Malignant Melanoma

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I. CASE REPORTS

1. MALIGNANT MELANOMA OF EAR

Case is 59 year old, white male admitted to University of Minnesota Hospitals November 14, 1932 and expired November 23, 1932 (9 days).

Benign-Malignant

1926 - Non-pigmented lesion on pinna of left ear.

1928 - Lesion activated when patient was struck on ear by flying sliver from latne. This caused ulceration as well as pain. Biopsy of lesion done and diagnosis of malignant melanoma made.

Excision - Radiation

8- -28 - Upper part of left ear, containing tumor, as well as regional lymph nodes excised. Course of deep x-ray treatment started (last treatment March 1931). Following operation, apparently felt well, but suffered from more or less continuous pain on left side of neck.

Metastasis

4- -32 - Experienced dull constant pain in right upper quadrant of abdomen. First noted weight loss, dropping from 208 to 170 lbs.

6- -32 - Gradual symmetrical enlargement of abdomen.

10-1-32 - Legs and ankles began to swell.

10- -32 - First became conscious of a yellowish discoloration of skin.

11-14-32 - Admitted.

Physical Examination

Well developed, moderately well nourished, somewhat listless. Skin and conjunctivae show icteric tinge. Upper third of left ear absent, skin being well healed. Large, indurated scar on left side of neck which extends along posterior margin of sternomastoid muscle. Just below left mastoid process, there is a hard, nodular mass which extends around angle of mandible and into region of parotid gland. There is a left-sided facial paresis. Chest - without special note. Abdomen - markedly distended and tympanitic, definite fluid wave elicited, liver edge palpated 7 to 8 cm. below costal margin in midclavicular line, mass about 10 cm. in diameter is palpated below liver margin which appears to be attached to the liver. Moderate edema of both lower extremities.

Laboratory:

Urine - specific gravity 1.025, cloud of albumen, no urobilinogen. Blood - hemoglobin 82%, erythrocytes 4,000,000. Blood Wassermann and Kahn tests positive. Icterus index - 188 units. Serum - shows a biphasic reaction to Van den Bergh test. Blood urea nitrogen - 10.9 mgs. Ascitic fluid - specific gravity 1.012. Impression on admission - malignant melanoma with metastases to regional lymph nodes, to liver and probably to lymph nodes adjacent to common bile ducts.

Progress

Condition rapidly became worse and he expired November 23, 1932.

Autopsy

The body is well developed, white male, 59 years of age, weighing approximately 160 lbs. Skin has marked icteric tinge. Slight edema in lower extremities.

Ascites

Peritoneal Cavity contains 3,500 cc. yellowish fluid.

Left Pleural Cavity contains 200 cc. straw colored fluid.

Syphilis

Heart weighs 350 grams. Aortic ring is slightly dilated and shows moderate separation of commissures, separation being about 2 mm. between each leaflet. Free margins of valves are not thickened. Root of Aorta shows severe degree of atherosclerosis as well as several longitudinally streaked whitish areas. Left coronary orifice is somewhat narrowed. There is a mild degree of atherosclerosis of the left coronary artery.

Lungs do not show metastases.

Spleen weighs 300 grams. No visible nodules on gross examination.

Liver weighs 3100 grams. The liver has a greenish appearance, is of a firm consistence and its surface is finely granular. No visible nodules on gross.

Common bile ducts and Gall-Bladder are markedly dilated. In the common bile duct about 1 cm. from the ampulla of vater, there is a nodular tumor mass extending into the lumen. There is a similar nodule about 2 cm. from the ampulla of vater. The nodules seem to have obstructed the common bile duct. At the junction of the cystic and common bile ducts, there is another tumor nodule about 1 cm. in diameter and there is a pigmented nodule in the ampulla of the gall-bladder.

Gastro-Intestinal Tract is filled with clotted and unclotted blood. Examination of the mucosa of the gastro-intestinal tract reveals no evidence of ulceration. No metastatic nodules in omentum.

Pancreas appears normal on gross examination.

Adrenals do not show any tumor nodules.

Kidneys show no metastatic nodules.

Lymph Nodes in the region of common bile ducts show a brownish pigmentation.

There is a soft nodule, 1 cm. in diameter, in the right lobe of the prostate.

Diagnosis:

1. Malignant melanoma of left ear with metastases to regional lymph nodes, bile duct and gall-bladder.
2. Mechanical obstruction of common bile duct.
3. Hemorrhage into bowel.
4. Prostatic hypertrophy.
5. Syphilitic aortitis.

2. MALIGNANT MELANOMA OF PREPUCE

Case is white male, 64 years of age, admitted to University Hospitals 2-13-29 and expired 2-23-29 (10 days).

1925 - First noted lesion on prepuce.

1927 - Lesion exhibited marked rapidity in growth. Ulcerated lesion excised from prepuce, as well as left inguinal nodes.

1929 - Showed dark pigmented lesions on skin of neck, chest, arms, abdomen and upper part of thigh.

2-15-29 - X-ray showed multiple metastases to lungs. Condition became rapidly worse.

