201 ©

ARTHUR PURDY STOUT SOCIETY

New York

May 15, 1974

Note: Please send your diagnoses to Dr. Vellios before May 10th.
Bring these abstracts with you. None will be available
at the meeting.

ABSTRACTS

CASE 1. Dr. Severance

1555-74. An 83 year old female was treated for urinary infection with antibiotics but entered the hospital complaining of inability to urinate for the previous 12 hours. Urine culture was negative. Urine examination showed 8-12 white cells and 25 to 35 red cells and a trace of albumin. I.V. Pyelogram showed negative kidneys.

At cystoscopy, a papillary tumor was seen along the urethra and extruding from the external urethral orifice, extending back to and a little bit above the bladder neck. The tumor seemed to be entirely within the urethra. Ten grams of pale reddish-grey fragments of tumor tissue were sent to the laboratory. (This is labeled 1402-74)

A few days later a complete removal of the urethra and removal of a lower portion of the bladder below the urethral orifice was carried out. (This is pathological number 1555-74). The specimen measured 5 x 3.7 x 3.0 cm. The tumor grossly and microscopically extended up to the lower portion of the trigone. It seemed to be incompletely removed.

CASE 2. Dr. Marshall

S-74-524. A 54 year old woman was admitted with acute urinary retention. Three week history of increasing difficulty in voiding was noted. There was no hematuria by history. She had a twenty pound weight loss in the last three months. She saw a local physician who treated her for urinary tract infection and referred her to the University of Texas Medical Branch.

PHYSICIAL EXAMINATION: Examination revealed blood pressure 96/66, pulse 92, respirations 24. A catheter was placed with 1300 cc.'s residual. On cardiac exam there was mitral stenosis with compensated congestive heart failure.

On pelvic exam the bladder wall was thickened but not fixed to the pelvic wall.

LABORATORY & X-RAY: On admission BUN was 21, hemoglobin 6.6, she was transfused to 12.4. IVP revealed the upper tracts to be within normal limits, cystogram revealed filling defects at bladder neck.

Cystoscopy revealed polypoidal lesions arising around the bladder neck and extending onto the anterior wall of the bladder, with gelatinous pieces easily dislodged. No ulcerated areas were found. The ureteral orifices were not involved with the process.

CASE 3. Dr. Nash

S72-5329A. A 34 year old Black woman noticed progressive swelling and cyanosis of her right arm while she was on oral contraception. The diagnosis of right subclavian vein thrombosis was made with the aid of a venogram and she was treated with anticoagulants and withdrawal of the contraceptives, with some improvement.

Within the next month she noticed painful swelling of her neck and right side of the face, followed by dyspnea, dysphagia and abdominal cramps and she was admitted to St. Luke's Hospital Center.

Case 3 (cont'd)

Her past history was unremarkable except for the periodic ingestion of desoxyn, an amphetamine for weight control, in the last 10 years.

On examination she had mild right facial and arm swelling and marked bilateral cervical swelling with hard, flat to nodular masses in the lateral cervical and supraclavicular regions, interpreted as matted lymph nodes. In addition there was a hard fixed mass palpable in the right iliac area. These masses increased perceptively in size within a few days of observation.

X-ray of the chest showed a widening of the superior mediastinum. IVP was normal except for a 4 x 4 cm. mass in the right lumbar area, displacing the ureter medially. A metastatic bone survey and a number of other laboratory tests were within normal limits.

Biopsies of the cervical and lower abdominal masses revealed identical histology, and a representative section is submitted.

CASE 4. Dr. Morales

S-69-4674. A 60 year old Black female, G3, Para 3003, LMP 14 years, was admitted for the third time to Jackson Memorial Hospital because of a six month history of postmenopausal bleeding. During two previous admissions, she had several biopsies of the endometrium, cervix and vagina which revealed only acute and chronic inflammation, and "necrotic angiomatous tissue with sickling". A hysterectomy disclosed two interstitial leiomyomas and a 6 cm. polypoid intra-cavitary mass of the uterus.

CASE 5. Dr. Azar

S74-415. A 65 year old patient was admitted to a psychiatric hospital for the second time on September 27, 1949. On April 12, 1972, an indurative mass was found on the upper outer quadrant of the left breast. After a frozen section, a left mastectomy with excision of axillary lymph nodes was performed. The breast mass appeared well delineated and measured 5 cm. in its greatest diameter. The left axillary lymph nodes were moderately enlarged and firm but not matted. No other masses were noted elsewhere in the body and on x-ray examination of the chest.

Serum electrophoresis revealed a small spike in the fast gamma region. Radial immunodiffusion assay of immunoglobulins showed the following:

		Normal Range
IgM	231 mg%	45 - 145mg%
IgG	900 mg%	570 - 1900 mg%
IgA	96mg%	60 - 330 mg%

The serum IgM appeared to be monoclonal in character on immunoelectrophoresis, although the monoclonal IgM could not be typed without further isolation and purification.

CASE 6. Dr. Ioachim

172-72. Cervical lymph node in a 59 year old white male. The patient had pneumonia, anemia and coagulation abnormalities. Laboratory data: Hemoglobin 9.6mg%, hematocrit 30%, WBC 5,400 with 73% granulocytes, 26% lymphocytes and 1% monocytes. Platelets 295,000. Sedimentation rate 60 mm in 60 minutes.

CASE 7. Dr. Huvos

70-8608. These are curettings from an expanding epiphyseal lesion of the lower end of the femur in a 14 year old boy. He had painful swelling of the knee for two months prior to examination.

CASE 8. Dr. Coffey

8466-73. This 67 year old man presented with symptoms of left nasal obstruction. In 1962 and mid-December 1970, he had excision of "nasal polyps" (no tissue examination). In January 1971, a left intranasal lesion was excised at another hospital (tissue essentially similar to the present material). Recurrent symptoms of nasal obstruction led to further surgery in October 1973 (present sections). Pre-operative X-rays showed opacification of the left maxillary sinus and left nasal cavity with questionable discontinuity of lateral wall of left maxillary sinus.

Using a Caldwell-Luc approach the tumor was removed. Tumor involved the left nasal cavity extensively with destruction of the wall between nose and maxillary sinus. There was extensive tumor within the maxillary and ethmoid sinuses, but the outer walls of these sinuses appeared to be intact.

CASE 9. Dr. Ackerman

738-735A. A 54 year old woman had a brownish patch on the posterior chest. The laboratory findings were within normal limits. There were no positive physical findings. A bone marrow was within normal limits.

ARTHUR PURDY STOUT SOCIETY
PROGRAM, SPRING MEETING, 1974

WEDNESDAY, MAY 15, 1974

3:00 P.M. - Visit Department of Surgical Pathology,
Vanderbilt Clinic, 16th Floor

SLIDE SEMINAR - 4:00 - 6:00 P.M. - Amphitheater (8th and 9th Floors)
College of Physicians and Surgeons
630 W. 168th St., New York City

COCTAILS FOLLOWED BY DINNER - 6:30 P.M. - Faculty Club - Rooms 17 C&D (17th Floor)
100 New Haven, New York City

BUSINESS MEETING - 8:30 P.M.

THURSDAY, MAY 16, 1974

Joint Meeting of the New York Pathological Society
and Arthur Purdy Stout Society
at
The New York Academy of Medicine
2 East 103rd Street, New York City (at 5th Avenue)

SEMINAR - 5:00 - 6:30 P.M. - Hosack Hall

(Illustrative material available at the meeting)

1. Evolution of Neoplasms in the Mammary Gland.
   Luciano Ozello, M.D., Chairman, Department of Pathology,
   Lausanne, Switzerland.
2. Evolution of Neoplasms of the Uterine Cervix.
   Ralph M. Richart, M.D., Professor of Pathology, College of
   Physicians & Surgeons, New York City

COCTAILS - 6:30 P.M. - Room 20

DINNER - 7:15 P.M. - Room 21

SCIENTIFIC SESSION - 8:15 P.M. - Hosack Hall

Role of Viruses in Neoplasia.
Dr. Donald Kufe, Senior Associate, Institute of Cancer Research,
College of Physicians & Surgeons, New York City

ARTHUR PURDY STOUT SOCIETY
BUSINESS MEETING
May 14, 1974 in New York City

The meeting was called to order by the President at 8:30 P.M. Those in attendance included Drs. Ackerman, Azar, Coffey, H. Dorfman, Ellis, Farinacci, Fine, Flynn, Garber, Huvos, Ioachim, Kay, Lattes, Lester, Luddecke, McBride, Marshall, Meissner, Melicow, Morales, Nash, Ozzello, Pelphrey, Perzin, Pickren, A.O. Severance, Sommers, Wolff, and Yannopoulos.

