

A STUDY OF NEOPLASMS

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## INTRODUCTION

During the past several years thirteen cows have died in the dairy herd at the Virginia Polytechnic Institute of malignant tumors of the lymphoid type. In view of research with respect to cancers of various types in man, any information relating to tumors acquired in this study should be of value not only to animal industry but also to similar conditions in man.

A problem such as this requires long study, probably several years. This paper is a preliminary report on early fundamental steps of the cancer problem in dairy cattle as applied to local conditions.

Because spontaneous cases of neoplasms in dairy cattle do not occur with any regularity, other phases of cancer research were instituted for investigation during the interval between cases.

REVIEW OF LITERATURE

"Well-known examples of specific etiology are seen in various tumors connected with occupations, as x-ray cancer, multiple epithelioma of skin of workers in paraffin and aniline dyes, scrotal cancer of chimney-sweeps, and the rare cancer of the lung in metal workers, weavers and cigar makers.

"Particular forms of chronic irritation and inflammation precede many well-known clinical forms of cancer, as epithelioma of tongue from jagged teeth, cancer of skin from chronic eczema, indolent ulcers, burns, or along chronic sinuses from necrosing bone.

"Mechanical trauma is an important factor in the causation of tumors. By trauma is here understood a single or repeated more or less contusing, crushing, or lacerating mechanical injury.

"Cancer has been attributed to lacerations by rough instruments, rusty nails and pins, thorn pricks, insect bites, surgical wounds, and blows without visible destruction of tissue." (1).

For several years it has been known that malignant tumors can be produced by artificial means. "From the original observations of B. Fischer on Sudan III, and of Yamagiwa and Ichikawa (in 1914) on coal tar, has arisen a new field of research, in which it has been shown that many chemical irritants,

especially the higher distillation products of coal tar, are capable of producing tumors in the lower animals in a high proportion of cases". (1).

Berenblum (2) produced malignant tumors in mice by repeated freezing and thawing of the skin with carbon dioxide snow. In later experiments, Berenblum (3) produced tumors in mice by use of a single application of carbon dioxide snow to skin that had been previously treated with coal tar. McIntosh (4) produced transplantable tumors of the sarcomatous type in fowls by weekly injections of tar and lard. Campbell (5) produced cancer of the skin and primary adenoma of the lungs in mice by exposing them to dust obtained from tarred roads. Recently it has been found that the active principle in coal tar is 1;2;5;6-dibenzanthracene. This brings about non-disjunction of chromosomes. (6). Berenblum and Kendal (7) produced spindle-cell sarcoma in fowls by repeated injections of a colloidal solution of 1;2;5;6-dibenzanthracene.

"It is highly suggestive of the factors determining the results of transplantation of tumors that the first success was with the most easily transplantable growth, the lymphosarcoma of dogs. Yet Novinsky, in 1876, had only two positive results in 42 attempts. Hanau's transplantation (in 1889) of epidermoid carcinoma of the vulva in a rat was rather more impressive, since he dealt with a better known

malignant tumor and secured extensive metastases." (1).

"In 1901 and 1902 the general revival of interest in the cancer problem gave to the studies of Loeb in America and Jensen in Denmark a special interest. Loeb (1900) carried a cystic sarcoma of the rats thyroid through 40 generations without observing change of structure or metastases. Jensen (1902-1903) reported the transmission of mouse carcinoma through 19 generations again without metastases." (1).

At the present time, there is much controversy about the causative agent of cancer. McCombs (8) advanced the theory that it is essentially a faulty cellular chemistry; Claude (9) found that the evidence indicates that a protein and a phospholipoid is the causative agent of a transplantable chicken tumor; Murphy (10) found that the carcinogenic substance of fowl tumors withstand considerably more ultraviolet energy and more drastic chemical treatment than any animal virus so far investigated. Murphy further stated that antigenic properties failed to show any close relationship to viruses. But Shope and Hurst (11) found an infectious papillomatosis in wild cottontail rabbits which disease they regard as due to a filterable virus. Rous and Beard (12) confirmed the work of Shope and Hurst. D'Aunoy, Von Haam and Lichtenstein (13) described what they called the virus of Lymphogranulosa Inguinale. Whatever the cause of these

conditions, they have been found by Purdy (14), Gye (15), and Rous and Beard (16), to be readily transmitted to animals of the same species, as well as to animals of different species, by means of cell-free filtrates.

Accumulating data indicate that certain types of neoplasms are hereditary. Lynch (17) made the following statement: "It seems clear that there are among mice constitutional types which differ in incidence of tumors of the lung and that the differences are inherited." Levit (18) observed that atheroma in a human family was hereditary. The tumors in his cases were all present from early childhood and appeared to be of a recessive character. Norday (19) observed a melanotic skin tumor in a family of swine which appeared to be 100 per cent congenital. Strong (20) produced a strain of mice by brother-sister matings in which every female for 19 generations had developed cancer of the mammary gland.

## INVESTIGATION

### Procedure

#### I. Rats

Rats are very numerous about the dairy barns and it was considered possible that they are acting as carriers of the neoplasms, although this appeared highly improbable. Consequently, 13 rats were caught and autopsied, and the organs examined macroscopically for tumors. Lesions were found in the livers of nine rats, or 69.2 per cent. Microscopical examination showed these lesions to be cysticercus of *Taenia taeniaeformis*, the tapeworm of the cat. No evidence of neoplastic tissue was observed in any of the rats. A photomicrograph of the cysticercus was taken (Plate I).



## II. Cattle

### A. Foreign Material

Mechanical trauma and prolonged irritation from foreign material are thought by some authors to be an important factor in the etiology of tumors. Dairy cattle are especially susceptible to internal injury caused by foreign material such as wire and nails picked up in their feed. When cattle ingest this material it passes to the reticulum, the function of which in ruminants is in part to aid in regurgitation of food. During peristaltic contractions this foreign material is probably forced forward through the wall of the reticulum, through the diaphragm which is situated directly anterior to it and on through the pericardium, and usually involves the myocardium. Nails and wires ingested with the food by ruminants frequently lodge in walls of the reticulum or rumen and remain in this location for a period of time. There is reasonable probability that the resultant irritation may act as a stimulus towards the development of malignant neoplasms such as has been found involving the digestive organs of dairy cattle. In order to investigate this theory, the following procedure was carried out.

Laparotomy was performed on cow No, 20940D on April 28, 1936, and a paper clip attached to the wall of the

rumen. This cow has been maintained in the quarantine herd and is apparently normal at the present time. Search has not been made to determine the status of the paper clip. This will be done at autopsy. Total blood cell counts were made as shown in Table I.

