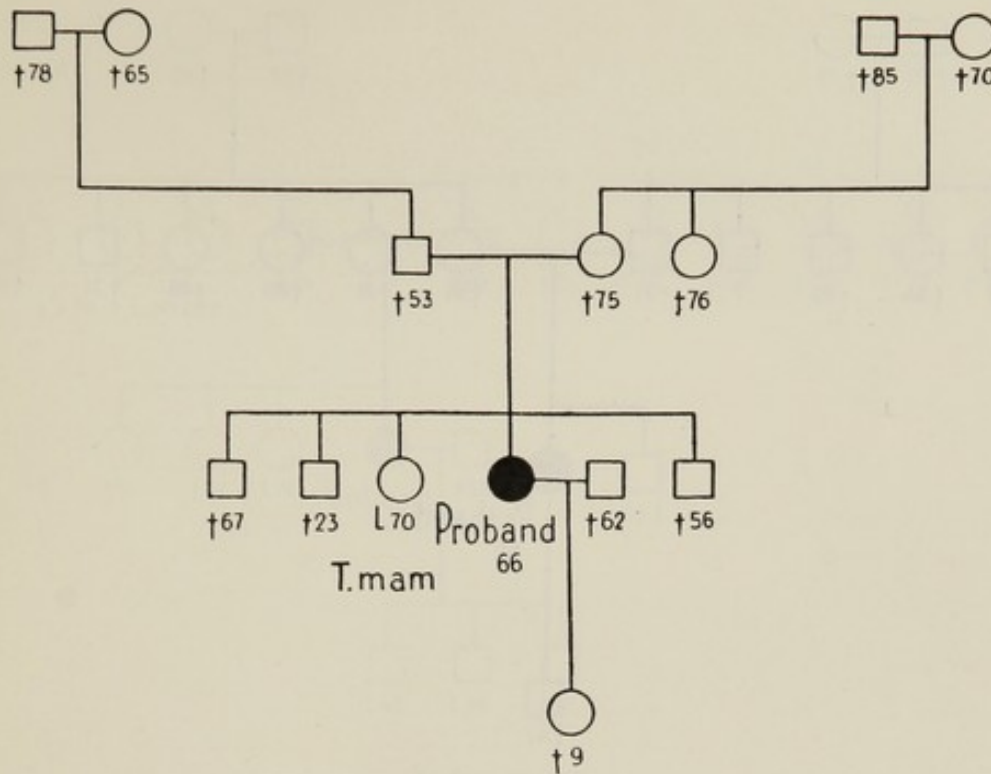
Pedigree 189.

PROBAND (Radium Center, Copenhagen; no. 20703).—○, born in Vejle June 29th, 1886. Policeman's widow. Formerly well. Menstruation from fourteenth to fifty-second year. Menopause normal. Four childbirths. Nursed respectively ten, twelve, four and fourteen months. During the second lactation, galactophoritis of left breast. In 1937 during three months treated with ovex (1 tablet 3 times daily) for nervousness. Had for over two years before admission noticed increasing retraction of the left nipple, but did not go to doctor until she got pains in the left axilla and upper arm, and paresthesia in the fingers of the left hand. June 1939, biopsy. Histologic diagnosis: adenocarcinoma. In May, 1943, she was still receiving ambulant treatment; there were now metastases to the skin extending all the way up into the left axilla, and metastases to the spinal column.



Pedigree 190.

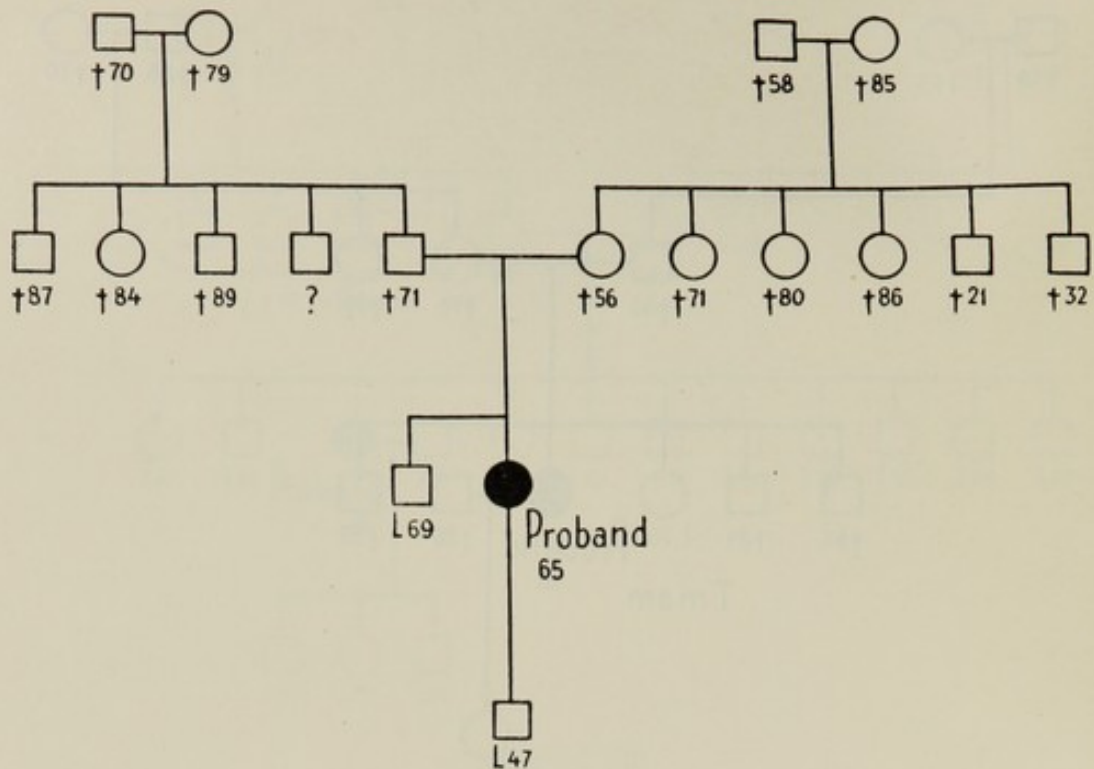
PROBAND (Radium Center, Copenhagen; no. 23836).—○, born in Ærøskøbing Jan. 14th, 1877. Physician's widow. Formerly well. Menstruation from fifteenth to fortieth year, regular. Three childbirths. Lactations normal. Has for over twenty years had a small cicatrix in the right breast, which she believes is due to pressure of a whalebone in her stays. About a year before admission, a small ulcer developed in its place, which refused to heal. Biopsy. Histologic diagnosis: scirrhus carcinoma.