Dr. Lattes presented a brief report of the financial state of the Society. The Society is solvent until the next meeting, but several bills are outstanding. The banquet for the May meeting is paid for by subscription ("Dutch treat").

Dr. Lattes moved that Dr. L. Ozzello, a member of the Society but participating by special request on the program, have part of his expenses defrayed by the Society. It was voted unanimously that one half of his fare be paid for.

Dr. Lattes moved that Dr. Ronald Dorfman, the special lecturer on the Wednesday afternoon program be given an honorarium of $200. The motion was recorded and passed unanimously.

The invited guests of the Society, including Ronald F. Dorfman, M.D., Earl Kasdon, James Magidson, Juan Rosai, and Ralph Snyder, were unanimously voted to membership in the A.P.S. Society. Invited guests Peter Rosen and Ralph Richart were unable to attend.

The President announced the list of invited guests of the A.P.S. at the Annual meeting, to be held in Washington, D.C. on October 10th. The guests include: George Banayan, Walter Bauer, Dale Bennett, Dianne Crocker, Franz Enzinger, Richard Kempson, Fred Kraus, Robert McDivitt, Richard Reed, Ralph Richart, Irene Roeckel, Peter Rosen, Charles (Pete) Schwinn, and Joseph Tomasulo.

The Arthur Purdy Stout Lecturer at the A.S.C.P. meeting on October 10th will be Dr. Harold L. Stewart, Consultant, National Cancer Institute. His subject will be "Comparative Aspects of Soft Tissue Tumors in Mouse and Man."

It was suggested that future A.P.S. Lectures be given at the International Academy of Pathology. The suggestion was referred to a committee on Planning and Scope.

The President, acting with the Past President as the Council, announced the formation of an Ad Hoc Committee for Planning and Scope. The Committee members include Drs. Ackerman, Hartman, Lattes, Meissner, Morales, Severance, and Vellios (ex officio). The committee has been requested to consider and make proposals for vote of the members at the October meeting on the following topics and any others: nominations for membership, changes in format of the meetings, relationship to the A.S.C.P., I.A.P., and New York Pathological Society, dues, slating of officers, etc. The Committee will meet in October. Suggestions from the membership to Committee members was invited.

It was moved by Dr. Ackerman that the arrangements for the Banquet at the Fall meeting be made by local members rather than the A.S.C.P. office. The motion carried unanimously.

Dr. Lattes requested reimbursement for the $100 he paid out of pocket for a gift certificate to his secretary, Mrs. Nora Thomann who has rendered services to the Society for more than 12 years. The members had previously voted that such notice be taken of her services, but provision for paying for the gift was not previously made. The members present each donated $3 to reimburse Dr. Lattes. He is still $10 short.

The meeting adjourned at approximately 9:30 P.M.

Frank Vellios, M.D.
President

ARTHUR PURDY STOUT SEMINAR
New York, May 15, 1974

Notes Prepared by Contributors

CASE 1. 1555-74 (Dr. Severance)
DIAGNOSIS: Papillary carcinoma, mucinous type, of posterior urethra.

There are two interesting features about this slide. One of the features is the presence of a papillary tumor in which we see fine papillary stalks, with small capillaries in the center of the stalk, and the stalk is made up of epithelial cells, which are pseudostratified, tall columnar in type. They have round or oval, vesicular nuclei, with small nucleoli. In some areas they show mucinous-appearing vacuoles in the cytoplasm of some tumor cells. In another area the tumor cells are forming small clusters in lakes of mucin. In these areas the tumor cells are smaller, with smaller, round or oval, moderately chromatic nuclei, and with small to moderate amount of eosinophilic, finely granular cytoplasm, and sometimes these cells also contain mucinous material. These tumor cells vary only slightly in size and shape. In these mucinous areas, mitotic figures were not seen. In the papillary areas, mitotic figures were seen occasionally. In some areas, the papillary tumor has a pattern somewhat reminiscent of the transitional cell tumors one sees in the urinary bladder. And yet, there is a difference. There is an occasional gland formed by these tumor cells at the bottom of some of the crypts of the papillary lesion. We see in one area some of the papillary tumor forming a cyst-like downward prolongation into the underlying stroma. In one of the sections I could see tumor in the center of what seemed to be a paraurethral gland, lined by transitional epithelium, and the tumor is forming the same papillary features. The tumor cells are darker staining than those of the paraurethral glands. The basal polarity of the nuclei in most of the papillary projections and gland-like structures is well maintained. An occasional focus shows slight loss of basal polarity of the nuclei.

In the first biopsy specimen, 1402-74, there is some stratified squamous epithelium, merging with the papillary and glandular tumor, and again in one of the areas we see invasion of the underlying submucosa by the glandular tumor. In some other areas in the original biopsy material, the tumor cells seem to have more mucinous material in the cytoplasm of the cells, and in some of these areas the tumor resembles very closely that of a villous adenoma of large bowel.

Comment: Carcinoma of the urethra is rare. According to Herbut, in his textbook on urological pathology, he believes that the first case of cancer of the female urethra was reported in 1833 by Boivin and Duges, while the first authentic case of cancer of the male urethra was reported by Hutchinson in 1861. Different series of cases of carcinoma of the male urethra were reported in articles, beginning with Kerwin in 1932, who collected 92 cases, to 1947, when Zaslow and Priestley had collected 208 cases in their paper. In 1932 Kerwin collected 96 cases from the literature of female urethral carcinoma. In 1935 Auer found 167 cases reported in the literature. In the Pondville State Hospital for Cancer in Massachusetts, over a 14-year period, Graves and Guiss encountered 10 cases of carcinoma of the female urethra in 19,000 admissions for cancer. In the female, most of the tumors seem to be near the external orifice, the meatus. In the male the posterior portion seems to be the most frequently affected. The tumor initially may be localized and start out as a papillomatous mass. It may then grow and spread and become ulcerated. Three other major forms of carcinoma are recorded, the fungating variety, the annular constricting variety, and the

ulcerating variety. In the fungating carcinoma, the tumor may be pedunculated or sessile and have a granular cauliflower-like, often ulcerated appearance. It may grow only slightly into the underlying tissues. The annular constricting type of carcinoma is found more often in the posterior portion of the male urethra and the proximal portion of the female urethra, away from the meatus. The ulcerating type of carcinoma may occur anywhere in the urethra, including the meatus. The carcinoma,in either male or female urethra, may arise from either the mucosa itself or from numerous periurethral glands. Therefore one may find a squamous cell carcinoma or a papillary transitional cell carcinoma or an adenocarcinoma. In a series of cases collected by Kreutzmann and Colloff there were 101 cases of squamous cell carcinoma, compared with 9 cases of transitional papillary carcinoma and 5 cases of adenocarcinoma. This applied to both sexes. In the female urethra, Auer reported 19 cases of squamous cell carcinoma and 2 cases of adenocarcinoma. Clayton, in 27 cases, recorded 12 cases of squamous cell carcinoma, 10 of columnar cell type, presumably adenocarcinoma, and 5 of undifferentiated variety. Watson's series consisted of 16 cases of squamous cell carcinoma and 1 of adenocarcinoma. The transitional papillary carcinoma of the urethra is similar in all respects to papillary carcinoma of the urinary bladder, the ureter and the renal pelvis. It is composed of finger-like projections of irregular transitional cells that rise above the surface of the adjacent mucosa.