On May 14, 1936, a trocar and canula were inserted into the rumen of cows Nos. 20941, 20942, and 21042D. The trocar was then removed and the following were introduced into the rumen through the canula: two pieces of hay bailing wire about 15 centimeters in length, two paper clips and two finishing nails.

On June 1, 1936, or 18 days following the above described procedure, cow No. 20941 showed a depressed appetite and clinical manifestations of a digestive disorder. A total blood cell count was made on June 6, 1936, as shown in Table II. The jugular veins were plainly visible and the brisket and submaxillary regions were edematous; upon auscultation a splashing sound was heard over the heart. The abdomen was "tucked up" and the animal was reluctant to move. A diagnosis of traumatic pericarditis was made. Forty-one days after the introduction of the foreign material, June 24, 1936, the animal died and was autopsied the following morning. The heart was greatly hypertrophied and dilated, the epicardium was rough and had a fuzzy appearance due to the deposition of

fibrous tissue. The pericardial sac was thickened and inflamed, and had numerous adhesions involving the adjacent lungs, heart and diaphragm. There were approximately two liters of semi-liquid purulent exudate in the pericardial cavity. One piece of wire and the two finishing nails were found in the anterior omental pocket of the rumen. Only one wire had penetrated the pericardium. Tissues were taken for pathological study from the neighborhood of the injury and also from a small nodule in the mesentary and the colon. None of these suggested a neoplastic condition upon microscopic examination, being primarily fibrous tissue.

Cow No. 20942 remained apparently normal until about the first of January, 1937, when she began showing progressive weakness in the pelvic limbs. On January 23, 1937, she was very much weaker and had difficulty in rising. Total blood cell counts were made as shown in Table III. She was destroyed on February 9, 1937. There were numerous small abscesses, 2.5 centimeters in diameter, in the liver and two large abscesses, 7.0 centimeters in diameter, in the spleen. A piece of wire had pierced the reticulum near the xiphoid cartilage of the sternum and resulted in an abscess. This animal exhibited typical symptoms of traumatic pericarditis. Microscopic examination of tissues from the wall of the

fistulous tract formed about the wire near the sternum revealed cells suggestive of tumor development.

Cow No. 21042D remained apparently normal for 19 months; then she began to have difficulty in rising. On December 21, she was unable to rise and was killed and autopsied. There was a large abscess involving the spinal processes of the last two thoracic vertebra. One wire was found on the ventral wall of the thoracic cavity walled off by fibrous tissue. The remaining wire and the finishing nails were found in the reticulum. Total blood cell counts were made as shown in Table IV.

#### B. Injections of Tar and Lard

It is an established fact that malignant tumors of the sarcomatous type can be produced in mice and fowls by intramuscular injections of coal tar and lard. The above described procedure has never been attempted in cattle; therefore, an experiment was set up to determine its effect upon these animals.

Three cows, Nos. 21038D, 21039D, and 21040D were given weekly injections of a four per cent solution of coal tar and lard (4grams tar and 96 grams lard). At each injection five cc. was given subcutaneously in the right side of the neck and five cc. intramuscularly in the right brisket. The

weekly injections were started on February 27, 1936, and given until January 2, 1937, at which time they were discontinued. On June 19, 1937, they were resumed and continued until July 31, 1937 inclusive. A total of forty-five injections were given.

The only external lesions in cow No. 21038D was several small nodules at the sites of the injections in the neck and brisket which were in the superficial fascia. Total blood counts were made as shown in Table V.

The only external lesion in cow No. 21039D was a soft cyst located in the superficial fascia at the site of injection in the brisket. Total blood cell counts were made as shown in Table VI. This animal was sold and further data on her are unavailable.

The only apparent lesions in cow No. 21040D were two nodules, 2.5 centimeters in diameter, in the superficial fascia at the site of the injection in the neck. Total blood cell counts were made as shown in Table VII.

On April 28, 1936, a laparotomy was performed upon cow No. 20939D and 15 cc. of the tar and lard solution were injected into the wall of the rumen. Total blood cell counts were made as shown in Table VIII. This animal was sold and further data on her are unobtainable.

### C. Spontaneous Neoplasms

A Holstein cow, No. 3819, died of generalized tumors on December 20, 1936. Some of the neoplastic tissue was shredded and frozen solid in the freezing unit of a refrigerator. The frozen tissue was macerated in normal, saline solution and filtered through a Seitz filter. On December 26, 1936, portions of the filtrate was injected as follows into a male Holstein calf, No. 23252Z, one-half cc. intratesticularly in the right testicle, one cc. intramuscularly and one cc. subcutaneously. This calf and calf No. 23251Z, (note below), were isolated for observation in a small pasture lot. Total blood cell counts were made of calf No. 23252Z as shown in Table IX. This calf was killed 13 months after the injections were made and the carcass was inspected; nothing suggestive of tumor formation was found.

A Jersey cow, No. 3918, developed a typical attack of indigestion on January 29, 1937, and was treated accordingly. Extensive and rapidly developing edema of the abdominal and sternal regions was noted on January 30, 1937. Cardiac and respiratory distress was evident on January 31, 1937. She stood with the fore feet elevated and the anterior thorax pushed solidly against the manger, but continued to eat and ruminate until February 7, 1937, and died February 8, 1937.

The force of the heart beat was greatly increased with some acceleration of rate. A total blood cell count was made as shown in Table X. The most notable lesion found at autopsy was a large tumor mass 18 centimeters by 7 centimeters involving the walls of the reticulum, abomasum, and omasum which was evidently responsible for the digestive disturbance. A photograph of this neoplasm in position was taken as shown in Plate III. The mediastinal, bronchial, mesenteric, cervical, hepatic, and most of the body lymph nodes were greatly enlarged and neoplastic. The right auricle was almost completely filled with a tumor mass that obstructed the posterior vena cava, which condition accounted for the sudden onset of edema and the peculiar position of the head. Photographs showing the external surface of the right auricle showing the obstruction of the vena cava are shown in Plates IV and V.

Microscopic examination of neoplastic tissue from cow No. 3819, showed a delicate reticulum in the meshes of which lie small round cells of lymphoid character. The capsule of lymph nodes and the wall of the rumen from which were taken are heavily infiltrated with round cells. Photomicrographs were taken as shown in Plates II and IIa.