Pedigree 191.

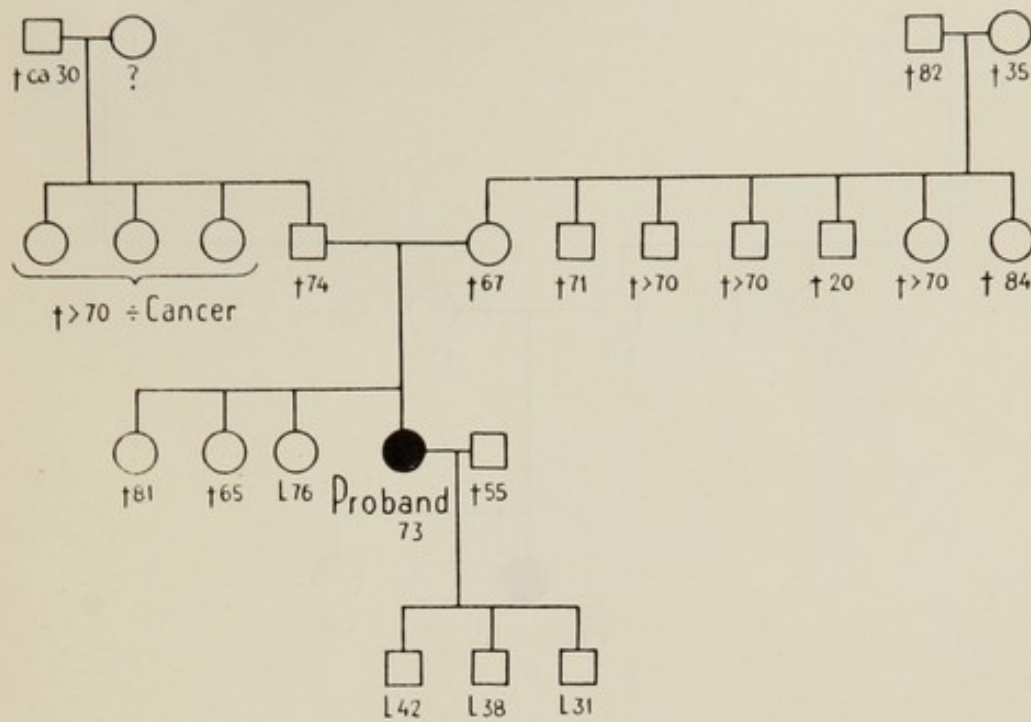
PROBAND (Deaconesses' Hospital, Copenhagen; service B, no. 678/42).—  
 ○, born in Svendborg July 4th, 1875. Farm overseer's widow. Since youth  
 a sufferer from bronchial asthma. In 1921 operation for gallstone. Mens-  
 truation from fifteenth to fifty-second year, regular. Menopause normal.  
 One childbirth. Nursed barely three months, owing to hypogalactia. Six  
 months before she noticed the tumor in her right breast, she had fallen  
 and hurt the breast badly against a door handle. No swelling or extra-  
 vasations. Apr. 22nd, 1942, ablation of the breast, with evacuation of the  
 axilla. Histologic diagnosis: solid carcinoma.

SISTER.—Born 1873 in Svendborg. Housekeeper. When she was recently  
 admitted to the Frederiksberg Hospital, Copenhagen, for another affection,  
 the examination revealed a tumor in the right breast, described in the  
 journal as circumscribed, hazelnut-sized, indolent and displaceable. No  
 retraction of the nipple. No enlarged lymph glands. As the patient refused  
 operation, it cannot be determined if the tumor was malignant.



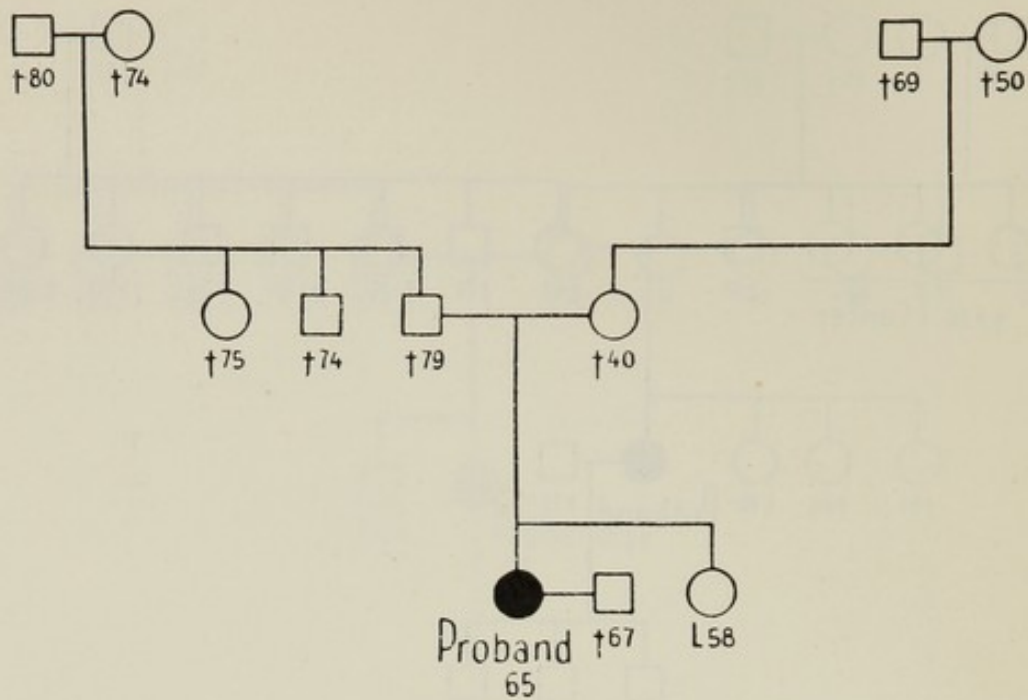
Pedigree 192.