The adenocarcinoma theoretically can originate in either the basal cells of the mucosa or in the periurethral glands, but probably it is from the latter. Usually a transition from normal mucosa to cancer is not ordinarily detectable. In some of the adenocarcinomas the cells may be piled up in layers of one or more cells thick and may be the cuboidal or columnar type. Some of them may contain mucoid material. The carcinoma of the urethra extends or spreads by extension, by lymphatic spread and by blood vessels. It extends in all directions. It may go distally toward the meatus or it may go proximally and involve the trigone of the bladder, although there is seldom involvement of the bladder itself. When the carcinoma metastasizes it is usually by lymphatic spread. It may spread to the external iliac lymph nodes and to the subinguinal nodes. In the female urethra the lymphatic vessels drain more to the hypogastric lymph nodes. In 17 out of 25 patients reported by Skjaerassen, reported by Ackerman in book on SURGICAL PATHOLOGY, they died of spread of the urethral cancer. The prognosis was worse for those with posterior lesions than those with vulvourethral tumors. Ackerman in his book on CANCER quotes L.E. McCrae as reporting 546 cases of carcinoma of the urethra in UROLOGY SURVEY, Vol. 2, 1952. He notes that the carcinomas are mostly epidermoid carcinoma, occasionally transitional cell carcinomas, and rarely adenocarcinomas, arising from paraurethral ducts or glands. He notes that they occur most frequently in women after the menopause. Interstitial irradiation has been successful in the treatment of carcinomas of the female urethra, and it is usually a combination of roentgen therapy and interstitial radium therapy, but remember most of the tumors were either epidermoid carcinomas or transitional cell carcinomas. Too little is known about radiotherapy in mucinous-producing adenocarcinomas. Harry Grabstald, et al, from Memorial Hospital in New York, in 1966, Journal of the A.M.A., Vol. 197, Sept. 12 issue, reported on a series of 79 patients with cancer of the female urethra, the largest single series reported up to that time. The most common symptoms were urinary bleeding, vaginal bleeding, frequency, and dysuria. The tumors were divided into location as to anterior or entire, and there were 12 adenocarcinomas in this series, 59 epidermoid carcinomas, 4 melanomas, 1 lymphosarcoma and 3 miscellaneous tumors. Of the 5 adenocarcinomas of the anterior portion of the urethra, 2 were thought to arise in Skene's glands; 1 from the entire urethra was thought to arise from a diverticulum. Twenty-two out of 79 patients, or 28%, showed histological proof of inguinal node metastasis, but 13 out of 79 had proven pelvic

node metastasis or 28, a total of 35%, had proven node metastasis. Distant metastases were diagnosed in 11 patients. Surgery or radiation or a combination of the two modalities was used. The most common operation was either partial urethrectomy or total urethrectomy and exenteration. Radiotherapy included external, interstitial, and intracavitary technic. Lymph node metastasis, especially pelvic, seemed to be more frequent when the tumor was covering the entire urethra than just the anterior tumors. The patients with entire urethral tumors showed a high incidence of lymph node involvement, 50%. These authors favor preoperative irradiation, followed by radical surgical procedures, for this type of urethral tumor. There was a comment by the editors that lymph node involvement is relatively infrequent in this tumor, and when the tumor is involving only the anterior third of the urethra, partial urethrectomy and irradiation yields good results.

Rogers and Burns in Jan., 1969, Obstetrics & Gynecology reported on 50 cases of carcinoma of the female urethra seen from 1950-1965 at M.D. Anderson Hospital. These were .7% of all cancers of the female genital tract. Fifteen of the 50 cases were recurrent. All were postmenopausal -- age 39-83. 86% were squamous or transitional in type and 14% were adenocarcinomas. Tumors over 3 cm. did poorly. Adenocarcinoma comes from the paraurethral glands. They preferred irradiation--needles in early cases; needles and external in more advanced cases. Six cases less than 3 cm. survived following radiation therapy. Four cases with posterior lesions and bladder neck involvement had needles and super-voltage irradiation. Only 1 survived (9 years) and it was $2\frac{1}{4}$ x $1\frac{1}{4}$ cm. Twelve patients had involvement of entire urethra--none survived 5 years. Suggest occasional radical surgery, Cytoxan and 5 FU for palliation.

Harry Grabstald in Cancer, Nov., 1973, reported again on tumors of the urethra. He added 17 cases to his previous series, bringing the total up to 96 for the carcinomas of the female urethra. They had 67 patients with squamous cell carcinoma and 18 with adenocarcinoma, 5 melanoma, and 1 lymphosarcoma. They believe all palpable lymph nodes are abnormal because when removed 24 of 25 nodes had cancer. Distant metastases more common in adenocarcinoma. None of the adenocarcinoma cases with positive nodes were cured. Entire urethral tumors are best treated by preoperative radiation and anterior exenteration; radical groin dissection if there is palpable disease.

In the December 1971 issue of the Journal of Urology Ney, Miller and Ochs reported a mucus-secreting adenocarcinoma arising in a diverticulum of the female urethra. They discussed briefly three other cases of adenocarcinoma arising in a diverticulum of the female urethra previously reported. They consider this tumor exceedingly rare. This case was treated with surgical excision, postoperative x-ray and radium therapy with transurethral resection of recurring urethral implants.

Roman Knoblish, in the American Journal of Obstetrics and Gynecology Vol. 80, 1960 reviewed the literature on primary adenocarcinoma of the female urethra and added three cases of his own to bring the total up to 44 at that time. Some were called papillary, colloid, papillary and gelatinous, glandular, columnar cell, adenocarcinoma, and adenoacanthoma.

Follow up 5-1-74. Foley catheter changed. Patient receiving Cobalt. 5-13-74 Cobalt planned 6,000 to 7,000 rads. No leakage at bladder neck which has stayed closed ok.

CASE 2. S-74-524 (Dr. Marshall)
DIAGNOSIS: Mesonephric Adenocarcinoma of the Bladder

The first consideration was whether it was malignant or benign. As most congeries of pathologists; staff and resident, the diagnosis was very adequately qualified. The diagnosis assigned eventually, as indicated above was with the support of Dr. Mostofi and Dr. Farrow and made independently. Although the occurrence of mesonephric "rests", mesonephric adenomas and adenocarcinoma in the female genital region have been well documented [1,2] this is a "peculiar" lesion in the bladder.

Dow and Young [3] reported "The first case" of a mesonephric adenocarcinoma of the bladder with brain metastasis. Subsequent reviews indicate the bladder may be the primary site [4,5] although the latter is a technical paper on exenteration and whether the mesonephric adenocarcinoma was primary in the bladder is not clear.

Shiller [6] originally characterized these tumors in the ovary as composed of tubular structures of various size and lined by low cuboidal cells. The epithelium was frequently hobnailed with "peg-like" intraluminal tufting interpreted as imperfect glomerulus formations (perfect for the mesonephros). It is of some interest that Teilum did describe elongated tubules with stratified epithelium. You may note the alteration of the transitional epithelium adjacent to the tumor.

Special stains showed the presence of glycogen, weakly positive mucin reaction and no other significant characteristics.

Electron microscopy demonstrated abundant glycogen, some colloid-like material, lysosomes et. al. in degenerating cells and no mucin production. Comparison with a renal cell carcinoma ultrastructurally showed greater anaplasia and less glycogen in the mesonephric carcinoma. Review of three "mesonephric carcinomas" of the vagina and ovary suggested not all clear cell tumors are mesonephric in origin and the differential should include: adenomatoid tumor (mesothelioma), adenocarcinoma of periurethral glands (Albarran's), and entodermal sinus tumor and lipoid cell tumor of ovary. The cloacogenic endocervical carcinomas extending to involve the trigone can be excluded. The embryologic, light microscopic, and ultrastructural studies of this neoplasm make it acceptable as a mesonephric adenocarcinoma.