Tissue from the tumor mass of cow No. 3918 was macerated in a mortar with sterile saline solution and in-

jected into a Holstein calf, No. 23251Z, one-half cc. subcutaneously. Total blood cell counts were made as shown in Table XI. This animal was killed 11 months after the injection and the carcass inspected; nothing suggestive of tumor development was found.

Microscopic examination of neoplastic tissue from cow No. 3918, showed a reticulum in the meshes of which lie round cells of lymphoid character. There are many small strands of fibrous tissue scattered throughout the neoplasms. Photomicrographs were taken as shown in Plates VI and VIa.

A Holstein cow, No. 5195, had been on a feeding experiment, the feed consisting of timothy hay and grain. She had several short periods of digestive trouble attributable to her ration. Although the symptoms were atypical, a neoplasm was suspected. She went off feed on May 15, 1937, and was not normal afterward, and died June 10, 1937. Total blood cell counts were made as shown in Table XII. Microscopical examination of the kidneys revealed cloudy swelling, fatty degeneration of the parenchymous tissue, and hemorrhage, and in the liver, fatty degeneration and cloudy swelling of the parenchymous tissue. Microscopic examination of tissue from cow No. 5195, showed loosely formed fibrous tissue infiltrated with round lymphoid cells. There are areas in which the



lymphoid cells are predominant. Photomicrographs were taken as shown in Plate VII and VIIa.

A cow six years old, No. 4138, developed a pathological condition in the left eye which was thought by the owner to be the result of an injury, or a barley beard. An extensive tumor mass involving the eye and ocular cavity developed and the eye along with contiguous tissue was enucleated on May 17, 1937. The cancer was tentatively diagnosed macroscopically to be an epithelioma which was confirmed by microscopical tissue examination. The cow was sold for slaughter during the latter part of July 1937, and further data on her are unobtainable. Total blood cell counts were made as shown in Table XIII.

#### D. Genetic Relationship

A study of the post mortem and pedigree records revealed that the cases of tumors had occurred primarily in two families of cattle, which indicated the possibility that genetic factors were involved. This theory is in agreement with work done by Norday, Lynch, Strong, and Slye. Norday observed melanotin skin tumors in swine which he believed to be 100 per cent congenital. Lynch concluded that in mice there are constitutional types of mice which differ in incidence of tumors of the lung and that the differences are

inherited. Strong produced a strain of mice by brother-sister matings through the fifty-fifth generation in which every female of the last 19 generations reported developed cancer of the mammary gland. Slye (21) stated in a recent paper: ".... we have spoken of cancer of the breast as though it were a single entity, whereas, it is now known to be controlled by two separate hereditary genes, one for the carcinoma and one for the breast localization, and only where both of these two genes are present does carcinoma of the breast occur; conversely, by the absence of either of these two genes breast carcinoma can be prevented. So with all other types and sites of malignancy, that is, bone sarcoma, lung carcinoma, hypernephroma, and so on".

With this possibility in mind, the genetic relationship of the animals that have died in the college herd was assembled in chart form for the Holstein breed as shown in Plate VIII, and for the Jersey breed as shown in Plate IX. Although the number here is too small to draw definite conclusions, it is of interest to note that most of the affected animals of each family were more or less closely related.

In the Holstein breed, one apparently normal cow had two daughters, a granddaughter, and a grandson to die from the neoplasms. Another cow, her daughter, granddaughter, and great granddaughter died of malignant tumors.

In the Jersey breed a mother and her daughter died with the neoplasms. Three other cows of this breed which died of the tumors were not closely related.

Microscopic examinations were not made of the early tumor cases that are recorded before this problem was begun, but the tumors were identical in gross appearance, hence included in the genetic study.

### III. Chickens

#### A. Tar and Lard Injections

It was decided to attempt to duplicate the work of McIntosh in the artificial production of tumors in fowls by injecting them with a solution made of four grams of coal tar and 96 grams of lard. Six Plymouth Rock hens were given weekly injections of the coal tar and lard solution, two-tenths of a cc. being injected into the breast muscles of three of the birds and one-tenth of a cc. into the breast muscles of the remaining three. Three of the birds were injected on alternate sides of the sternum, in the remainder all the injections were given on the right side only.

In chicken No. 884, the weekly injections were started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and continued until September 16, 1936 inclusive, twenty-five injections being given. Two-tenths of a cc. was given at each injection intramuscularly in the breast muscles, using alternate sides. On April 23, 1936, a tumor-like mass was found directly on the xiphoid cartilage of the sternum. On July 28, 1936, a biopsy was performed and some of the tumor tissue removed, cut into small pieces, suspended in normal saline solution and injected both subcutaneously and intra-

peritoneally into chicken No. 463, a Plymouth Rock cock. A total blood cell count was made as shown in Table XIV. Bird No. 463 died on September 3, 1936. The liver and spleen was enlarged and light in color, the xiphoid cartilage was spongy, the bone marrow was hyperaemic, the sciatic nerves apparently were normal. A diagnosis of lymphomatosis was made. Some of the tissue removed from chicken No. 884 was cut into small pieces and frozen in the freezing unit of a refrigerator over night. The next day it was ground in a sterile mortar with sterile physiological salt solution, filtered through a Berkfeld filter, and stored in a refrigerator. On August 1, 1936, one and one-half cc. of the filtrate was injected subcutaneously and one and one-half cc. intramuscularly into the right breast muscle of chicken No. 460. A Total blood cell count was made as shown in Table XV. The bird was destroyed in December, 1936. No evidence suggestive of tumor development was found.

Bird No. 884 was found dead on September 21, 1936, several hours after it had died. There was an old unhealed lesion from which tissue was taken, decalcified, sectioned and stained. Three accumulations of tar and lard were found in the breast muscles. Sections were taken from a dark area of the muscle, one long muscle cyst, the liver and the spleen.

The spleen was normal but the liver showed cloudy swelling and fatty degeneration on microscopic examination. The muscle contained patches of tar between the fibers with a heavy cellular infiltration; in places, the striations were present but in other areas they were absent and there was considerable fatty degeneration. The wall of the cyst consisted of fibrous tissue. The microscopic characteristics of the tissue transplanted and the autopsy findings indicated that the original pathological condition was the result of traumatism. A total blood cell count was made as shown in Table XVI.