2-23-29 - Expired.

Autopsy

Shows skin metastases already noted. There is a grayish tumor mass in greater omentum. There are metastases in the liver, pancreas and right adrenal. The brain shows metastases in the right lobe of the cerebellum and both cerebral hemispheres. There are numerous metastases in the meninges.

II. ABSTRACT

MALIGNANT MELANOMA

By Louise G. Frary, M.D.

Definition

A highly malignant tumor of melanotic cells with a tendency to widespread dissemination (sometimes early) which is usually radio-resistant and not very responsive to surgical excision which may or may not arise on the basis of a previous benign melanoma.

Incidence

Frequency of malignant melanoma: McWhorter and Cloud (Bellevue Hospital)

reviewed 13,500 necropsies; 865 were on malignant tumors, 9 were on melano-carcinomas (malignant melanoma).

Gleave (Leeds General Infirmary) noted 36 cases in a series of 136,609 in-patient admissions.

Pack and Le Fevre (Memorial Hospital) found that among 3,137 skin tumors, (2,857 malignant) malignant melanoma comprised 208 cases.

About one-third of all melanomas originate in the choroid; the choroid is the most frequent site of ocular melano-mas (cited by Ewing). However, Winter-steiner has noted that the disease is relatively rare, occurring in only 0.58% of ophthalmic patients.

Pathology

Classification (Becker)

Neoplasms formed by melanoblasts or related cells.

Benign

Nevus pigmentosus

Non-elevated (no nevus cells)

Elevated (with nevus cells)

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Malignant

Lentigo maligna

Melano-carcinoma or nevocarcinoma

Melanosarcoma or nevosarcoma

Pigmented

Non-pigmented

Histology of Pigmented Nevus:

1. The flat, brown mole may contain no nevus cells and be composed of in-creased number of melanoblasts with hyper-pigmentation of the overlying epithelium.

2. The elevated nevus contains nevus cells in the dermis. The nevus cells are round, oval or polyhedral with pale staining nuclei and pale staining cyto-plasm. The cell size varies with the growth and age of the nevus. An older type contains occasional atrophic nevus cells and fibrous tissue.

The microscopic evidence of malig-nancy consists of increased size of cells (increased cytoplasm), hyperchromatism, increased vascularity and mitoses. Becker has recently shown that in malignant melanomas there is early in-creased pigmentary activity without hyperpigmentation. This feature can be discovered by the use of the dopa reaction. He also demonstrates an in-creased number and disintegration of melanoblasts and hyperpigmentation of the epidermis. Finally, there is dis-integration of epithelial cell structure and penetration of melanoblasts into the epidermis.

Histologic types of malignant melanoma

There are two main types: (1) sar-comatous - spindle shape cells, (2) epidermoid or so-called carcinoma cells - polyhedral shape. The types may also be pigmented and non-pigmented. The sarcomatous form is usually deeply pigmented. Most melanomas will exhibit pigmentation in some portions but it may be masked by the ordinary hema-toxylin-eosin stain. Special stains will show the pigmentation. The silver stain which colors the melanin black is usually employed. The dopa reaction may also be used on fresh tissue. Dopa is 3 - 4 dioxyphenyl alanine, the cyclic amino acid most closely related to adrenalin. By placing thick frozen sections containing melanoblasts, in dopa, non-pigmented melanoblasts may be brought out. This is called a positive dopa reaction and is specific for melanoblasts (myelogenous leukocytes also give a positive dopa reaction). Bloch interprets a positive dopa reac-tion as the formation of dopa melanin by an oxidative ferment in the melano-blast acting on the dopa. Cells con-taining melanin pigment but not the ferment give a negative dopa reaction. Thus, chromataphores (pigment phagocytes) give a negative reaction.

Genesis of pigmented nevi

There are 2 leading theories today:

1. Epithelial (Unna, Bloch and others): The nevus cell is an altered basal cell with descent into the dermis.

(These authors admit a mesodermal origin for the blue nevus.)

2. Neuro-epithelial (Soldan and Masson): Masson as the result of detailed histologic studies concludes that the epithelioid cells in a nevus of the scalp are comparable to the cells of Merkel-Ranvier. He shows corpuscles in the nevus of the scalp comparable to the Wagner-Meissner tactile corpuscles. He concludes that the epithelioid cells and the corpuscles are associated in a "symplaste" by a system of plexiform and amyelinic fibres continuous with myelinated nerves of the dermis. He has carried his studies over to other nevi and he states that "naevi are neuroneurinomas of tactile nerves."

Masson believes that nevi are related to neurofibromata. He says, "In naevi, as in the neurofibromata of the nerve trunks, the characteristic element is the syncitium of Schwann, the peripheral neuroglia of Nageotte, emigrated from the neural crest; but, in the naevi, the Schwann cells are partially neurotized."

It is a question whether malignant melanomas of the skin always arise from previous pigmented nevi or lentigines. Dawson believes that malignant melanomas arise either from carcinomatous change in actual nevus cells derived from the epidermis or from a genetic process, starting in the epidermis and progressively undergoing morphologic change as they migrate into the dermis. Becker has shown that when malignant change occurs in a nevus the change takes place at the epidermodermal junction and not in the nevus cells in the dermis.