1. Teilum, G. Histogenesis and classification of mesonephric tumors of the female and male genital system and relation to so-called (wishy-washy) adenomatoid tumors (mesotheliomas); comparative histological study. ACTA Path, et Microbiol. Scand. 34:431,1954.

2. Novak, E., Woodruff, J.D., & Novak, E.R. Probable mesonephric origin of certain female genital tumors. Amer. J. Obst. & Gynec. 68:1222, 1954.

3. Dow, J., and Young, J. Mesonephric adenocarcinoma of the bladder. J. of Urol. 100:466, 1968.

4. Christoffersen, J. and Moller, J., Adenomatoid tumors of the urinary bladder. Scand. J. of Urology, 6:295, 1972.

5. Galante, M. and Hill, E. Pelvic exenteration. Amer.J.Obst. & Gynec. 110:180, 1971.

6. Shiller, W. Mesonephroma ovarii. Amer.J.Cancer 35:1, 1939.

7. Williams, D. Development of the trigone of the bladder. Brit.J. Urol. 23:123, 1951. (not sited.)

CASE 3. S72-5329 (Dr. Nash)
DIAGNOSIS: Multifocal fibrosclerosis involving soft tissues of neck, mediastinum and retroperitoneum.

Addendum to Clinical History: The Patient was started on Prednisone, 60 mgm. O.D.; within the next ten days her cervical and abdominal masses receded dramatically and her mediastinal shadow disappeared on chest x-ray. She was discharged symptom-free on steroid maintainance and has been followed since by a private physician. He reports that although he was able to gradually taper her dose of Prednisone to 5mgm. without recurrence, when he stopped medications, there was prompt reappearance of the symptoms, necessitating re-institution of steroid therapy up to the present, fifteen months after diagnosis.

Discussion: The histologic features of this case consist of a diffuse growth of relatively avascular fibrous connective tissue, without distinctive pattern, but characteristically containing areas of acute and chronic type of inflammatory cells. In some areas, there is active fibroblastic cell growth whereas in others broad bands of hyalinized collagen, resembling those of keloid scars are seen.

The gross appearance of this condition presents pale, hard scar-like tissue with a "wooden" texture, forming encasing flat plaques or round "tumor" like masses.

A case of mediastinal sclerosing fibrosis from the autopsy files of St. Luke's Hospital Center is shown to illustrate the infiltrative qualities of this type of lesion; the process had invaded the major pulmonary veins at the hilum thus causing massive terminal hemoptysis, after a 5 year course of recurrent hemoptysis and progressive pulmonary hypertension. This case also illustrates the tragic and fatal outcome this condition may take if undiagnosed, as the seminar case emphasizes the importance of early diagnosis and treatment.

In the light of many recent reports in the literature, it is evident that this condition may manifest itself locally or with simultaneous multiple sites of involvement, thus meriting the term "multi-focal fibrosclerosis", first proposed by Comings in 1967. Some of the better known analogies of the condition have been named in the past by such topographic designations as: sclerosing mediastinitis or cholangitis, retroperitoneal fibrosis, Riedel's struma and orbital pseudo-tumor.

The etiology of the disease is not clearly understood, and some of the possible contributory factors such as infections, drugs and autoimmunity, are discussed.

Differential diagnosis from malignancies such as desmoplastic carcinoma and Hodgkin's Disease as well as early diagnosis and the effective therapeutic response to use of steroids are emphasized.

1. Buckberg, G.D.: The protean manifestations of sclerosing fibrosis. Surg. Gynec. Obstet. 1966, 123, 729-736.

2. Comings, D.E., Skubi, K.B., Van Eyes, J., Motulski, A.G.: Familial multifocal fibrosclerosis. Ann. Intern. Med. 1967, 66, 884-892.

3. Cutler, B., Donaldson, G.A.: Primary sclerosing cholangitis and obliterative cholangitis. Amer. J. Surg., 1969, 117, 502-511.

4. Gleeson, M.H., Taylor, S., Dowling, R.H.: Multifocal fibrosclerosis. Proc. Royal Soc. Med., 1970, 63, 1309-1311.

5. Graham, J.R.: Fibrotic disorders associated with methysergide therapy for headache. New Eng. J. Med., 1966, 274, 359-368.

6. Hache, L., Woolner, L.B., Bernatzm, P.B.: Idiopathic fibrous mediastinitis, J. Dis. Chest, 1962, 41, 9-25.

7. Kittredge, R.D., Nash, A.D.: The Many Facets of Sclerosing Fibrosis. Amer. J. Roent., Rad. Ther. & Nucl. Med. accepted for publication, 1974.

8. Kunkel, W.M., Clagett, O.T., McDonald, J.R.: Mediastinal granulomas. J. Thor. Cardiov. Surg., 1953, 27, 565-574.

9. Mitchison, M.J.: Pathology of retroperitoneal fibrosis. J.Clin.Path., 1970, 23, 681-689.

10. Morandi, L.P., Grob, P.J.: Retroperitoneal fibrosis. Arch. Intern. Med. 1971, 128, 295-298.

11. Que, G.S., Mandema, E.: A case of idiopathic retroperitoneal fibrosis, presenting as a systemic collagen disease. Amer. J. Med., 1964, 36, 320-329.

CASE 4. (S-69-4674)(Dr. Morales)
DIAGNOSIS: Plexiform tumorlet of the uterus.

This tumor is made up of cords of cells with scant cytoplasm and uniform round nuclei lying in abundant hyalinized stroma. Reticulum stain demonstrated fibers around groups of cells rather than separating individual cells as one would generally expect in mesenchymal lesions. There was no evidence of invasion of the myometrium and peripherally the tumor blended with the adjacent endometrium. Sections from the interstitial leiomyomas revealed the routine histologic pattern of uterine leiomyomas unlike the above described intracavitary mass.

Histologically, the tumor under consideration is identical to the lesion originally described by Borghard-Erdle and Hirsch [1] who considered the lesion a glomus tumor. In 1965 Larbig, et al.[2] described five cases and named it "plexiform tumorlet" which seems to be the term presently accepted for this rare uterine lesion. The literature now contains 20 reported cases of this condition. [1-4] All of them have been incidental findings and unlike the present case have measured no more than 0.5 cm. in largest dimension. Nearly one-third of the published cases have been associated with foci of adenomyosis and more than half had associated leiomyomas of the uterus.

The histogenesis of the lesion is uncertain. It has been considered a glomus tumor, "solid angioma" variant of leiomyomas, and a benign endometrial stromal tumor. Most of the participants in the seminar favored the diagnosis of leiomyoblastoma. However, ultrastructural study of this case showed none of the characteristics of smooth muscle tumors [5] but numerous cellular junctional complexes

akin to epithelial and/or stromal cells. The latter origin seems also to be supported by the reported instances of the tumor in association with foci of adenomyosis.

1. Borghard-Erdle, A.M. and Hirsch, E.F.: Glomus tumor of the uterus. Arch.Path. 65: 244, 1958

2. Larbig, G.G., et al.: Plexiform tumorlets of endometrial stromal origin. Am. J. Clin. Path. 44: 32, 1965.

3. Patchefsky, A.S.: Plexiform tumorlet of the uterus. Obst. Gynec. 35: 592,1970.

4. Cera, P.J., Jr.: Plexiform tumorlet of the uterus: Report of two cases. Am. J. Clin. Path. 59: 263, 1973.

5. Morales, A.R., et al.: The ultrastructure of smooth muscle tumors with a consideration of the possible relationship of glomangiomas, hemangiopericytomas and cardiac myxomas. Path. Ann. 1975 (in press).

CASE 5. (S74-415)(Dr. Azar)
DIAGNOSIS: Malignant lymphoma with plasmacytic differentiation (lymphoma with mixed plasmacytic and lymphocytic components) involving the breast and axillary lymph nodes.

A year following mastectomy the patient developed a progressive IgM lambda type monoclonal gammapathy. There is also radiologic evidence of involvement of the lung by tumor. The clinical picture is not yet that of classical Waldenström's macroglobulinemia.