In chicken No. 834 the weekly injections were started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and continued until October 7, 1936, inclusive. Two-tenths of a cc. was given intramuscularly in the right breast muscle at each injection. A total blood cell count was made as shown in Table XVII. The bird died on November 1, 1936. The breast muscles were heavily impregnated with tar and the cartilage of the sternum was involved. The abdominal organs presented the appearance of a generalized toxemia. Tissues were taken from the muscles of the breast, cartilage of the sternum, the liver, and the spleen. The spleen was apparently normal. The liver was heavily infiltrated with lymphocytes and contained areas of tar. The

section from the sternum was found to be a fibroma.

In chicken No. 860, the weekly injections were started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and continued until October 7, 1936, inclusive. Two-tenths of a cc. was given intramuscularly in the right breast muscle at each injection. A total blood cell count was made as shown in Table XVIII. The bird died January 11, 1937. There were two caseous masses on either side of the breast. The breast muscles were almost completely atrophied. One mass of dense tissue, greyish white in appearance, was found deep in the muscle. Sections of the mass were taken for microscopical examination and it was found to be a fibroma.

In chicken No. 882, the weekly injections were started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and continued until October 7, 1936, inclusive. One-tenth of a cc. was given intramuscularly in the breast muscles, alternating the sides. Total blood cell counts were made as shown in Table XIX. The bird was destroyed on August 14, 1937. The only lesions found were areas of tar in the breast muscles and emphysema in the lungs.

In chicken No. 803, the weekly injections were

started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and continued until September 6, 1936, inclusive. One-tenth of a cc. was given intramuscularly in the breast muscles at each injection, the sides being alternated. Total blood cell counts were made as shown in Table XX. The bird was destroyed on September 10, 1936, after an illness of several days. The autopsy reveals a generalized peritonitis and a large cyst on the cloaca. The peritonitis was due to an egg in the abdominal cavity.

In chicken No. 898, the weekly injections were started on February 24, 1936, and given until March 30, 1936, at which time they were discontinued. On May 4, 1936, they were resumed and given until July 8, 1936 inclusive. One-tenth of a cc. was given intramuscularly in the right breast muscle at each injection. On April 8, 1936, a hard tumor was found in the right breast muscle. It grew rapidly and on April 13, 1936, was measured to be six centimeters by three centimeters. On April 23, 1936, a biopsy was performed and some of the tumor tissue removed. The tissue was cut into small pieces, suspended in physiological salt solution and injected intraperitoneally and intramuscularly into chicken No. M6132, a White Leghorn cock. A total blood cell



count of the cock is shown in Table XXI. This bird was destroyed in December 1936, and was found to be free of tumors at autopsy.

Bird No. 898 died on July 13, 1936. The heart was slightly enlarged; the liver was much enlarged and pale and contained several white nodules. The spleen was light in color. Sections from the heart, liver, spleen and a tumor from the breast were removed for microscopical examination. The sections of the liver showed cloudy swelling, fatty degeneration and lymphoid infiltration; in some areas the normal structure had entirely disappeared. There was extensive fatty degeneration in the heart. The tumor was found to be a lymphofibroma.

It was decided to repeat the experiment with chickens. Consequently, three White Leghorn hens, Nos. 31943, 31931, and 142542, were given weekly injections of two-tenths of a cc. of four per cent solution of coal tar and lard intramuscularly in the right breast muscles. The injections were started on June 23, 1937, and continued through July 28, 1937, six injections being given to each bird.

Total blood cell counts were made of chicken No. 31943 as shown in Table XXII. After an illness of several days the bird died on August 2, 1937. The body was extremely emaciated and dehydrated. The breast muscles were almost

completely atrophied; the remains of the right breast muscle was heavily impregnated with tar. The kidneys were somewhat enlarged and firm; the liver contained several lesions of necrosis. No evidence of neoplastic tissue was present.

Total blood cell counts were made of chicken No. 31931 as shown in Table XXIII. On August 10, 1937, the bird was killed and autopsied. The body was emaciated and the breast muscles atrophied to a great extent. The right breast muscles were impregnated with tar. The heart was probably slightly hypertrophied. No other lesions were found.

Total blood cell counts were made of chicken No. 142542 as shown in Table XXIV. The bird was killed and autopsied on August 10, 1937. It was in good physical condition with the abdominal cavity filled with fat. The liver which was a pale mottled yellow color, was friable and contained small white nodules scattered throughout the organ. There were numerous small tumors in the ovary and mesenteries. The bone marrow was soft and easily torn. The spleen was apparently normal. The right breast muscle contained masses of tar. Sections of the liver, bone marrow, breast muscle, and tumors from the ovary and mesenteries were taken for microscopical examination. The liver showed cloudy swelling and focal fatty degeneration which was responsible for the mottled appearance. The bone marrow was hyperplastic.

There was a fibrous cyst in the breast muscle. The cyst wall and adjacent muscle showed a heavy cellular infiltration and tar impregnation. The tumors of the ovary and mesentary were essentially identical histologically. They were adeno-fibromas and were probably of ovarian origin.

## DISCUSSION

During the past several years thirteen cows, an average of almost two cows each year, have died of malignant tumors of the lymphoid type. With one exception, all the affected animals were adults.

The possibility of rats being the carrier of the neoplasms was investigated merely as an elimination factor with respect to their etiology. Thirteen rats were caught in the dairy barns and autopsied. The cysticercus of *Taenia taeniaeformis* was found in the livers of nine of these rats.

Cancer has been attributed to prolonged irritation from foreign material. Since wires, nails and other forms of foreign matter are so frequently found in the digestive organs of dairy cattle, this theory was investigated.

A paper clip was attached to the wall of the rumen of one cow. She is maintained in the quarantine herd and is apparently normal at the present time.

A trocar and canula were inserted into the rumen of three cows, the trocar was then removed and the following were introduced into the rumen through the canula: two pieces of hay bailing wire about 15 centimeters in length, two finishing nails and two paper clips. Eighteen days following the above described procedure, one of the cows developed

symptoms typical of traumatic pericarditis. Fifty-one days after the introduction of the foreign material the animal died. Upon post mortem examination the heart was found to be greatly hypertrophied and dilated. The epicardium was roughened and had a fuzzy appearance. The pericardium was thickened and inflamed, and had numerous adhesions involving the heart, diaphragm and adjacent lungs. There were about two liters of semi-liquid purulent exudate in the pericardial cavity. Both pieces of wire and the two finishing nails were found in the anterior omental pocket of the rumen. Only one wire had penetrated the pericardium. None of the several tissues taken for microscopic examination suggested a neoplastic condition, being primarily fibrous tissue.

One of the cows remained apparently normal for almost eight months; then she developed a typical case of traumatic pericarditis. One of the pieces of wire had pierced the reticulum near the xiphoid cartilage of the sternum. Microscopic examination of tissue from the fistulous tract about this wire revealed cells suggestive of tumor development.