Incidence of origin of malignant melanoma from benign molds

Coley and Hoguet in a series of 91 cases report history of moles in 36 of 76 malignant melanomas of the skin.

Broders and McCarty - 70 cases, of which 35 originated in the site of previous moles. Note how these agree with our hospital series, not with Department of Pathology.

Amadon in 27 cases reports a history of moles in 21 (even more).

University of Minnesota Hospitals Cases

Case	Site	History of Pigmented Mole
1	Palmar surface, left thumb	None
2	Tip of auricle, left ear	Yes
3	Right anterior axillary border	Yes
4	Calf, left leg	Not stated
5	Inner canthus, left eye	Not stated
6	Prepuce	None
7	Back	None
8	Eye	—
9	Under chin	None
10	Left ear (helix)	Yes
11	Behind left ear	None
12	Calf, right leg	Not stated
13	Scalp	None
14	Right temporal region	Yes
15	Angle of left jaw	None
16	Just below angle left jaw	None

Summary:

No history of pigmented mole in 8 skin cases (about half). History of previous mole in 4 skin cases. In 2 of these cases, the mole had been present since childhood. In 3, the history of the presence of moles was not stated.

Department of Pathology, University of Minnesota

One hundred and twenty-one operative cases and 32 autopsy cases are reviewed. Site of the primary in order of frequency is as follows:

1. Head and neck - 77 cases, of these 35 (45%) involved the eye.

2. Lower extremity - 36 cases, of these 21 (60%) were on the foot.

3. Trunk - 16 cases, 7 were scrotal

and interscapular.

4. Upper Extremity - 13 cases, with no special site of predilection.

5. Genitalia - labia 2 cases, prepuce 1.

6. Central nervous system - spinal cord 1 autopsy case, pia arachnoid and brain, 1 operative case (primary?).

7. Visceral - ampulla of vater 1 case, jejunum 1.

8. Undetermined primary site - 4 cases.

Note: Of 102 skin melanomas, 85 operative and 17 autopsy cases, there was history of mole in 17 cases (very low?), no history of mole in 35, not definitely stated in 50.

Diagnosis

a. Clinical

The lesion was described in our series by the patient or the doctor as (1) hemorrhagic nodule, (2) hemangioma, (3) blood blister, (4) blood tumor, (5) granulating ulcer, (6) blue-black ulcer, (7) soft corn, (8) infected foot, (9) scabbing sore.

Malignant melanoma develops on any portion of the body but the face and extremities are the common sites. Although pigmented nevi occur in over 95% of people, only a small proportion become malignant. Many times the malignant neoplasm arises in apparently normal skin.

History of trauma cannot always be obtained but in certain sites (foot and scapular regions) trauma seems to play a part in initiating malignant change. In those cases preceded by moles, the patient's attention is frequently aroused by three features: (1) increase in size of mole, (2) increased vascularity manifested by bleeding, (3) increased pigmentation. There may be ulceration or scabbing. Frequently, the increase of pigmentation shows itself by a pigmented areola (melanotic halo) about the mole rather than by increased depth of pigmentation. This is an important feature in malignant changes.

Melanemia and melanuria may be present early. Considerable quantities of melanin in the tumor may cause mobilization of melanin in the blood plasma and cause its excretion in the urine. However, melanuria cannot be taken as conclusive proof of the presence of malignant melanoma. It is a result of protein disintegration and may occur at times in widely different clinical conditions (Stout).

(Test for melanin in urine: add Ferric chloride. This forms a gray precipitate which blackens on standing.)

Melanotic whitlow is a clinical form of malignant melanoma which begins as a swelling on the lateral nail fold of the finger or toe. At first it may be only slightly pigmented and appear as a paronychia. The regional lymph nodes are involved early. Womack (1927) reviewed the literature on melanotic whitlow. Sixty percent of subungual melanomas occurred in the thumb. Pain was not a special feature.

Rectal melanomas

These apparently form 2 to 3% of all malignant melanomas. These tumors are low in the rectum and often pedunculated, usually mobile and do not tend to invade the mucosa but distant metastasis is an important feature. About 80% will have metastases, especially to the liver, at the time of examination.

Ocular melanomas

are either conjunctival or intraocular. These melanomas are said to arise from pigmented nevi (Melanosis oculi).

Primary melanomas may involve the central nervous system. They present no special clinical features.

Treatment

Amadon observed 27 cases, treated with an electric needle. All showed recurrence at the site of the primary lesion. He concludes that treatment by such

procedures as by electro-coagulation, electric needle and actual cautery are dangerous and that wide surgical excision is the procedure of choice. This has wide acceptance.