Haagensen (1) in his Diseases of the Breast (2nd ed.) states that "there are occasional soft part tumors composed of plasma cells that are not associated with plasma cell myeloma. None has been reported in the breast". Occasionally, however, a breast tumor may be the first presenting sign of multiple myeloma (2). Also according to Haagensen (1), "all types of lymphosarcoma have appeared initially in the breast, without concurrent manifestations of the disease elsewhere. In such cases the disease usually soon appears in other areas of the body, in lymph nodes, or in the chest, and follows its characteristic course." In Haagensen's nine personal cases, all were of the reticulum cell type, seven had involvement of axillary lymph nodes and seven died with persisting or generalized lymphosarcoma.

The presence of "myeloma-type" serum protein (in modern language: M-component, paraprotein or monoclonal immunoglobulin) has been reported by Azar, Hill and Osserman (3) in 1957 in 13 patients with malignant lymphoma or chronic lymphocytic leukemia. These M-components were not classified immunoelectrophoretically at the time of publication of this report but later 3 of these M-components were found to be 19S macroglobulins.

The association of monoclonal immunoglobulins or paraproteins have been subsequently described by a number of authors: In 1966, Krauss and Sokal (4) reported 9 patients with malignant lymphomas and various types of paraproteinemia. In 1970, Moore et al (5) analyzed the evidence of monoclonal gammapathies in various forms of malignant lymphoma: of 333 patients with diffuse lymphoma, 3.6% had an IgM monoclonal protein; a prevalence estimated to be about 60 times more frequent than that in normal subjects. Only 1.5% had an IgG monoclonal

protein. Monoclonal proteins were more frequent in older patients. Interestingly, no monoclonal IgM proteins were observed in sera of 345 patients with nodular lymphoma or Hodgkin's disease. The association of IgM monoclonal proteins with reticulum sarcoma evolving from Sjögren's syndrome has been stressed by Talal et al (6).

More recently, Kim, Heller and Rappaport (7) analyzed 15 patients with lymphoproliferative diseases of various types and associated monoclonal gammapathy. Eleven of these patients had an IgM monoclonal gammapathy, 10 of the lambda type and one Kappa type. Nuclear PAS-positive globules were found in only 3 patients with IgM monoclonal gammapathy; in 2 of these, they were found after a prolonged search. The presence of plasmacytoid or pyroninophilic cells, and of PAS-positive globules within the nucleus or cytoplasm were considered to be helpful in predicting the association of malignant lymphoma with a monoclonal gammapathy.

The plasmacytoid differentiation of this malignant lymphoma was so striking that electrophoretic and immunoelectrophoretic studies were requested immediately after the operation. Although there was a marked increase in IgM level during the immediate post-operative period, a monoclonal IgM was satisfactorily demonstrated only a year later.

Because of the present emphasis on classifying lymphocytes and other immunocompetent cells into T (thymus-dependent) and B (thymus-independent) cells, immunologic surface markers have been utilized to investigate the morphogenesis of the lymphomas. It has been suggested that neoplastic lymphoreticular cells also bear surface markers or receptors and their presence or absence may establish the origin of these neoplastic cells. A recent study by Jaffe et al (8) of the cellular origin of nodular lymphoma revealed that a high proportion of the neoplastic cells had IgM receptors, not unlike those of B-type lymphoid follicular cells.

1. Haagensen, C.D.: Diseases of the Breast (2nd edition). W. B. Saunders Co., Philadelphia, 1971, pp. 315-323.

2. Rosenberg, B., Attie, J.N. and Mandelbaum, H.L.: Breast tumor as the presenting sign of multiple myeloma. N. Engl. J. Med. 269:359-361, 1963.

3. Azar, H.A., Hill, W.T. and Osserman, E.F.: Malignant lymphoma and lymphatic leukemia associated with myeloma - type serum proteins. Amer. J. Med. 23:239-249, 1957.

4. Krauss, S. and Sokal, J.E.: Paraproteinemia in the lymphomas. Amer. J. Med. 40:400-413, 1966.

5. Moore, D.F., Milgliore, P.J., Schullenberger, C.C. and Alexanian, R.: Monoclonal macroglobulinemia in malignant lymphoma. Ann. Int. Med. 72:43-47, 1970.

6. Talal, N., Sokiloff, L. and Barth, W.F.: Extrasalivary lymphoid abnormalities in Sjögren's syndrome (reticulum cell sarcoma, "pseudolymphoma", macroglobulinemia). Amer. J. Med. 43:50-65, 1967.

7. Kim, H., Heller, P. and Rappaport, H.: Monoclonal gammapathies associated with lymphoproliferative disorders: a morphologic study. Amer.J.Clin.Path., 59:282-294, 1973.

8. Jaffe, E.S., Shevash, E.M., Frank, M.M., Berard, C.W. and Green,I.: Nodular lymphoma-evidence for origin from follicular B lymphocytes. N. Engl. J. Med. 290:813-819, 1974.

CASE 6. (172-72)(Dr. Ioachim)
DIAGNOSIS: Lymphadenopathy, consistent with Waldenström's macroglobulinemia (W.M.)

Sections show a lymph node which appears to be quite enlarged with abundant lymphoid parenchyma and large, well-defined sinusoids filled with histiocytes. Peripheral sinuses are present, but the capsular collagen and the fibrofatty tissue peripheral to this are heavily infiltrated with cells. Most of these are mature lymphocytes, but there are also scattered histiocytes, plasma cells and mast cells. The lymphoid tissue of the nodes themselves, is also infiltrated with histiocytes and plasma cells. Many histiocytes, in and around the sinuses are filled with hemosiderin pigment. Germinal centers are present, but rather obscure.

A. Pathological criteria for diagnosis of W.M. in lymph nodes:

1. Histology
   - moderately enlarged
   - perinodal fat infiltrated
   - follicles obliterated
   - sinuses preserved
   - plasma and serum PAS +

2. Cytology
   - not uniformly lymphocytic
   - well differentiated
   - infrequent mitoses
   - plasma cells
   - mast cells
   - hemosiderin
   - lymphocytoid plasma cells
   - intranuclear PAS + inclusions

B. Immunological criteria for diagnosis of W. M.:

- increased total proteins
- increased gammaglobulins
- presence of M proteins
- presence of monoclonal spike of fast gammaglobulins
- marked increase of gamma M globulins on immunoelectrophoresis

C. Clinical symptoms and their pathogenesis in W.M.:

1. Proliferation of atypical lymphocytes
   - anemia
   - leukopenia
   - hemorrhagic diathesis
   - impaired antibody synthesis

2. Hyperviscosity
   - cardiac failure
   - thrombosis
   - slowed circulation
   - retinal changes
   - impaired mentality
   - incr. ESR., rouleaux
   - impaired leuk. phagoc.
   - impaired platelet function
   - impaired antibody release

1. Argani I. and Kipkie, G.F.: The cellular origin of macroglobulins. Lab. Invest. 14:720-6, 1965.

2. Dutcher, T.F. and Fahey, J.L.: The histopathology of the macroglobulinemia of Waldenström - J. Nat. Cancer Inst. 22:887-917, 1959.

3. Harrison, C.V.: The morphology of the lymph node in the macroglobulinemia of Waldenström. J. Clin. Path., 25:12-16, 1972.

4. Osserman, E.F. and Fahey, J.L.: Plasma cell dyscrasias: current clinical and biochemical concepts. Amer. J. Med., 44:256, 1968.

5. Rappaport, H.: Tumors of the Hematopoietic system - Atlas of Tumor Pathology, fasc. 8, A.F.I.P. 1966.

6. Samaracq, P.R.: Anatomie pathologique de la maladie de Waldenström, Sang 31: 473-489, 1960.

7. Tanaka, Y. and Goodman, J.R.: Electron microscopy of human blood cells, Harper & Row, 1972.

8. Waldenström, J.: Incipient myelomatosis or "essential" hyperglobulinemia with fibrinogenopenia - new syndrome? Acta Med. Scand., 117:244-261, 1944.