The remaining cow with foreign material implanted in the rumen remained apparently normal for nineteen months; then she died of an abscess involving the spinal column.

To transplant neoplasms, the material should be obtained before or immediately after the death of the affected animal. The material should be ground in a sterile mortar with sterile physiological saline solution and injected into another animal of the same species and preferably the same variety and genetic family. Possibly the reason that better results were not obtained in these experiments is that it was very difficult to get fresh tumor material.

In the blood picture of the neoplastic animals it is of interest to note the marked decrease of the per cent of hemoglobin and the numbers of erythrocytes, but the great increase of leucocytes. Differential counts of the leucocytes revealed an increase of polymorphonuclear neutrophil granulocytes and monocytes with a relative decrease of lymphocytes.

It is a known fact that certain types of neoplasms are hereditary. Probable heredity is the most important factor in the etiology of the tumor epidemic in the dairy herd. Although the same type of neoplasms occurring in two different breeds may throw suspicion upon this theory, the fact that most of the affected animals of each breed are related adds to it.

The nodules in the superficial fascia at the sites of the weekly injections of the tar and lard solution in the

three cows may have been due to non-absorption of the tar and lard or to trauma. However, at the time which the experiment had to be discontinued the nodules apparently were undergoing rapid development. Blood pictures of these animals show the normal number of erythrocytes, and a substantial increase of leucocytes in two of the cows and normal leucocyte counts in the remaining cow. They also indicate that the percentage of hemoglobin was probably low. Differential counts of the leucocytes revealed an increase of lymphocytes in two of the animals and of polymorphonuclear eosinophil granulocytes in the remaining cow.

The only apparent change in the cow which received the injection of tar and lard in the wall of the rumen was a slight increase of erythrocytes and leucocytes and a probable decrease in the per cent of hemoglobin. Differential leucocyte counts showed a slight increase of polymorphonuclear neutrophil and eosinophil granulocytes with a relative decrease of lymphocytes.

Of the six chickens in the first experiment that received weekly injections of the tar and lard solution, four developed tumors, of which three were fibromas and one was a lymphofibroma. The attempts to transplant two of the fibromas were unsuccessful. Blood pictures of the injected

bird showed a decrease in the numbers of erythrocytes, and with one exception a decrease of the per cent of hemoglobin. The differential counts varied greatly.

Of the three chickens receiving weekly injections of tar and lard solution in the second experiment, only one developed tumors. They were adenofibromas of the ovary and mesenteries. No attempt was made to transplant them. The blood pictures of these birds were normal with the exception of an increase of polymorphonuclear leucocytes in two of the birds, one of which was the fowl having the tumors.

From the blood pictures of the chickens receiving the tar and lard injections it is impossible to distinguish the birds that develop tumors.



### CONCLUSIONS

From the results of the previously described experiments, the following conclusions were drawn:

1. There was no evidence whatever of the neoplasma occurring in the rats about the dairy barns.

2. The attempts to produce neoplasms in dairy cattle due to foreign bodies implanted in the rumen were unsuccessful.

3. Attempts to transplant some of the tumors occurring naturally in the dairy cattle were unsuccessful.

4. Attempts to produce neoplasms in dairy cattle by weekly injections of four per cent solution of tar and lard were unsuccessful.

5. Attempts to produce tumors in fowls by weekly injections of four per cent solution of tar and lard were successful in five of the nine birds. Attempts to transplant two of these tumors were unsuccessful.

6. Occurrence of tumors in the members of the two families indicates possible genetic relationship.

DESCRIPTION OF PLATES

Plate I

Photomicrograph of the cysticercus of *Taenia taeniaformis*. x80.

Plate II

Photomicrograph of tumor tissue from Cow No. 3819, showing a delicate reticulum in the meshes of which lie small round cells of lymphoid character. x80.

Plate IIa

Same as Plate II. x336.

Plate III

Photograph of the neoplasm of Cow No. 3918, involving the walls of the reticulum, omasum, and abomasum.

Plate IV

Photograph of the neoplasm of Cow No. 3918, involving the right auricle, showing the external surface.

Plate V

Photograph of the neoplasm of Cow No. 3918, involving the right auricle; internal view showing the obstruction of the vena cava by the tumor mass.

Plate VI

Photomicrograph of tumor tissue from Cow No. 3918, showing small round cells of lymphoid character; fibrous tissue infiltrated with round lymphoid cells. x80.

Plate VIa

Same as Plate VI. x336.

Plate VII

Photomicrograph of tissue from Cow No. 5195,  
showing loosely formed fibrous tissue infiltrated with round  
lymphoid cells. x80.

Plate VIIa

Same as Plate VII. x336.

Plate VIII

Photograph of the chart showing the genetic relation-  
ship of the animals of the Holstein breed that died of malignant  
neoplasms.

Plate IX

Photograph of the chart showing the genetic relation-  
ship of the animals of the Jersey breed that died of malignant  
neoplasms.