Note on Treatment by Dr. K. W. Stenstrom

Malignant melanomas as a rule are very resistant to radiation. Stewart from Memorial Hospital, New York City, states that they are almost uniformly highly radio resistant but that about 2% have some degree of sensitivity. "They are apt to be as resistant or more resistant than the surrounding normal tissues and may sprout up under sufficient interstitial irradiation to destroy the tumor bed. Fast growing, widespread, hematogenous metastasis to the skin and subcutaneous tissues may be sensitive." Unfortunately the microscopic picture does not give us much information about the sensitivity. The only satisfactory treatment is radical surgical removal of the primary lesion and the regional nodes. If the disease is widespread it must be considered incurable. Enough statistics are not available to decide whether prophylactic radiation therapy following the surgical removal is of value. There seems to be no contra indication to postoperative prophylactic radiation and it is believed to reduce the number of recurrences.

We have several far advanced cases in whom radiation therapy was used as a palliative treatment. Metastasis to the lungs have responded temporarily and pain has been relieved in bone metastasis. In some cases where the disease was limited to a local lesion and regional nodes, the patients have been well for the time they have been followed after radical surgery plus prophylactic radiation. The longest duration is, however, as yet only four years.

Malignant melanoma of the conjunctiva seems to be an exception to the rule of radioresistance as it often has responded favorably to radiation. This may, however, be explained by the fact that the lesion is superficial and can be treated with a very heavy dose of soft rays, for instance, beta rays from radium.

Prognosis

The average duration of generalized disease is 3 years. The intervals vary between the malignant onset and the appearance of secondary lesions. In a series of 50 cases (Butterworth and Klauder), metastases occurred on the average of 25 months after malignant onset.

There are cases reported of unusual duration, one case of 20 years before metastasis occurred, another 26 years with 4 local recurrences but no evidence of metastasis.

Pregnancy is said to hasten the process.

Variability in prognosis according to site:

Ocular melanomas are less malignant than the skin melanomas. Enucleation before glaucoma appears results in 60 - 80% cures (Ewing). However, when metastasis occurs or recurrences appear, the progress of the disease is about the same as in skin cases.

In subungual melanomas, the average length of life after diagnosis is 14 months.

Malignant melanomas of the mouth usually have metastases to the nodes at the time of observation, first to the nodes of the neck and then to the axillary nodes. The usual course is death 1 to 2 years, the latest 3 years.

Metastasis

The skin is the chief seat of the first metastatic lesion (Ewing). The regional nodes are usually involved early, tumor cells being noted in the nodes before growth manifests itself clinically. As in other malignant tumors, the possibility of the metastasis being the presenting tumor should be borne in mind. This feature is especially significant in malignant melanomas. A supposedly benign mole may have been removed previously or the primary may be so insignificant that it does not attract the patient's attention.

Metastases in order of frequency (32 autopsies): University of Minnesota

Liver	21	Gall-bladder	4
Lymph nodes	19	Omentum and mesentery	4
Lungs and pleura	17	Stomach	3
Subcutaneous	14	Peritoneum	3
Heart	13	Skeletal muscles (including diaphragm)	3
Spleen	13	Large intestine	2
Kidneys	12	Vagina	2
Small intestine	8	Uterus	2
Adrenals	7	Prostate	1
Bone	6	Ovary	1
Pancreas	5	Common bile duct	1
Brain	5		
Thyroid	4		

Note: High incidence in heart and spleen - unusual sites in metastatic lesions.

Bone involvement

1. Melanoma of eye to all ribs, 2. melanoma of left shoulder to calvarium, ribs, vertebrae and right femur, 3. melanoma of right eye to sphenoid, posterior-ethmoid and right maxillary sinus. Lymph node involvement was limited to the regional nodes in only 3 cases. Adrenal involvement was bilateral in 4 cases.

Impressions

1. Malignant melanoma is not a common tumor (1% of all - 7% of skin tumors).

2. Melanomas may be divided into benign and malignant, pigmented and non-pigmented types. While two sub-groups of the malignant form are recognized (sarcomatous and carcinomatous), there is a tendency to classify them all as malignant melanoma.

3. A microscopic distinction can be made between the benign and the malignant form. The "dopa" reaction may be of great assistance in border-line cases. (melanoblasts). Most melanomas will exhibit pigmentation in some portions but it may be obscured by ordinary stains.

4. There are 2 theories of origin of pigmented nevi: epithelial and neuro-epithelial. Masson believes that nevi are related to neurofibromata. "In nevi as in neurofibromata of the nerve trunks, the characteristic element is the syncitium of Schwann."

5. When good histories are available, approximately one-half of all malignant melanomas develop from a benign melanoma. There is a tendency in many records to neglect this point. This is especially true of the Department of Pathology series?

6. There are certain special points of origin which must be kept in mind (head, neck, eye, about ear region, lower extremities - chiefly the foot, scapular and interscapular regions and upper extremities). Apparently benign melanomata are uncommon on the foot. If this is true then the number which become malignant is great and benign melanomas of this region should be removed routinely. The most frequent site of malignant melanoma was the head and neck, including eye. Approximately 25% in this series occurred in the lower extremity. Of 36 cases on the lower extremity, 21 were on the foot.

7. Transformations of benign to malignant growth are characterized in our series by vascularity, bleeding, ulceration, crusting and a suggestive history of trauma. The increased pigmentation may be a halo rather than a change in the mole itself.