9. Waldenström, J.G.: Benign monoclonal gammapathies 247-286, in Multiple myeloma and related disorders, edit. H.A. Ažar and M. Potter, Harper & Row, 1972.

10. Zucker-Franklin, D., Mullaney, V.: Structural features of cells associated with the paraproteinemias. Seminars in Hematology 1:165-198, 1964.

11. Macris, N.T., Capra, J.D., Frankel, G.J., Ioachim, H.L., Satz, H., and Bruno, M.S.: A lambda light chain agglutinin cryomacroglobulin occurring in Waldenström's Macroglobulinemia. The Am. J. of Med., 48:525-29, 1970.

CASE 7. (70-8608)(Dr. Huvos)
DIAGNOSIS: Chondroblastoma

Histologically the primary lesion is that of a typical benign chondroblastoma and it was entirely unsuspected that the lesion metastasized to the lungs in multiple foci after local recurrence. Local recurrence with soft tissue tumor implantation rarely occurs and does not in itself signify a potential metastasizing tumor. Malignant transformation in chondroblastomas in the absence of radiotherapy are extremely rare and are summarized in the enclosed table. It is interesting to mention that the histological study of the metastasizing pulmonary lesions in this case showed evidence of "maturation" characterized by mature cartilage and bone formation. Some pertinent references follow:

1. Dahlin, D.C. and Ivins, J.C.: Benign chondroblastoma. A study of 125 cases. Cancer, 30:401, 1972.

2. Huvos, A.G. and Marcove, R.C.: Chondroblastoma of bone. Clinical Orthopaedics, 95:300-312, 1973.

3. Kahn, L.B., Wood, F.M. and Ackerman, L.V.: Malignant chondroblastoma: Report of 2 cases and review of the literature. Arch. Pathol. 88:371, 1969.

4. Schajowicz, F. and Gallardo, H.: Epiphysial chondroblastoma of bone. A clinicopathological study of 69 cases. J. Bone Joint Surg. (Br.) 52:205, 1970.

METASTATIC "BENIGN" CHONDROBLASTOMA OF BONE

Primary tumor		Metastatic tumor		Follow - up	Author + yr.
Site	Treatment	Site	Treatment		
Fibula	Local excision Amputation	Lung (solitary)	Lobectomy	NED 5½ yrs.	Sweetnam & Ross 1967
Femur	4 curettages + partial excision	Lung and other organs	None	Died in 15 yrs.	Kahn et al. 1969
Tibia	Amputation	Lung (multiple)	Biopsy	No F.U.	Dahlin & Ivins 1972
Tibia	Amputation	Lung (multiple)	Excision of 1 nodule	Alive 5 yrs.	Riddel et al. 1973
Femur	2 curettages	Lung (multiple)	Excision of nodules	Alive 5 yrs.	Huvos et al. 1974

CASE 8. (8466-73)(Dr. Coffey)
DIAGNOSIS: Well differentiated mucin producing adenopapillary carcinoma of minor salivary gland origin, left nasal cavity and paranasal sinuses.

This 67 year old man (Occupation: lawyer) underwent excision of a large tumor that involved left nasal cavity, maxillary sinus and ethmoid sinus. The lateral nasal wall was partially destroyed, presumably by pressure since no direct bone invasion was demonstrable grossly or microscopically.

Histologically, the tumor contained mucinous cyst spaces and areas lined by focally papillary and markedly cellular neoplasm. In some areas the neoplasm was acceptable as mucin secreting adenoma. Other areas showed nuclear atypia and focal stromal invasion leading to the diagnosis of well differentiated adenocarcinoma. In some foci there was superficial resemblance to colonic carcinoma.

Electron microscopic study showed that the tumor was clearly of salivary gland origin. The overall appearance was that of stratified epithelium. The luminal surfaces contained focally abundant microvilli but no cilia. Two types of secretory granules, similar to those described in human parotid tissue (7), and myoepithelial cells (5) were identified.

While certain areas resemble the well-recognized entity of nasal adenocarcinomas that closely simulate colonic carcinomas (4,8,9) the demonstrated origin from seromucinous glands suggests that this lesion is more likely the nasal counterpart of mucous producing adenopapillary carcinoma of parotid gland as described by Blanck et al.(3) In the report by these authors it is noteworthy that the histology of the parotid gland tumor is characterized as "mucous producing adenocarcinoma rather similar to adenocarcinoma of the gastrointestinal tract but with a greater tendency to formation of cystic and papillary structures." These tumors were considered to be closely related to mucoepidermoid carcinoma and separable by the lack of squamoid differentiation and a better survival for mucoepidermoid carcinoma. However, the survival rate for the subgroup of low grade malignancy adenopapillary carcinoma was excellent (94% at 5 years; 80% at 20 years).

In the series of twenty cases of nasal adenocarcinomas that closely simulate colonic carcinomas reported by Sanchez-Casis et al (8) certain differences from the present lesion are apparent. The twenty cases as well as other similar cases in the literature (1,2,4,6,8,9) have shown a predilection for ethmoid sinus region as the site of origin. The present tumor most likely originated in the lateral nasal wall. Sanchez-Casis et al state that the tissue of origin for the colonic type carcinoma is from either surface epithelium or submucosal glands and that the tumors have little similarity to salivary gland tumors. In 14 of their patients death was attributable to tumor (local invasion) with in some instances initial recurrence up to 5 years following therapy. The authors recommended lateral rhinotomy as the approach of choice. Four of these patients, however, were alive and well without evidence of tumor 5 to 15 years after varied forms of therapy. Possibly some of these less lethal tumors included in this series as well as other series in the literature may represent tumors similar to the present case.

This patient has shown no evidence of further recurrence 6 months after local excision of the tumor.
(Dr. Gordon Kaye of the Department of Pathology, College of Physicians & Surgeons performed the electron microscopic study).

1. Batsakis, J.G., Mucous Gland Tumors of the Nose and Paranasal Sinuses. Ann. Otol., Rhinol. and Laryngol. 79:557-562, 1970.

2. ----------, F. Holtz and R.H. Sueper, Adenocarcinoma of Nasal and Paranasal Cavities, Arch. Otolaryngol. 77:625-633, 1963.

3. Blanck, C., C-M. Eneroth and P.A. Jakobsson, Mucus-Producing Adenopapillary (Non-Epidermoid) Carcinoma of the Parotid Gland, Cancer 28:676-685, 1971.

4. Goepfert, H. and R.E. Fechner, Pathologic Quiz Case, Arch. Otolaryngol. 98:137-138, 1973.

5. Hubner, G., H.J. Klein, O. Kleinsasser and H.G. Schieffer, Role of Myoepithelial Cells in the Development of Salivary Gland Tumors, Cancer 27: 1255-1261, 1971.

6. Jarvi, O. Heterotopic Tumors With an Intestinal Mucous Membrane Structure in the Nasal Cavity, Acta Otolaryngol. (Stockholm) 33:471-485, 1945.

7. Riva, A. and F. Riva-Testa, Fine Structure of Acinar Cells of Human Parotid Gland, Anat. Rec. 176:149-165, 1973.

8. Sanchez-Casis, G., K.D. Devine and L.H. Weiland, Nasal Adenocarcinomas that Closely Simulate Colonic Carcinomas, Cancer 28:714-720, 1971.

9. Simard, L.C. and Jean, A., Adenocarcinoma With Argentaffin Cells of the Nasal Cavity, Giving Widespread Metastases, Cancer 6:699-703, 1953.

CASE 9. (738-735)(Dr. Ackerman)
DIAGNOSIS: Skin: Lymphocytic leukemic infiltration.

This case was of great interest to me because of the differential diagnosis between pseudolymphoma and leukemic infiltrate of the skin. At the time of the biopsy, all of the laboratory findings were negative, including the bone marrow. The bone marrow was later reviewed and it was agreed that it was within normal limits. It also should be emphasized that the patient did not have generalized lymphadenopathy. Two months later, the patient blew up with typical chronic lymphocytic leukemia with a white blood count of over 90,000. The bone marrow was involved.