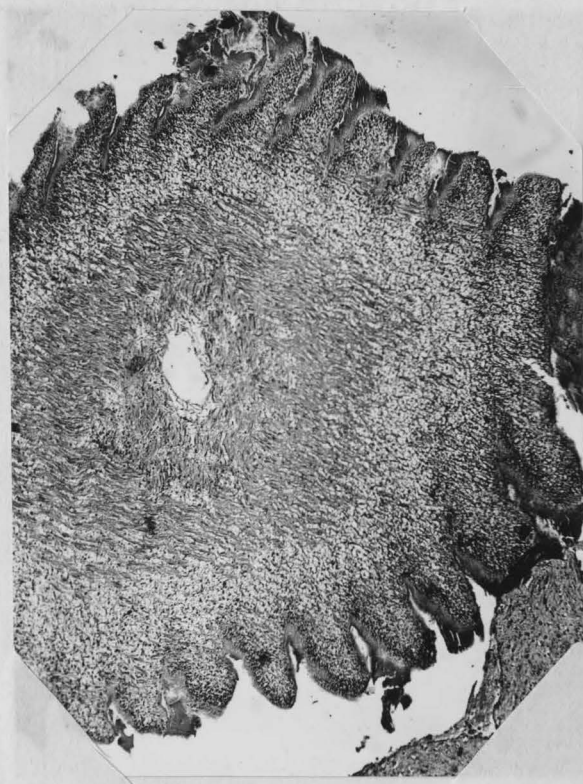


Plate I

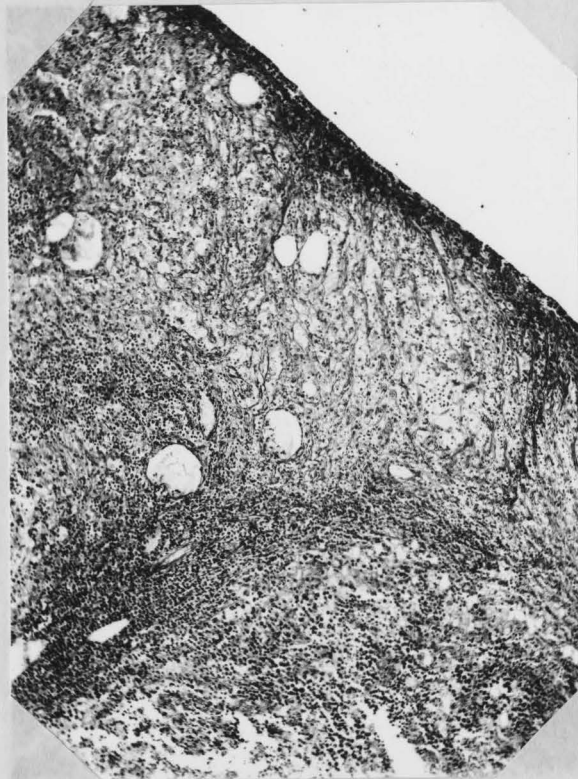


Plate II

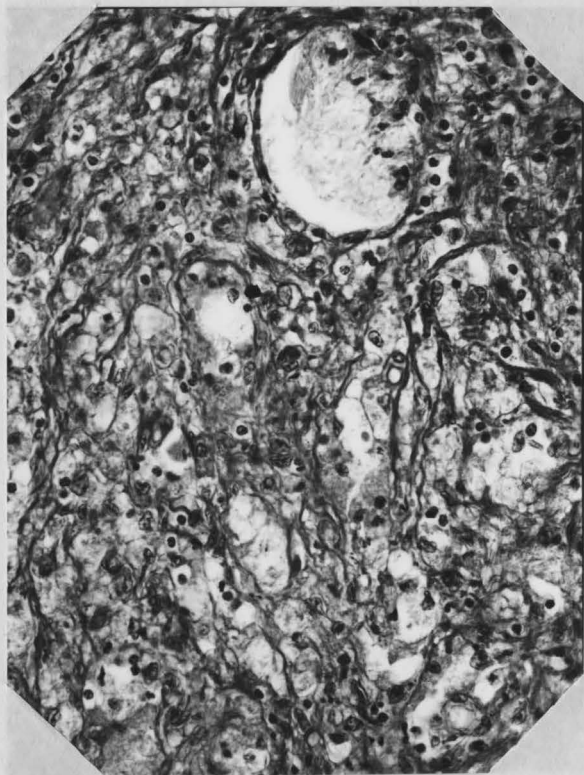


plate IIa



Plate III

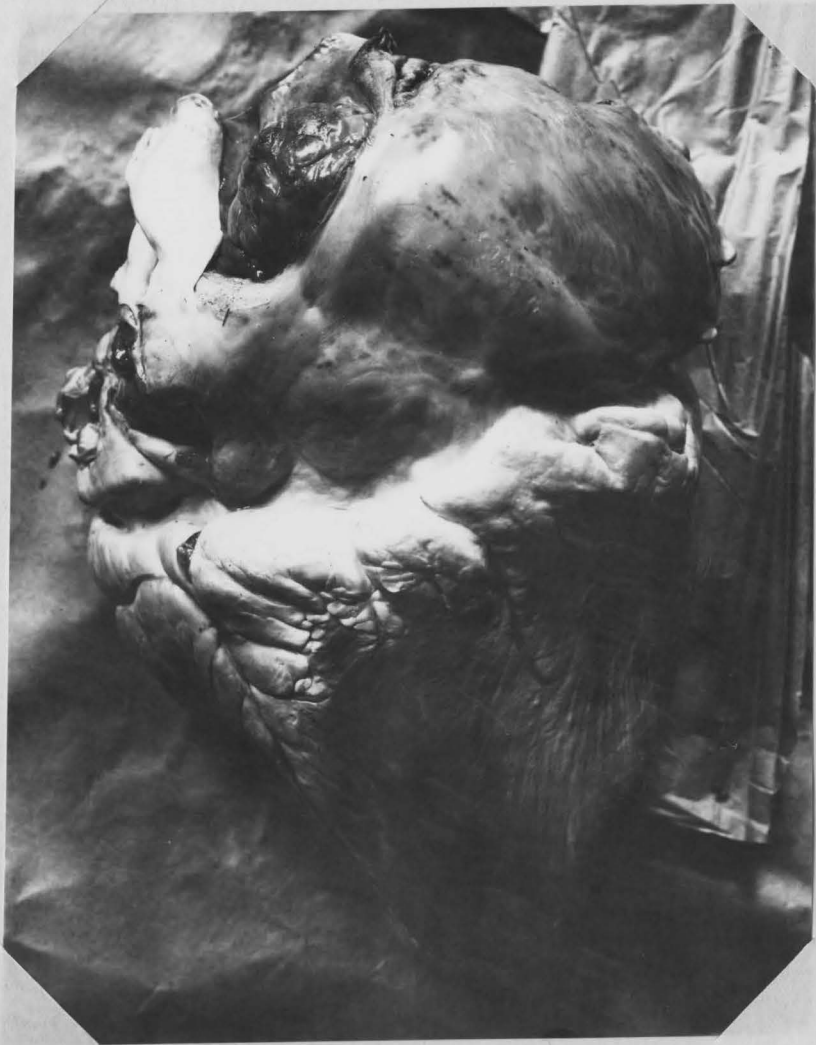


Plate IV





Plate V

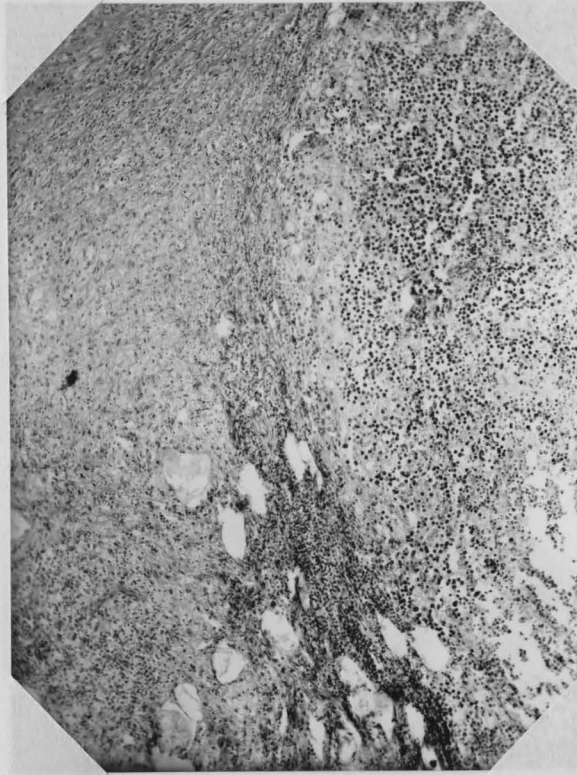


Plate VI



Plate VIa

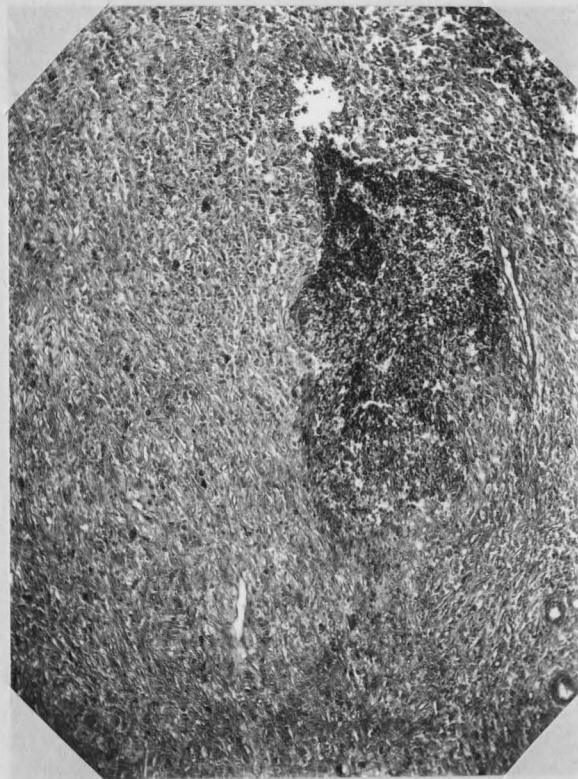


Plate VII

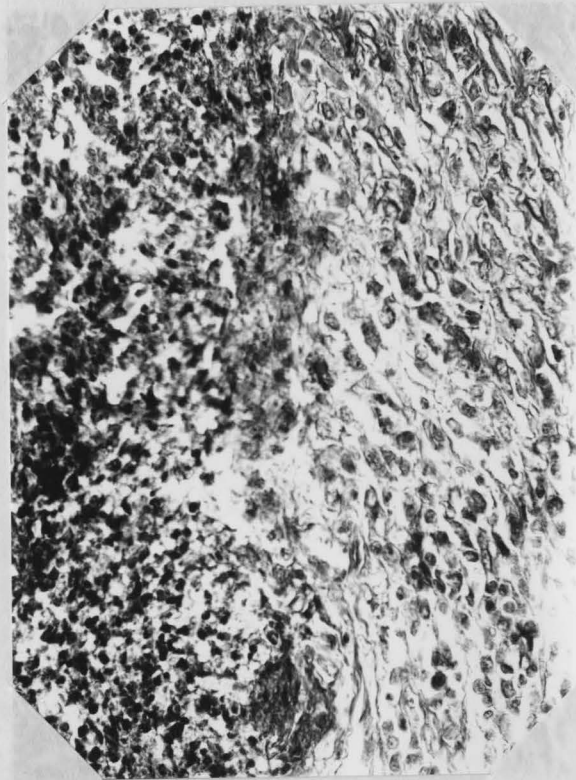


Plate VIIa

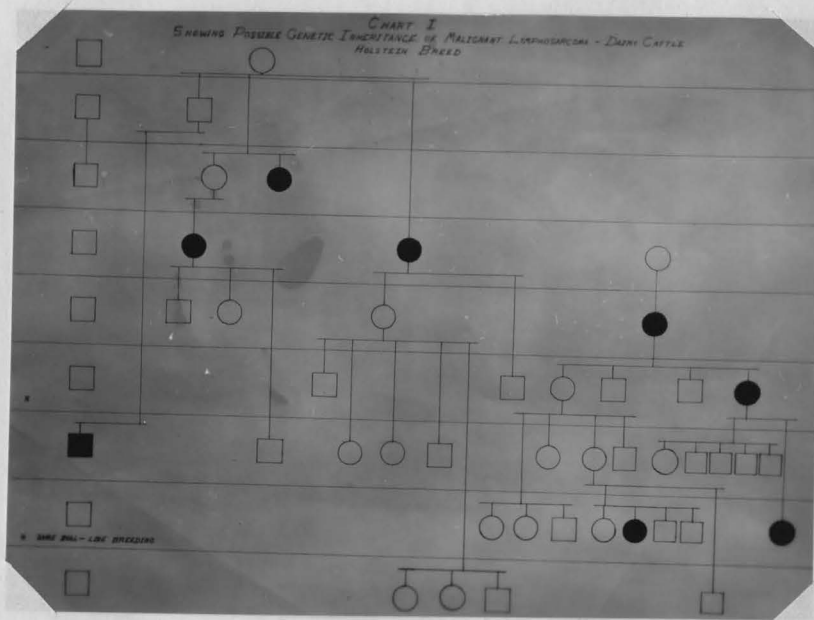


Plate VIII



Table I - Blood Cell Counts of Cow No. 20940D

Date	Total			% Hemo.	Leucocytes				
	Leucocytes	Erythrocytes			Neut.	Lymph.	Eosin.	Baso.	Mono.
July 21, 1936	27,000	5,190,000		75	66	22	10	0	2
Aug. 18, 1937	18,520	6,220,000		72	7	70	18	0	5
May 11, 1938	11,680	6,830,000		68	6	85	5	0	4

Table II - Blood Cell Counts of Cow No. 20941

Date	Total			% Hemo.	Leucocytes				
	Leucocytes	Erythrocytes			Neut.	Lymph.	Eosin.	Baso.	Mono.
June 5, 1936	22,700	5,470,000		45	60	25	3	0	19