8. Melanemia and melanuria may be present early. Melanuria is not conclusive proof of the presence of malignant melanoma as it may be due to other conditions.

9. Special clinical forms should be kept in mind (melanotic whitlow, rectal melanoma, ocular melanoma and melanoma of nervous system).

10. Most malignant melanomas are radio-resistant. Surgical excision is usually not effective and electric needle, electrocoagulation and electrocautery are condemned.

11. The question of prophylactic radiation following surgical removal is still debatable. There seems to be no contra-indication and a certain amount of palliation has been obtained in some cases.

12. Malignant melanoma of the conjunctiva is the exception to the rule of radioresistance as it usually responds favorably.

13. The skin is the chief site of the first metastatic lesions. Regional nodes are usually involved early and a metastatic nodule may be the presenting tumor.

14. The average duration of the generalized disease is 3 years. Metastases occur on the average of 25 months after malignant onset.

15. There are reported cases of unusual duration.

16. The site of origin is of importance in prognosis. Ocular melanomas are less malignant than skin melanomas. Enucleation before glaucoma appears results in a high percentage of temporary cures. It must be kept in mind that late metastasis (as long as 20 years after operation) have been recorded.

17. In 32 autopsy cases (Department of Pathology), the liver was the leading metastatic focus with nodes next. The heart and spleen (unusual sites) are close behind. Any part of the body may be affected. Metastasis to the bones is found in our series.

Note: In addition to the following references 16 cases from the hospital records and 121 operative and 32 autopsy records from the Department of Pathology were studied.

References

1. Becker, S. Wm.
Cutaneous melanoma.
Arch. Derm. u. Syph. 21: 818-835
(May) '30.

2. Becker, S. Wm.
Melanotic neoplasms of the skin.
Am. J. of Cancer 22: 17-40
(Sept.) '34.

3. Laidlaw, G. F.
The dopa reaction in general pathology.
Am. J. Path. 8: 477-490 (Sept.) '32.

4. Amadon, Philip D.
Electrocoagulation of the melanoma and its dangers.
Surg., Gyn. and Obs. 56: 943-946,
(May) '33.

5. Masson, P.
Giant neuro-naevus of the hairy scalp.
Ann. Surg. 93: 218-222, '31.

6. Laidlaw, G. F. and Blackberg, S. N.
A simple technique for the dopa reaction.
Am. J. of Path. 8:491-498, (Sept.)'32.

7. Dawson, J. W.
The melanomata.
Edinburgh M. J. 32: 2, 501-732,
(Oct.), '25.

8. La Melanogenese et les Ferments cutanes.
L. H. Dejust,
Ann de dermat et syph. 9:241-267,
(Apr.), '28.

9. K. Lindberg
Autor de la question du pigment cutane.
Ann. de dermat. et de syph. 4: 353-373, 448-483, '23.

10. Percival, G. H. and Stewart, C. P.
Melanogensis, a review.
Edinburgh M. J. 37: 497-523,
(Sept.) '30.

11. Peck, S. M.
Pigment (melanin) studies of the human skin after application of thorium x with special reference to the origin and function of dendritic cells.
Arch. Derm. u. Syph. 21 #6: 916-956,
(June) '31.

12. McWhorter, J. E. and Cloud, A. W.
Malignant tumors and their metastases, a summary of the necropsies on 865 cases performed at the Bellevue Hospital of New York.
Ann. Surg. 92: 434-443, (Sept.) '30.

13. Gleave, H. H.
Prognosis in malignant melanoma. A report of 40 consecutive cases.
The Lancet 2: 658-659, (Sept. 28) '29.

14. Pack, G. T. and Le Fevre, R. G.
The age and sex distribution and incidence of neoplastic diseases at the Memorial Hospital, New York City.
The J. of Cancer Research 14: 167-294, (June) '30.

15. Bloch, B.
The problem of pigment formation.
Am. J. Med. Sc. 177: 609-618, (May) '29.

Bloch, B.
Der. Zetzige stand der pigmentlehre.
Zentralbl. f. haut u Geschlechtskr 8: 1-10, 1923.

16. Miescher, G.
Ein Beitrag zur epithelialen Genese der malignen melanome der Haut.
Centralbl f allgemeine Path u Path Anat. 30:#14, 353-364, (Oct.) '19.

Miescher, G.
Die Enstehung der bösartigen melanome der Haut
Virchow's Arch. 264: 86-142, (Mar.) '27.

17. Ewing, J.
Neoplastic disease, Philadelphia
W. B. Saunders Co., Ed. 3, 1928.

18. Coley, W. B. and Hoguet, J. P.
Melanotic Cancer with a report of 91 cases.
Ann. Surg. 64: 206-241, (Aug.) '16.

19. Broders, A. C. and McCarty, W. C.
Melano-epithelioma, a report of 70 cases.
Surg., Gyn. and Obst. 23: 28-32, (July) 1916.

20. Laidlaw, G. F. and Murray, M. R.
Melanoma studies III, a theory of pigmented moles. Their relation to the evolution of hair follicles.
Am. J. Path. 9:827-838, (Nov.) '33.