The diagnosis of possible lymphoma was made on the original slide because of homogeneous infiltrate. There were no germinal centers, and there were no admixtures of inflammatory cells. Since seeing this case, I have learned of several others. Therefore, the pathologist must be extremely careful in making a diagnosis of pseudolymphoma.

NEW YORK PATHOLOGICAL SOCIETY

Organized in 1844 Incorporated in 1886

NEOPLASIA

Arthur Purdy Stout Meeting

May 16, 1974

Vol. I #6

S E M I N A R

EVOLUTION OF NEOPLASIA IN THE FEMALE MAMMARY GLAND

* * *

EVOLUTION OF NEOPLASIA IN THE UTERINE CERVIX

* * *

Raffaele Lattes, M.D.
Professor of Surgical Pathology
College of Physicians and Surgeons
Columbia University

* * *

Luciano Ozzello, M.D.
Professor and Chairman
Department of Pathology
University of Lausanne Medical School
Lausanne, Switzerland

* * *

Ralph M. Richart, M.D.
Professor of Pathology
Director of Obstetric and Gynecologic
Pathology and Cytology
College of Physicians and Surgeons
Columbia University

* * *

Donald Kufe, M.D.
Assistant Professor Human Genetics and
Development - Institute of Cancer Research
College of Physicians and Surgeons
Columbia University

* * *

Paul Krieger, M.D.
Fred Silva, M.D.
Department of Pathology
College of Physicians and Surgeons

* * *

New York Pathological Society

May 16, 1974

* * *

FORWARD

This is the last meeting this year of the New York Pathological Society and we are pleased to have the Arthur Purdy Stout Society act as co-sponsors.

The Pathological Society has had a very successful year in terms of the attendance and general interest in the program, the syllabi, microscopic slide sets and the microfiche. We hope to introduce additional new innovations next year and welcome your suggestions.

To maintain a strong financial base we need an increase in membership in all categories and urge all of you who have participated this year to consider active membership in the Society.

An application blank is enclosed on the last page of this syllabus.

May 1974 Donald West King

TABLE OF CONTENTS

ARTHUR PURDY STOUT

Arthur Purdy Stout, A.B. Yale '07, M.D. P&S '12, retired Professor of Pathology, Emeritus Professor of Surgery, died in New York on December 20, 1967 at age 82.

Probably no other individual in his generation has had a greater impact on the development of that branch of clinically oriented pathology which we know of as Surgical Pathology. His original training in Clinical Surgery, and the influence of his predecessor, Dr. William Clarke, played a decisive role in developing his life-long interest: the correlation of tissue changes seen in the surgical specimen with the clinical course of disease. More especially, he devoted himself to the histological classification of human tumors and the predictability of tumor behavior on the basis of morphology. His influence in this country and abroad on young pathologists and surgeons was great, imparting to them a modern, practically useful knowledge of human neoplastic diseases.

Dr. Stout and his collaborators, including Virginia Kneeland Frantz, Cushman Haagensen and Margaret Murray were responsible for the development of the laboratory of Surgical Pathology at P&S. The Laboratory was originally a Division of the Department of Surgery and was completely independent of the Department of Pathology until well after his "retirements" in 1951 and 1954.

When in 1951, Dr. Stout reached the age limit of 65 as Professor of Surgery, he became Professor and Director of Pathology at the Francis Delafield Hospital, a position which he occupied until 1954. Then, having reached the age limit as Professor of Pathology, he asked to be made Emeritus Professor of Surgery. This appointment was granted in recognition of his lifetime identification with the Department of Surgery.

Following the second retirement, his activity as a teacher, author, and practicing pathologist kept on increasing. He had an ever expanding consultation practice, referred from all parts of the world, of which he always took personal care. He could write long, learned discussions to the referring pathologist or surgeon summarizing the results of his experience and knowledge. This he was able to do with such an unassuming and natural simplicity, that he was never overbearing.

During these later years, he became a member of many important national committees including the subcommittee on oncology of the National Research Council. He was Chairman of this Committee in 1954 and to it he devoted unbelievable energy, aimed at the creation and publication of the fascicles of the

Atlas of Tumor Pathology. The high standard and the great success here and abroad of these fascicles, now numbering about forty, is due to a great extent to the devotion and enthusiasm which he was able to impart to the other committee members and to the authors. He was himself the author of four of these fascicles.

Dr. Stout was a member or honorary member of more than twenty medical or scientific societies. He was consultant to the Armed Forces Institute of Pathology, to the Surgeon General and to dozens of hospitals in the New York area. He served at different times as a member of at least ten editorial boards.

His publications, including the book "Human Cancer" published in 1932, number more than three hundred. His major contributions were in the field of tumors of soft tissues, tumors of children and a study of the morphological changes in the membranes of the respiratory tract in cigarette smokers.

The imprint that Dr. Stout has left as author and tumor specialist is by itself a lasting monument to his memory. But all of us, those who had the fortune of living and working near him and with him for many years, will remember him also, and perhaps especially so, as the exceptional human being he was. He was a teacher in the humanistic tradition, a teacher of respect and compassion for human life, respect for the opinion of the most junior associates and colleagues, absolute scientific and professional honesty, and especially, to all of us a great friend. Testimony for these qualities is the Arthur Purdy Stout Society, founded about twenty seven years ago by a group of former residents, associates and admirers who gathered around him once a year coming from all parts of the country. They came to attend the scientific session, in the form of a seminar, conducted by him, but also for the peasure of the reunion with the "chief".

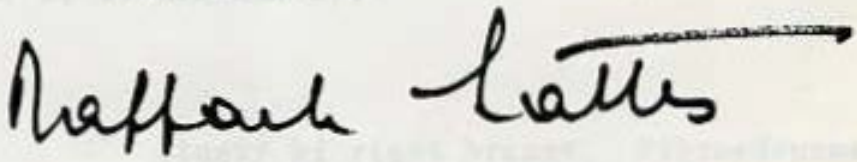
After Dr. Stout's death, the activities of the Stout Society changed format. An A.P. Stout Scholarship Fund was established in Columbia University. The interests generated by this Fund are used every year to help P&S medical students in financial need. An "Arthur Purdy Stout Memorial Lecture" is given every year, at the time of the Annual Meeting of the American Society of Clinical Pathology. The lecturers so far (F. Stewart, W. Boyd, C.D. Haagensen, B. Castleman, L. Ackerman) represent a Who's Who in American Pathology and Cancer Surgery, and have been attended every year by hundreds of pathologists. At that time, the members of the A.P. Stout Society hold their annual meeting, in which nominations for new members are presented, and future activities are planned.

One of the new activities, first started in 1973, has been an interim meeting in New York, in conjunction with the New York Pathological Society. The 1973 meeting was devoted

to Diseases of the Thyroid and consisted of a slide seminar conducted by Dr. William Meissner, and of a clinical pathological panel discussion, in which the panelists were Drs. C. Feind, P. Johnson, W. Meissner and S. Werner.

This year, the second joint meeting of the New York Pathological Society and the Arthur Purdy Stout Society will consist of a seminar on the Evolution of Neoplasia in the Mammary Gland and Cervix Uteri, conducted respectively by Dr. Luciano Ozzello and Dr. Ralph Richart, followed by a formal lecture on Neoplasia, which will be delivered by Dr. D. Kufe of our Institute of Cancer Research.

Raffaele Lattes



Breast with/atn/b/hyperplasia = 18 times higher risk of inv CA

Case 1

This 34-year-old woman underwent a routine physical check-up during which the gynecologist discovered a dominant lump of 2 cm in diameter in the right breast and ill-defined area of induration in the left breast. Biopsies revealed a fibroadenoma of the right breast and bilateral dysplastic lesions with atypical lobular hyperplasia and lobular neoplasia (lobular carcinoma in situ). Bilateral simple mastectomies were then performed. On macroscopic examination of the two breasts only gross cystic disease could be detected. Specimen radiography disclosed one suspicious area in the right breast which proved to be a small infiltrating lobular carcinoma on histologic examination. In addition, there were bilateral foci of lobular neoplasia and diffuse hyperplastic lesions. The patient was symptom-free one year after mastectomy.