Table III - Blood Counts of Cow No. 20942

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 22, 1936	16,120	5,630,000	60	45	47	5	0	2
Jan. 1, 1937	28,280	3,160,000	Too low to read					
Jan. 23, 1937	46,120	2,860,000	"					
Feb. 1, 1937	36,200	3,300,000	"					
Feb. 8, 1937	41,080	3,240,000	"					

Table IV - Blood Cell Counts of Cow No. 21042D

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 22, 1936	11,880	5,180,000	54	57	35	6	0	3
Aug. 18, 1937	8,120	5,220,000		26	49	21	0	4

Table V - Blood Cell Counts of Cow No. 21038D

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 21, 1936	19,250	6,080,000	75	10	83	3	0	4
July 2, 1937	21,340	5,130,000	62	22	62	7	0	4
Aug. 16, 1937	12,920	5,140,000	65	26	58	17	2	2
May 10, 1938	21,600	5,840,000	65	21	63	11	0	5

Table VI - Blood Cell Counts of Cow No. 21039D

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 24, 1936	9,900	5,480,000	90	8	70	16	5	1
July 17, 1937	8,660	4,420,000	65	24	40	29	1	6
Aug. 16, 1936	9,920	5,030,000	62	25	53	18	0	3

Table VII - Blood Cell Counts of Cow No. 21040D

Date	Total			Leucocytes				
	Euocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 16, 1936	20,720	5,430,000	73	35	46	8	4	7
July 3, 1937	12,000	6,590,000	64	29	55	9	1	6
Aug. 17, 1937	17,080	6,220,000	69	34	43	12	0	6
May 10, 1938	13,920	6,740,000	62	20	59	9	1	11

Table VIII - Blood Cell Counts of Cow No. 20939D

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
July 24, 1936	8,540	6,135,000	84	35	47	11	0	7
Aug. 17, 1937	12,280	6,320,000	69	39	45	14	0	2

Table IX - Blood Cell Counts of Calf No. 23252Z

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
Dec. 26, 1936	10,920	6,070,000	56	31	30	22	0	17
Aug. 16, 1937	10,840	6,710,000	69	10	70	1	1	18

Table X - Blood Cell Counts of Cow No. 3028

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
Feb. 1, 1937	42,000	4,360,000	50					

Table XI - Blood Cell Counts of Calf No. 23251Z

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
April 17, 1937	15,320	8,900,000	68	24	55	6	2	13
Aug. 17, 1937	11,720	9,270,000	89	35	55	4	2	5

Table XII - Blood Cell Count of Cow No. 5195

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
May 17, 1937	38,360	7,280,000	63	67	25	0	4	4
May 25, 1937	31,520	5,740,000	53	58	25	3	3	11
June 4, 1937	45,120	5,130,000	50	44	41	3	2	12

Table XIII - Blood Cell Count of Cow No. 4138

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Neut.	Lymph.	Eosin.	Baso.	Mono.
May 24, 1937	6,480	5,030,000	53	27	57	5	4	12
June 17, 1937	10,400	6,550,000	54	45	37	3	2	13

Table XIV - Blood Cell Count of Cock No. 463

Date	Total			Leucocytes				
	Leucocytes	Erythrocytes	% Hemo.	Poly.	Lymph.	Eosin.	Baso.	Mono.
Aug. 12, 1936		3,320,000	80	54	40	0	1	5

Table XV - Blood Cell Count of Cock No. 460

Date	Total	Erythrocytes	% Hemo.	Leucocytes				
				Poly.	Lymph.	Eosin.	Baso.	Mono.
Aug. 12, 1936	2,250,000		75	54	40	0	1	5

Table XVI - Blood Cell Count of Chicken No. 884

Date	Total	Erythrocytes	% Hemo.	Leucocytes				
				Poly.	Lymph.	Eosin.	Baso.	Mono.
Aug. 6, 1936	2,030,000		68	74	25	0	0	1

Table XVII - Blood Cell Count of Chicken No. 834

Date	Total	Erythrocytes	% Hemo.	Leucocytes				
				Poly.	Lymph.	Eosin.	Baso.	Mono.
Aug. 10, 1936	630,000		38	45	50	0	0	5

Table XVIII - Blood Cell Count of Chicken No. 860

Date	: Total : Erythrocytes	: % Hemo.	: Leucocytes				
			: Poly.	: Lymph.	: Eosin.	: Baso.	: Mono.
Aug. 5, 1936	: 2,320,000	: 79	: 45	: 39	: 0	: 3	: 13

Table XIX - Blood Cell Count of Chicken No. 882

Date	: Total : Erythrocytes	: % Hemo.	: Leucocytes				
			: Poly.	: Lymph.	: Eosin.	: Baso.	: Mono.
Aug. 5, 1936	: 2,000,000	: 72	: 70	: 27	: 0	: 1	: 2
Aug. 14, 1937	: 3,310,000	: 81	: 58	: 29	: 5	: 4	: 3

Table XX - Blood Cell Count of Chicken No. 803

Date	: Total : Erythrocytes	: % Hemo.	: Leucocytes				
			: Poly.	: Lymph.	: Eosin.	: Baso.	: Mono.
Aug. 6, 1936	: 2,490,000	: 56	: 59	: 36	: 0	: 0	: 5
Sept. 6, 1936	: 2,520,000	: 50	: 34	: 51	: 2	: 7	: 6

Table XXI - Blood Cell Count of Cock No. M6132

Date	Total	% Hemo.	Leucocytes				
	Erythrocytes		Poly.	Lymph.	Eosin.	Baso.	Mono.
Aug. 10, 1938	2,590,000	90	43	53	0	0	4

Table XXII - Blood Cell Count of Chicken No. 31943

Date	Total	% Hemo.	Leucocytes				
	Erythrocytes		Poly.	Lymph.	Eosin.	Baso.	Mono.
June 22, 1937	2,670,000	74	16	75	0	1	6
July 31, 1937	3,270,000	90	80	11	2	1	7



Table XXIII - Blood Cell Count of Chicken No. 31931

Date	Total	% Hemo.	Leucocytes				
	Erythrocytes		Poly.	Lymph.	Eosine	Baso.	Mono.
June 22, 1937	2,970,000	66	63	6	0	0	31
Aug. 2, 1937	2,880,000	63	16	72	1	1	11

Table XXIV - Blood Cell Count of Chicken No. 142542

Date	Total	% Hemo.	Leucocytes				
	Erythrocytes		Poly.	Lymph.	Eosin.	Baso.	Mono.
June 21, 1937	2,940,000	72	36	57	0	2	7
Aug. 3, 1937	2,900,000	91	40	55	1	2	2



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