PROBAND (Radium Center, Copenhagen; no. 31559).—○, born in Copenhagen July 3rd, 1877. Old age pensioner; single. As child and young well. Receiving invalidity pension on account of emphysema of the lungs and arterial hypertension. Menstruation from fourteenth to thirty-eighth year, regular. One childbirth. Did not nurse, owing to puerperal fever. At the same time bilateral galactophoritis. Tumor in right breast noticed three months before admission. Trephine biopsy. Histologic diagnosis: adenocarcinoma and solid carcinoma.



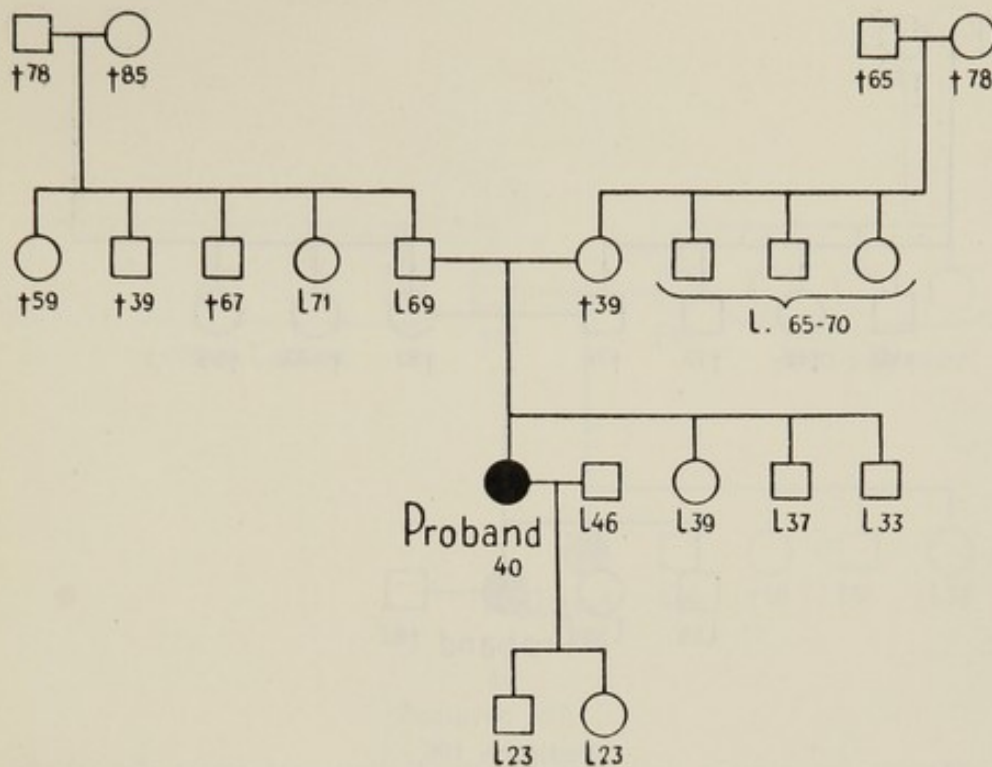
Pedigree 193.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 3828/42).—  
 ○, born in Løgstør Oct. 7th, 1869. Farmer's widow. Formerly well. Menstruation from fourteenth to forty-seventh year, regular. Menopause normal. Three childbirths. Lactations normal. Tumor in left breast not noticed until three days before admission. Trephine biopsy. Histologic diagnosis: solid carcinoma.



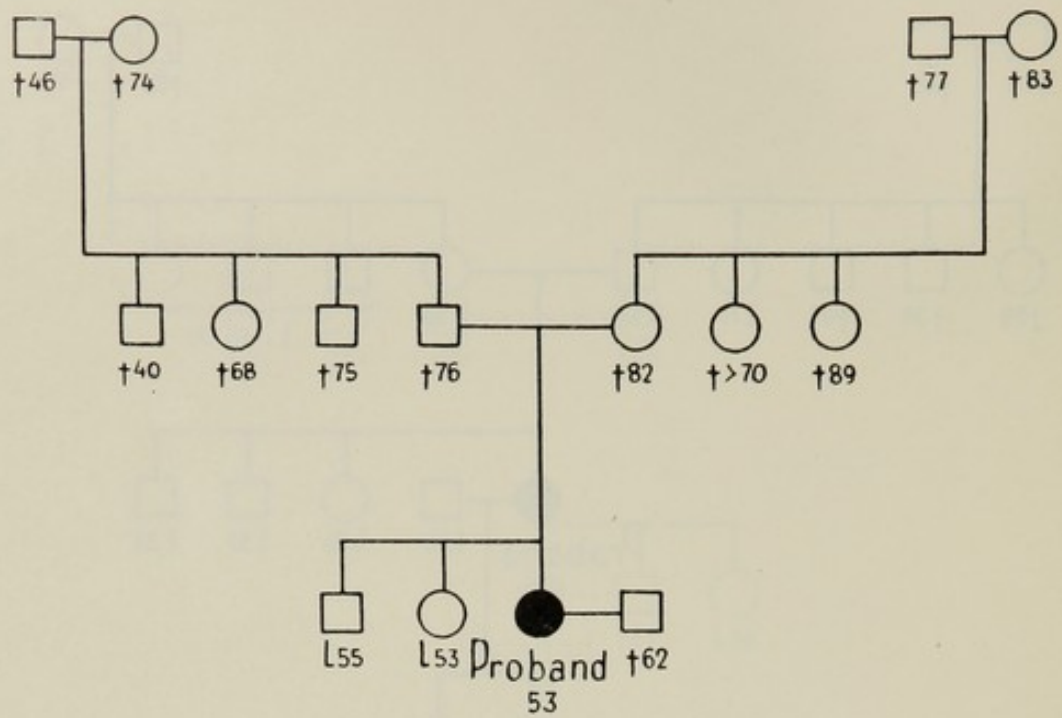
Pedigree 194.