21. Broders, A. C. and Fletcher, E. M.
Evidence in support of neuro-epithelial nature of moles
3: 29-39 (Jan.) '33.

22. Human Cancer
Stout, A. P.
Lea and Febiger, Phila. '32.

23. Bell, E. T.
Textbook of pathology.
Lea and Febiger, Ed. 2, '34.

24. Masson, P.
Les naevi pigmentaires, Tumeurs nerveuses.
Ann. d'anat. path. 3:417-453, (May) 1926; 657-696 (July) 1926.

25. Fuhs, H. and Kumer, L.
Uber Melanosarkome der Mundschleimhaut.
Dermat. Wchnschr. 89: 1867-1899, (Nov. 23) '29.

26. Womack, N. A.
Subungual melanoma; Hutchinson's melanotic whitlow.
Arch. Surg. 15: 667-676 (Nov.) '27.

III. STAFF MEETING

Date:	October 4, 1934
Place:	Recreation Room, Nurses' Hall.
Time:	12:15 to 1:15
Attendance:	75
Program:	Purpose of Staff Meetings. Sound Movie Dean Goodrich New Interns Comprehensive Teaching Case Analysis

Case I: Diagnosis - Lead Poisoning

In response to an open question as to what further information the staff desired, Cecil Watson asked the question -- Was basophilic stippling present in the blood smear? It was: approximately 30% of the red cells showing stippling. Moses Barron then described the case as he was the pathologist at the time she was examined here. She was brought in in a stuporous condition. Routine blood smear showed a large number of stippled cells. Blood poisoning was suspected and the history revealed that the female members of the family had been using a cosmetic consisting chiefly of lead carbonate. The women volunteered the information that they used it because it stayed on so well. It gave a dead white appearance to their face so the preparation is probably not used at the present time. The name was "Flake White." Absorption was thought to have occurred through the nostrils although the skin may be a factor.

R. W. Koucky then reviewed the autopsy findings (see report).

The case was then opened for general discussion. An interesting observation was made in Japan where a large number of women had what was called "Epidemic Meningitis." It was learned that they were using a type of face preparation which contained lead and the diagnosis was changed to "lead poisoning." Another interesting source was uncovered last year in which home brew made in glazed crocks (lead used) was a source of lead poisoning. A child observed at the University of Minnesota Hospitals was found to have been poisoned by playing with tin foil. He collected between 5 and 6 pounds within six months. He constantly played with this material and eventually developed all the signs of lead poisoning, including the wrist drop. At the present time, he is making a very slow recovery. Lead encephalopathy may not be a specific histological picture. Analysis of the brain of a person dying with lead poisoning may not show lead. In some, apparently it is a toxic reaction. In other cases in which the changes are present, there is no marked involvement except for minor cell changes. It should be remembered, therefore, that the absence of any specific pathological picture does not rule out lead encephalopathy. The lead line in the epiphyses of the bones of growing children is a very characteristic finding. Whenever lead poisoning is suspected in children, x-rays of the long bones may reveal deposits at this point. Although basophilic stippling is seen in other blood dyscrasias, very few show the severity of lead poisoning. It is found in some cases of pernicious anemia, myelocytic anemia, etc.

Discussion by: H. A. Reimann, Harold S. Diehl, A. B. Stoesser, Willis Thompson, Alex Blumstein, L. G. Rigler, Cecil Watson.

Case II. Diagnosis: Actinomycosis

O. H. Wangensteen made the diagnosis that the lesion was undoubtedly a pelvic infection which has spread to the liver by way of the portal vein. The cause was pyogenic organisms or actinomycosis, probably the latter.

R. W. Koucky then reviewed the autopsy findings.

In the discussion which followed, the point of origin was of particular interest. The loop of bowel down in the pelvis may have been the focus. Many cases of actinomycosis come in after the primary focus has healed and only the secondary manifestations are present. Some 60 to 70 cases of primary urogenital tuberculosis are in the literature. In many of these cases, the question comes up as to whether or not the genital organs were the primary site of the disease. Many authors favored the cecum or rectum as the original site. Criticism of the transpleural route of opening the liver abscess was made. It appears that this method once used in this institution was not found satisfactory because of the secondary contamination of the pleural cavity. The best approach is low down below the pleura (12th rib). If frank empyema is present, the transpleural route may not be open to so much question.

Discussion by: O. H. Wangensteen.

Case III. Diagnosis: Right Heart Failure Secondary to Chronic Infection Lung Process (Bronchiectasis and Pneumonitis) with Secondary Epileptiform Seizures.

L. G. Rigler read the films. It was noted that the man had a long chest, showed emphysema and the process completely obscured the heart outline. Although there was suggestive increase in the size of the left ventricle, this was really pleura and not heart. The heart was hidden by the extensive process in the lung. Fluoroscopic examination of the heart did not reveal any conus change. In this way, it was seen that the left ventricle was not enlarged.