PROBAND (Bispebjerg Hospital, Copenhagen; service A, no. 141/42).—  
 ○, born in Copenhagen Dec. 31st, 1876. Manufacturer's widow. As child and young well. Menstruation from fifteenth to fifty-second year, regular. Menopause normal. In 1938, operation for gallstone. Aware of a slowly growing tumor in her right breast for over two years before she consulted a physician. Dec. 22nd, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhus adenocarcinoma.



Pedigree 195.

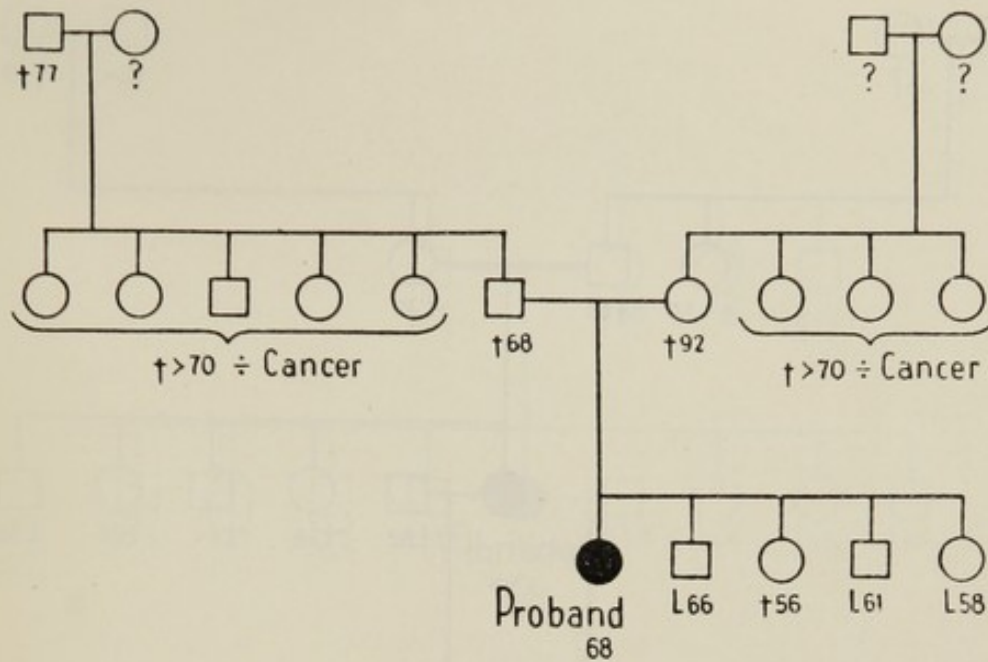
PROBAND (Radium Center, Copenhagen; no. 22163.—○, born in Copenhagen Aug. 14th, 1899. Factory worker; divorced. Formerly well. Menstruation from fourteenth to thirty-ninth year, regular. Menopause normal. One childbirth (twins). During the lactation suppurating mastitis of right breast, treated with incisions. Had for six months before admission noticed retraction of the nipple and increasing shrinking of the entire right breast. June 20th, 1940, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: scirrhous carcinoma.



Pedigree 196.

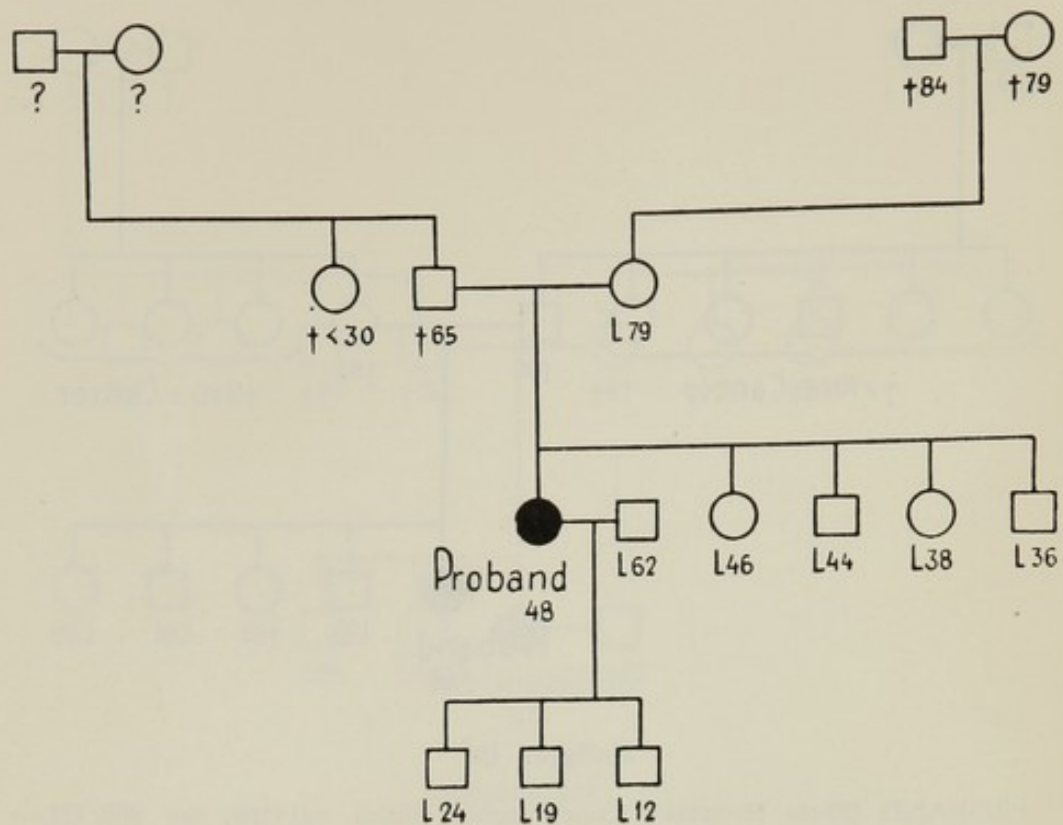
PROBAND (Deaconesses' Hospital, Copenhagen; service A, no. 78/42).—  
 ○, born Feb. 1st, 1888. Widow. Formerly well. Menstruation from thirteenth to fifty-third year, regular. For two years (1939-1941) treated with ovex, for climacteric disorders, in periods of three months during which she was given 1 tablet (2000 I.U.) daily, alternating with three months' suspension of treatment. Tumor in right breast noticed a month before admission. Jan. 29th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: milk duct carcinoma.





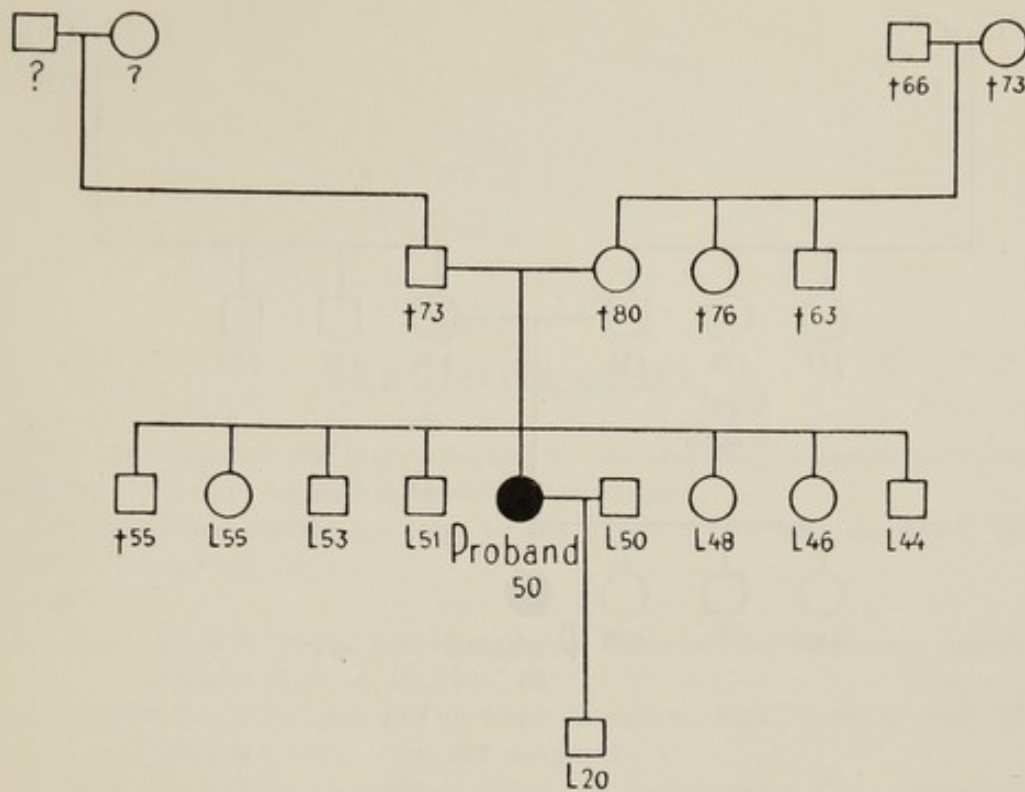
Pedigree 197.

PROBAND (State Hospital, Copenhagen; radiol. service, no. 360/42).—  
 ○, born in Copenhagen Nov. 23rd, 1873. Dressmaker; single. Formerly well.  
 Menstruation from fourteenth to forty-fifth year, regular. Menopause normal.  
 Never pregnant. Tumor in right breast noticed three weeks before admission.  
 May 26th, 1942, ablation of the breast, with evacuation of the axilla.  
**Histologic diagnosis:** solid scirrhus carcinoma.



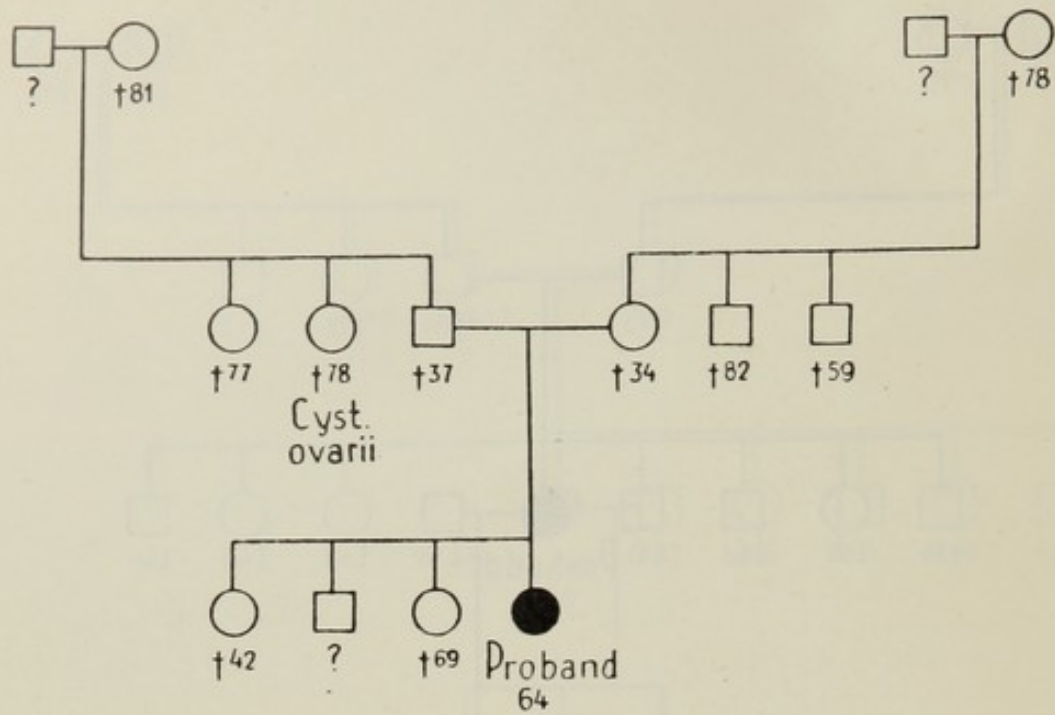
Pedigree 198.