Richard Johnson made a diagnosis of right heart failure with secondary epileptiform seizures on a vascular basis, the primary lesion being in the lungs on an infectious basis.

R. W. Koucky then reviewed the post-mortem findings. In the discussion which followed, it was pointed out that the history of asthma was atypical. Note inspiratory difficulty. This suggested to some a mediastinal process of an obstructive type. It was also suggested that the cerebral lesions might be metastatic abscess or tumor. Lung tumor was also suggested but ruled out by the x-ray findings. Echinococcus cyst was another possibility although the lesion in the left lower lung was probably not of this nature (x-ray). There was no special consultation with the cardiologist. Sinus infection was considered a possible etiological feature for the lower respiratory involvement. In our experience, we have seen several cases of right heart failure with epileptiform seizures. In the absence of proof that another lesion was not present, it was assumed that this was brought about by the secondary cerebral irritation due to the change in the circulation on the right side.

Discussion by: Ralph Ellis, L. G. Rigler, H. A. Reimann, O. H. Wangensteen, Richard Johnson, R. W. Koucky.

A summary of the autopsy findings in the three cases now follows:

Case I.

Pathologist - Moses Barron

Autopsy summary:

The viscera showed nothing of particular importance with the exception of the kidney which had a few abscesses.

Brain was grossly negative.

The histological sections showed no encephalitis but the presence of this was not considered essential to establish the diagnosis of lead encephalitis.

Chemical analysis of the organs showed a large amount of lead.

(The data left out in this case is that the erythrocytes showed marked basophilic stippling. On the day after admission, the patient developed wrist drop. Family history: All of the women in the family used the face powder which on chemical analysis proved to be lead carbonate.)

Case II.

Pathologist - N. H. Lufkin.

Autopsy summary:

The entire peritoneal cavity was fused by recent and old adhesions with numerous collections of pus. The small bowel was bound to the pelvic organs. One tube and opposite ovary contained abscesses. Liver was filled with multilocular abscesses. Small nodules were present in both lungs.

The histological sections showed actinomycosis.

Case III.

Pathologist - W. A. O'Brien.

Autopsy summary:

Chest was deformed as in chronic emphysema. Recent purulent pleurisy and pericarditis were present.

The heart weighed 515 grams and showed hypertrophy of the entire right side.

The lungs showed emphysema. The bronchi were dilated and infected and the pulmonary arteries not sclerosed.

The liver weighed 2150 grams and showed no chronic passive congestion.

Microscopic sections showed diffuse fibrosis in the lung parenchyma with constriction of the capillary bed. There was no arteriosclerosis in the larger vessels.

Bronchi showed no evidence of asthma.

Conclusions: Chronic pulmonary fibrosis, bronchiectasis, right-sided heart hypertrophy and failure.

IV. ANNOUNCEMENTS

1. SOUND MOVIES

Title: Oxidation and Reduction, by Dr. Hermann I. Schlesinger and Dr. Harvey B. Lemon, of the University of Chicago, shown through the courtesy of the Department of Visual Education, University of Minnesota. One reel.

2. CARL W. LAYMON, M.D.

Announces
the opening of his office
on September Tenth, Nineteen Thirty-Four
615 Medical Arts Building
Minneapolis

Practice Limited to Dermatology

Office	Residence
Bridgeport 3535	Kenwood 1884

Congratulations and Best Wishes!

3. FELLOWS

Last week we presented the Interns. Today we want you to know the Fellows. The development of the Graduate School at the University of Minnesota is synonymous with better teaching and a better clinical service. Before our present senior full-time staff was developed the Fellows used to carry the heaviest part of the clinical load. Although conditions are different at the present time the Fellowship men are taking an even greater part in the development of our clinical services and research. The following names are on file in the Superintendent's Office. We trust that there are no omissions. Any corrections will be appreciated.

Fellows:

Abraham, Arden L. - Minneapolis, Minn.
B.M. - U. of Minn. - '27.
B.S. - U. of Minn. - '27-'28.
Intern - San Francisco City and County Hospital '27-'28.
M.D. - U. of Minn. - '28.
Private Practice, Gibbon, Minn. '28-'34 (July).
Radiology.

Anderson, John A. - Sioux Falls, S. Dak.
U. of S.D. - 2 yrs.
B.S. - U. of Minn. - '31.
B.M. - U. of Minn. - '32.
M.D. - U. of Minn. - '33.
Intern at Mpls. Gen. Hosp. - 3 mos. (Obstetrics)
Intern at Univ. Minn. Hosp. - '33-'34 (Pediatrics)
Research Assistant, Dept. of Peds. - '34-'35.