PROBAND (Frederiksberg Hospital, Copenhagen; service A, no. 1835/42). —○, born in Copenhagen Apr. 14th, 1894. ∞ electrician. Formerly well. Menstruation since fourteenth year, regular. Two childbirths. Nursed nearly a year each time. Tumor in right breast noticed a year before admission. Aug. 30th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.



Pedigree 199.

PROBAND (Radium Center, Copenhagen; no. 28146).—○, born in Copenhagen Jan. 17th, 1892. ∞ shipping agent. Formerly well. Menstruation since fourteenth year, regular. The bleeding now rather slight and intermittent, accompanied by climacteric symptoms in the form of headaches, vertigo and sudden hot flushes. Five-six months before admission treated for about three months with ovex, 1 tablet of 1000 I.U. 3 times daily; 200 tablets in all. Tumor in left breast noticed two months before admission. Oct. 29th, 1942, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid carcinoma.



Pedigree 200.

PROBAND (Radium Center, Copenhagen; no. 20568).—○, born in Copenhagen Dec. 28th, 1875. Former domestic servant; single. Formerly well. Menstruation from fourteenth to forty-fifth year, regular. Menopause normal. Never pregnant. Four months before admission she had fallen and hurt her left breast, and a few days afterwards she noticed a lump in it. Sep. 12th, 1939, ablation of the breast, with evacuation of the axilla. Histologic diagnosis: solid scirrhus carcinoma.

## BIBLIOGRAPHY

The abbreviations are those adopted by the Quarterly Cumulative Index Medicus, Chicago. American Medical Association.

The bracketed figures ( ) refer to the pages in the text on which the authors are quoted.

1. Adair, F. & H. Bagg: Breast stasis as cause of the mammary cancer. *Internat. Clin.* 4. 19, 1925. (13).
2. Auvray, M.: A propos de l'hérédité du cancer. *Bull. Acad. de méd.* 97. 420, 1927. (19).
3. Bang, F.: Kræftsygdommenes Klinik og Pathogenese. Kbh. 1924 Disp. Pp. 301.
4. Bartels, E.: Heredity in Graves' disease. Kbh. 1924 Disp. Pp. 384.
5. Bashford, E.: Heredity in cancer. *Lancet.* 2. 1508, 1908. (18).
6. Bauer, E. E. — Fischer, F. — Lenz: *Menschliche Erblehre und Rassenhygiene.* 5. Aufl. Springer, Berlin 1940.
7. Bauer, J.: Erblichkeit und Disposition. *Wien. klin. Wchnschr.* 83. 1058, 1931.
8. Bauer, K.: *Mutationstheorie der Geschwulstentstehung.* Springer, Berlin, 1928, Pp. 79.
9. Bayle, G. L.: *Traité de maladies cancéreuses. Ouvrage Posthume.* Paris 1833, p. 107-299 and 471-495.
10. Behan, R.: *Cancer of the breast.* H. Kimpton, London 1938, Pp. 844.
11. Berencsy, G. & K. Wolff: Über die Verbreitung des Carcinoms auf Grund von 19908 Sectionen... *Ztschr. f. Krebsforsch.* 21. 109, 1924.
12. Bernstein, F.: Über die Erblichkeit und Natur des Krebses. *Med. Klin.* 26. 1583 und 1621, 1930.
13. Bittner, J. J.: Mammary tumours in mice in relation to nursing. *Am. J. Cancer,* 30. 530, 1937. (12).
14. — Relation of nursing to the extra-chromosomal theory of breast cancer in mice. *Am. J. Cancer,* 35. 90, 1939. (12).
15. — Breast cancer in mice. *Am. J. Cancer,* 36. 44, 1939. (12).
16. Bonser, G.: Effect on oestrone administration on the mammary glands of male mice. *J. Path. and Bact.* 42. 169, 1936.
17. Britz, H.: Über Krebsentstehung mit Berücksicht der Vererbung und Rassendisposition. Disp. Berlin, 1937. Pp. 35. (84).

18. Broca, P.: *Traité des tumeurs*, Bd. 1. p. 149, Paris 1866. (15).
19. Burkard, H.: Gleichzeitige und gleichartige Geschwulstbildung in der linken Brustdrüse bei Zwillingsschwestern. *Deutsche Ztschr. f. Chir.* 169. 166, 1922.
20. Buschke, A. & E. Langer: Tumorartige Schleimhautveränderungen in Vormagen der Ratten infolge von Teereinwirkung. *Ztschr. f. Krebsforsch.* 21. 1, 1924.
21. Butlin, H.: Report of the inquiry No. 33 cancer (of the breast only) *Brit M. J.* 1. 463, 1887. (17).
22. Carrel, A.: Action du principe filtrant d'un sarcome... *Compt. rend. soc. de biol.* 93. 491, 1925.
23. Caspari, W.: Das Problem der Entstehung des Krebses. *Arch. f. klin. Chir.* 146. 711, 1924.
24. Cholewa, J.: Krebskrankung und Vererbung. *Ztschr. f. Krebsforsch.* 37. 214, 1932. (19).
25. Claypon, E. Lane: *Minist. of health rep. on public. health and med. subjects* 32, 1926. (22-39).
26. Clemmesen, J.: Moderne Svulstforskning. *Ugesk. f. Læger.* 101. 664, 1939.
27. — Cancer and occupation in Denmark. *Kbh.* 1941, Pp. 74.
28. — Familiært malignt Hypernephron i en Slægt med hereditær Cystennyre. *Nord. Med.* 14. 1472, 1942. (19).
29. Cramer, W. & W. E. Gye: Oestrin. and cancer. *Lancet.* 2. 1365, 1936.
30. Dahlberg, G.: On the heredity of malignant tumours. *Upsala Läkareför. Förhandl.* 46. 21, 1941.
31. Dahl-Iversen, E.: Kønshormonernes Betydning for fysiologiske og patologiske Tilstande i Corpus mammae. *Nord. Med. Tidskr.* 9. 745 og 785, 1935.
32. Deelmann: Heredity and cancer. *Ann. Surg.* 93. 30, 1931. (19).
33. Dobrovolskaja-Zawadskaja, N.: Heredity of cancer. *J. cancer.* 18. 356, 1933. (12).
34. Engelbreth-Holm, J.: Om Hyppigheden af dobbeltsidig Brystkræft og om Brystkræftens Sammentræf med andre Kræftformer. *Ugesk. f. Læger.* 104. 456, 1942. (28).
35. Essen-Møller, E.: *Kompændium i statistik för medicinare*, Lund 1932, Pp. 85.
36. Ewald, C.: Ist das Krebsleiden ansteckend? Ist die Anlage zu dieser Krankheit erblich? *Wien. klin. Wchnschr.* 5. 134, 1931. (19).
37. Fabre, J.: *De la contagion du cancer*. Paris 1892. (17).
38. Farland, M. & T. Meade: The genetic origin of tumours supported by their simultaneous and symmetrical occurrence in homologous twins. *Am. J. M. Sc.* 184. 66, 1932. (22).
39. Fischer, R. & F. Yates: *Statistical tables for biological, agricultural and medical research*. London 1938, Pp. 98. (46).
40. Florschütz, G.: *Allgemeine Versicherungsmedizin* 1914. (Cit. Cholewa. *Ztschr. f. Krebsforsch.* 37. 24, 1932). (19).
41. Frykholm, K.: En Cancerslægt. *Svenska Läk.tidning.* 46. 2673, 1943. (19).

42. Gardner, W.: Estrogenes in carcinogenesis. *Arch. Path.* 27. 138, 1939.
43. Guelliot, O.: *Union Méd. de Nord-Est*. 1881. (Cit. Wolff, J. *Lehre von der Krebskrankheit*. Bd. 2. P. 46, 1911). (16).
44. Habs, H.: Krebs und Vererbung. *Ztschr. f. klin. Med.* 135. 676, 1939. (22).
45. Hadfield, G. & L. Garrod: *Recent advances in pathology*. 4. ed. London 1943, Pp. 346.
46. Hanharte, E.: Auffallend geringe Bedeutung der Belastung mit Krebs. *Schweiz. med. Wchnschr.* 15. 446, 1943. (21).
47. Hanriot, H.: Statistique des cancers familiaux. *Bull. Acad. de méd.* 97. 389, 1927.
48. Hartmann, H.: Sur un travail de M. Chaton: Contribut. a l'étude étiologique du cancer. *Bull. Acad. de méd.* 97. 344, 1927. (19).
49. Heidenhain, L.: Über das Krebsproblem. *Deutsch. Ztsch. f. Chir.* 252. 604, 1939.
50. Hoffmann, F.: *Opera omnia*. . . Geneva 1740. (Cit. Wolff, J. *Lehre von der Krebskrankheit*. Bd. 1. 2. Aufl. 1929, P. 73). (14).
51. Hunt, E.: Oestrin and toxic goitre. *Lancet*. 2. 1302, 1936.
52. Häberlin, H.: Über Vererbung und Etiologie des Magenkrebses. *Deutsches Arch. f. klin. Med.* 44. 461, 1889. (19).
53. Kappelgaard, P.: Om magligne Mammatumorer hos Mænd. *Nord. Med.* 24. 2021, 1944.
54. Kaufmann, E.: *Lehrbuch der spec. Pathol. Anatomie*. 10. Aufl. Berlin 1931. Bd. 1-2.
55. Kemp, T.: *Statistiske Metoder i Medicin og Biologi*, Kbh. 1942. Pp. 172. (45).
56. — *Arvelighedslære for Studerende og Læger*. Kbh. 1943, Pp. 285. (83).
57. Kennaway, E. & N. Kennaway: Some factors affecting carcinogenesis. *Acta Intern. Union against cancer*. 2. 101, 1937.
58. Kranz, H.: Tumoren bei Zwillingen. *Ztschr. f. indukt. Abstammungs- und Vererbungslehre*. 62. 173, 1932. (22).
59. Körbler, J.: Zur Frage der Vererbung und der Kontagiosität bei Krebs. *Ztschr. f. Krebsfor.* 47. 84, 1938. (19).
60. Laccasagne, A.: A comparative study of the carcinogenic action of certain oestrogenic hormones. *Am. J. Cancer*. 28. 734, 1936. (12).
61. — Influence d'un facteur familial dans la production, par la folliculine, des cancers mammaires chez la souris male. *Compt. rend. Soc. de biol.* 114. 427, 1933. (12).
62. — Sur la pathogénie de l'adénocarcinome mammaire de la souris. *Compt. rend. Soc. de biol.* 115. 937, 1934. (12).
63. Laurence, J.: *The diagnosis of surgical cancer*. 2. ed. London, 1858, Pp. 126. (15).
64. Lefevre, H.: Om multiple primære Carcinomer. *Ugesk. f. Læger*. 103. 822, 1941. (28).
65. — Acceleration of the development of spontaneous tumours in mice. Kbh. 1945, Disp. Pp. 248. (13).
66. Letulle, M.: Les familles à cancers. *Presse méd.* 32. 761, 1924. (19).