Borman, C. L. - Minneapolis, Minn.
B.A. - U. of N.D. - '27 (Medicine).
B.S. - U. of N.D. - '29 (Medicine).
B.M. - U. of Minn. - '30.
M.D. - U. of Minn. - '31.
Rotating Intern, Mpls. Gen. Hosp., '31-'32.
Practice, Jordan, Minn., '32-'33.
Fellow in Radiology '33-

Clark, H. E. - Minneapolis, Minn.
B.A. - Dartmouth - '24.
Medicine, Dartmouth - 2 yrs.
M.D. - U. of Minn. - '29.
M.S. - U. of Minn. - '34.
Fellow in Ophthalmology and Otolaryngology '32 -

Dyson, Ralph - Manilla, Iowa.
Jr. Intern, Lutheran Hospital, Des Moines - Summer '31.
M.D. - U. of Iowa - '32.
Intern on Pediatrics, Univ. of Minn. Hosps., '32-'33.
Research in Pediatrics, Univ. of Minn. Hosps., '33-'34.
Teaching Fellow in Pediatrics, Univ. of Minn. Hosps., '34-'35.

Eklund, Carl - Minneapolis, Minn.
St. Olaf, 2 yrs., '21-'23.
B.A. - U. of Minn. - '25.
B.S. - U. of Minn. - '29.
B.M. - U. of Minn. - '32.
Rotating Intern, Mpls. Gen. Hosp., '32-'33.
M.D. - U. of Minn. - '33.
Fellow in Medicine, Univ. of Minn. Hosps., '33 -

Hibbard, J. S. - Wichita, Kansas.
Rotating Intern, St. Francis Hosp., Wichita - '29-'30.
N.D. - U. of Kansas - '29.
Presbyterian Hosp., College of Phys. and Surg., Columbia, July '30-Jan. '32.
Fellow in Surg., U. of Minn. Hosps., Jan. '32 -

Hynes, John E. - Minneapolis, Minn.
B.A. - U. of Minn. - '29.
B.M. - U. of Minn. - '30.
M.D. - U. of Minn. - '31.
Rotating Intern, Detroit, '32.
Fellow in Obstetrics and Gynecology, Univ. of Minn. Hosps., Jan. '33 -

Lee, H. E. - Northfield, Minn.
U. S. Naval Service - '17-'18.
B.A. - St. Olaf - '19.
Taught School, North Dakota, 2 yrs.
B.S. - U. of Minn. - '27.
B.M. - U. of Minn. - '29.
Intern, Univ. of Minn. Hosps., '29-'30.
M.D. - U. of Minn. - '29-'30.
Private Practice, Vergas - '30-'33.
Fellow in Ophthalmology, Univ. of Minn. Hosps., July '33 -

Paine, John - Dallas, Texas.
B.A. - Harvard - '27.
M.D. - Harvard - '31.
Surgery, U. of Minn. Hosps., '31-'32.
Research Assistant, Dept. of Surg., Univ. of Minn. Hosps., '32-'33.
Intern, Mpls. Gen. Hosp., July to Jan. '33 (Medicine).
Fellow on Surg., U. of Minn. Hosps., '34-

Pass, Isadore - Minneapolis, Minn.
B.A. - U. of Minn. - '29.
M.A. - U. of Minn. - '32.
M.B. - U. of Minn. - '32.
M.D. - U. of Minn. - '32.
Rotating Internship, Mpls. Gen. Hosp., '34.
Dept. of Pathology, Mpls. Gen. Hosp., Jan. to June '34.
Fellow in Medicine, U. of Minn. Hosps., July '34.-

Rea, Charles - St. Paul, Minn.
B.S. - U. of Minn. - '28.
B.M. - U. of Minn. - '30.
Intern. Mpls. Gen. Hosp. - '30-'31.
M.D. - U. of Minn. - '31.
Dept. of Pathology, Fellow, '31-'32.
M.S. - U. of Minn. - '32.
Fellow, Physiology, U. of Ill. - '32-'33.
Experimental Surgery, - '33-'34.
Fellow in Surgery, U. of Minn. Hosps., '34 -

Ritchie, Wallace P. - St. Paul, Minn.
B.A. - Yale Univ. - '27.
M.D. - Johns Hopkins - '31.
Intern Union Memorial Hospital, Baltimore - '31-'32.
Fellow in Surg., U. of Minn. Hosps., '32 -

Rossen, Ralph - Minneapolis, Minn.
B.S. - U. of Minn. - '31.
B.M. - U. of Minn. - '33.
M.D. - U. of Minn. - '34.
Intern Pediatrics, U. of Minn. '33-'34.
Fellow in Neurology, U. of Minn. Hosps., '34 -

Russell, Sydney B. - Minneapolis, Minn.
B.A. - U. of Minn. - '25.
M.D. - U. of Minn. - '30.
Rotating Intern, St. Mary's Hosp., Mpls. - '30.
Epidemiologist, State Board of Health, Minnesota - Jan. to July '31.
Division of Mobile Indian Health Survey August '31 to June '32.
Resident in Ophthalmology, Presbyterian Hospital, Chicago, June to Sept. '32.
Fellow in Ophthalmology and Otolaryngology at present.

Semansky, E. J. - Shenandoah, Penn.
B.S. - Georgetown University, Washington, D.C. - '28.
M.D. - Georgetown University, Washington, D.C. - '32.
Intern G. F. Geisinger Memorial Hospital, Penn. - '32 - '33.
Intern U. of Minn. Hosps., '33 - '34 (Surgery).
Fellow in Surg., '34 -