67. Little, C.: The inheritance of a predisposition to cancer in man. *Eugenics, genetics and the family. 1.* 186, 1923. (19).
68. Little, C.: Evidence that cancer is not a simple mendelian recessive. *Cancer Research. 12.* 30, 1928. (12).
69. Loeb, L. & A. Lathrop: The effect of continued inbreeding on the tumor rate in mice. *Proc. Soc. Exper. Biol. and Med. 15.* 72, 1918.
70. Lundsgaard, R.: *Leber's disease.* Kbh. 1944, Disp. Pp. 306.
71. Lynch, C.: Studies on the relation between tumor susceptibility and heredity. *J. Exper. Med. 39.* 481, 1924. (12).
72. — Studies on the relation between tumor susceptibility and heredity. *J. Exper. Med. 42.* 829, 1925. (12).
73. Macklin, M.: Can we breed out cancer in human race? *Edinburgh M. J. 45.* 587, 1938.
74. Maisin, J.: *L'étiologie du cancer d'après l'expérimentation.* Paris méd. 71. 249, 1929.
75. Martynova, R.: Studies in genetics of human neoplasms, cancer of the breast. . . *Am. J. Cancer. 29.* 530, 1937. (22-26).
76. Miche, F.: *L'hérédité mendélienne des tumeurs chez l'homme.* Bull. Acad. de méd. 97. 510, 1927.
77. Morgan, T.: *Contributions to the genetics of drosophila melanogaster.* Carnegie Institution of Washington. 1919. (Cit. Schinz und Buschke: *Krebs und Vererbung*, p. 34). (11).
78. Murray & C. Little: Chromosomal and extra-chromosomal influence in relation to the incidence of mammary tumor in mice. *Am. J. Cancer. 37.* 536, 1939. (12).
79. Møller, P.: *Carcinome pulm. prim. chez les rats. . .* Acta path. et microbiol. Scandinav. 1. 412, 1924.
80. Paget, J.: *Lecture on cancer and cancerous disease.* Brit. M. J. 2. 1091, 1887. (16).
81. — *Lecture on tumours.* P. 328-391 and 460-462 and 487-542. (16).
82. Paulsen, J.: *Konstitution und Krebs.* Ztschr. f. Krebsforsch. 21. 119, 1924. (19).
83. Pearson, K.: *Tables for statisticians and biometricians.* 3. ed. London. Part. 1-2. 1930-31. (46).
84. Peiser, H.: *Zur familiären Häufung des Carcinoms.* Med. Klin. 7. 193, 1915. (19).
85. Peller, S.: *Die Ergebnisse der von Oster. Gesellschaft f. Erforschung und Bekämpfung der Krebskrankheit veranstalteten Sammel-forschung.* Wien. klin. Wchnschr. 35. 121, 1922. (19).
86. Peyrilhe, B.: *Dissert acad. de cancro.* 1773. (Cit. Wolff: *Lehre von der Krebskrankheit.* 2. Aufl. Bd. 1. 1929, p. 65). (14).
87. Piorry, P.: *L'hérédité dans les maladies.* Paris 1840.
88. Poulsen, K.: *Om Svulster i mamma.* Kbh. 1890, Pp. 179. (16-64).
89. Puig, H.: *Contribution a l'étude de l'hérédité des tumeurs.* Lyon 1885. (18).
90. Recamier, J. C.: *Recherches sur le traitement du cancer* Bd. 2. 217, Paris 1829. (17).



91. Regaud, C.: Revue critique des quelques travaux sur le cancer. Paris méd. 67. 237, 1928.
92. Roffo, A.: Biology and etiology of cancer. Bolletino de med. exp. para el estud. y trat. del cáncer 11, 635, 1934 (Abstract in Am. J. Cancer 28. 793, 1936).
93. Roussy, G.: Der Krebs. Rascher, Zürich 1943, Pp. 290.
94. Rust, J. Nepomuk: Helkologie oder über die Natur, Erkenntniss und Heilung der Geschwüre. P. 39. Wien 1811. (14).
95. Schinz, H. & F. Buschke: Krebs und Vererbung. Georg Thieme, Leipzig 1935. Pp. 280.
96. Schnorrbusch, M. & B. Kujath: Untersuchungen in den Familien jugenlicher Krebskranker. Ztschr. f. menschliche Vererb. und Konstit.lehre. 21. 676, 1938. (27).
97. Schreiner, B. & A. Stenstrom: End results in 563 cases of breast cancer. Surg. Gynec. Ost. 44. 608, 1927.
98. Sibley, J.: Tr. Med. and Chir. Soc. London p. 110, 1859. (15).
99. Slye, M.: Incidence and inheritability of spontaneous cancer in mice... J. Cancer Research. 1. 109, 1916. (12).
100. Strong, L.: General considerations on the genetic study of cancer. Cancer Rev. 12. 49, 1927.
101. Taylor, G.: Cancer of the breast. Internat. Abstract Surg. 55. 1, 1932. (50).
102. Waaler, G.: Über die Erblichkeit des Krebses. Skrifter udg. af det Norske Videnskapsakademi i Oslo, Mat. Naturv. Klasse, 1931, Nr. 2. Pp. 75. (20).
103. Waaler, G.: Om kreft og arvelighet. Nord. med. Tidskr. 4. 761, 1932. (20).
104. Wachtel, H.: Zur Frage der Erblichkeit des Krebses. München. med. Wchnschr. 71. 852, 1924. (84).
105. Wainwright, I. M.: A comparison of conditions associated with breast cancer in Great Britain and America. Am. J. Cancer. 15. 2610, 1931. (22, 39, 50).
106. Warren, J. C.: Praktische Bemerkungen über die Diagnose und Kur der Geschwülste. Berlin 1829. (Cit. Wolff, J.: Lehre von der Krebskrankheit. 2. Aufl. Bd. 1, p. 358, 1929). (14).
107. Warthin, A.: Heredity with reference to cancer. Arch. Int. Med. 12. 546, 1913. (19).
108. Warthin, A.: The further study of a cancer family. J. Cancer Research. 9. 279, 1925. (19).
109. Wassink, W. F.: Cancer et hérédité, Genetica. 17. 103, 1935. (22-25).
110. Weitz, W.: Über die Erblichkeit des Krebses. Monatschr. f. Krebsbekämpfung. 10. 385, 1933. (22).
111. — Die Vererbung innerer Krankheiten. Stuttgart 1936. Pp. 197.
112. Velpeau, A.: Traité des maladies du sein. Paris 1854, p. 695. (14).
113. Verneuil: Diathese néoplasique. Rev. scient. Paris 1884. (17).
114. Werthemann, A.: Über die Veranlagerung zum Krebs. Bull. des Eidgen. Gesundheitsamtes. 9. 122, 1942.

115. Wienberg, W.: Pathologische Vererbung und genealogische Statistik. Deutsche Arch. f. klin. Med. 78. 521, 1903. (18).
116. Williams, W. Roger: The natural history of cancer. Heinemann, London, 1908, Pp. 534. (14-22).
117. Virchow, R.: Die krankhaften Geschwülste. Berlin. 1863. Pp. 543.
118. Wolff, J.: Die Lehre von der Krebskrankheit. Bd. 1-3, Jena 1911. 1929.