Microfiche

A-1	Biopsy of right breast. Fibroadenoma and atypical lobular hyperplasia.
A-2	Biopsy of right breast. Higher magnification of the atypical lobular hyperplasia.
A-3	Biopsy of right breast. Lobular neoplasia.
A-4	Biopsy of left breast. Adenosis.
A-5	Biopsy of left breast. Cystic disease with a focus of lobular neoplasia.
A-6	Right simple mastectomy. Infiltrating lobular carcinoma.
A-7	Right simple mastectomy. Hyperplastic lobule containing numerous calcifications in the vicinity of the carcinoma.

References

Ashikari, R., Huvos, A.G., Snyder, R.E., Lucas, J.C., Hutter, R.V.P., McDivitt, R.W. and Schottenfeld D.: A clinicopathologic study of a atypical lesions of the breast. Cancer 33: 310-317, 1974.

Black, M.M., Barclay, T.H.C., Cutler, S.J., Hankey, B.F. and Asire, A.J.: Association of atypical characteristics of benign breast lesions with subsequent risk of breast cancer. Cancer 29: 338-343, 1972.

Haagensen, C.D.: Family history of breast carcinoma in women predisposed to develop breast carcinoma. J. Natl. Cancer Inst. 48: 1025-1027, 1972.

Haagensen, C.D., Lane, N. and Lattes, R.: Neoplastic proliferation of the epithelium of the mammary lobules. Adenosis, lobular neoplasia, and small cell carcinoma. Surg. Clin. North Amer. 52: 497-524, 1972.

Izuo, M., Okagaki, T., Richart, R.M. and Lattes, R.: Nuclear DNA content in hyperplastic lesions of cystic disease of the breast with special reference to malignant alteration. Cancer 28: 620-627, 1971.

Ozzello, L.: Electron microscopic study of functional and dysfunctional human mammary glands. Adv. Biol. Skin 15, 1974, in press.

mutant mice (athymic)

Case 2

A 38-year-old woman first discovered a lump in her right breast 28 months earlier. The tumor increased gradually in size and, at the time of admission to the hospital, it measured 7 cm in diameter. No axillary lymphadenopathy could be detected clinically. A radical mastectomy was performed. Detailed histological examination revealed an intraductal carcinoma with no evidence of stromal invasion. Nevertheless, one axillary lymphnode measuring 0.4cm in diameter was almost entirely replaced by metastatic carcinoma. The patient was alive and clinically free of disease 10 years after mastectomy.

Microfiche

B-1 and 2	Intraductal carcinoma featuring a cribiform pattern.
B-3	Intraductal carcinoma with a focus of papillary growth.
B-4	Neoplastic ducts surrounded by intact "basement membranes" (colloidal iron-PAS without nuclear couterstain).
B-5	Other neoplastic ducts of the same tumor of "basement membranes" (colloidal iron-PAS without nuclear counterstain).
B-6	Axillary metastasis.

References

Carlile, T., Farrow, J.H., Hutter, R.V.P., Gonzales, R., Minagi, H. and Venet, L.: Problems in early diagnosis and treatment: case presentations with commentary. South. Med. Bull. 59: 34-37, 1971.

Ozzello, L.: The behavior of basement membranes in intraductal carcinoma of the breast. Am. J. Path. 35: 887-899, 1959.

Ozzello, L.: Ultrastructure of intraepithelial carcinomas of the breast. Cancer 28: 1508-1515, 1971.

Case 3

This woman was first seen at the age of 36 when diffuse lumpiness of the left breast was noted. A biopsy revealed an extensive papillary proliferation of the ductal epithelium which was interpreted by several pathologists as a worrisome hyperplasia "potentially pre-cancerous". A left "prophylactic simple" mastectomy was performed and disclosed the same histological lesion throughout the breast. The patient was well until the age of 48 when she noticed a deep-seated nodule in the lower left axillary region. The nodule, measuring 1cm in diameter, was removed and proved to be an infiltrating ductal carcinoma with a few foci of intraductal growth. No metastases were found in two adjacent lymph nodes. At this time, however, a chest x-ray disclosed bilateral pulmonary metastases. The subsequent course was characterized by alternating periods of regression and reactivation of pulmonary and intracranial metastases which were treated by oophorectomy, hormonotherapy, hypophysectomy, and radiotherapy. At present (18 months after removal of the axillary carcinoma), the patient is alive with questionable persistence of cerebral metastases. During all this time the opposite breast has remained clinically and radiographically unremarkable.

Microfiche

C-1, 2, 3	Intraductal papillary carcinoma in original biopsy.
C-4	Infiltrating ductal carcinoma in axillary mammary tissue removed 12 years later.
C-5	Focus of intraductal growth next to infiltrating carcinoma.

References

Gallager, H.S. and Martin, J.E.: Early phases in the development of breast cancer. Cancer 24: 1170-1178, 1969.

Haagensen, C.D.: Diseases of the breast, 2nd ed., W.B. Saunders Co., Philadelphia, 1971, ch. 28, pp. 528-544.

Kraus, F.T. and Neubecker, R.D.: The differential diagnosis of papillary tumors of the breast. Cancer 15: 444-445, 1962.

Case 4

A mammography performed on a 39-year-old woman as part of a periodical check-up disclosed a small cluster of suspicious calcifications in one breast. Clinical examination of both mammary glands was entirely unrevealing. A biopsy of the suspicious area was performed disclosing grossly unremarkable mammary tissue. Specimen radiography revealed calcifications comparable to those seen in the mammogram and led to the demonstration of a minute intraductal carcinoma. Thorough histological study of the remainder of the biopsy and of the simple mastectomy that followed revealed no other foci of carcinoma.

Microfiche

D-1	Radiograph of one of the slices of the biopsy specimen showing minute calcifications (photographic enlargement).
D-2, 3, 4	Intraductal carcinoma with intraepithelial extension to adjacent lobules corresponding to the area with calcifications seen in the radiograph.

References

Rosen, P., Snyder, R.E., Urban, J. and Robbins, G.: Correlation of suspicious mammograms and x-rays of breast biopsies during surgery. Result in 60 cases. Cancer 31: 656-659, 1973.

Silverberg, S.G. and Chitale, A.R.: Assessment of significance of proportions of intraductal and infiltrating tumor growth in ductal carcinoma of the breast. Cancer 32: 830-837, 1973.

Wellings, S.R. and Jensen, H.M.: On the origin and progression of ductal carcinoma in the human breast. J. Natl. Cancer Inst. 50: 1111-1118, 1973.

Discussion - 5

C.I.N.

CERVICAL INTRAEPITHELIA NEOPLASIA

There is abundant evidence that the precursors to invasive cervical cancer form a continuum, the subsets of which are indistinguishable from one another except by arbitrary histological definition. The newer concepts regarding cervical intraepithelia neoplasia (CIN), including the recognition that at least 95% of the cases are unifocal and most are unicellular in origin, has led to a striking change in the role of the pathologist in the clinical management of this disease, analagous to the change his role has undergone in the management of trophoblastic disease. When one accepts the view that CIN is a continuous process, that the grade of dedifferentiation is principally a statement of the proximate probability of invasive carcinoma, but that this aggregate probability statement is meaningless in the individual patient, then it becomes apparent that it is the distribution and ease of eradication of the lesion which is important for optimal patient care rather than histological diagnosis. Hence the important diagnoses are normal cervix, cervical intraepithelial neoplasia, microinvasion, and invasive carcinoma.

Microfiche

E-1 Comparison of classical terminology with CIN terminology.

E-2 Schematic of the difference in histological diagnosis using classical terminology and with reference to CIN. Note that classical terminology divisions are indicated by solid lines representing the rigid criteria which have customarily been used in distinguishing the grades of intraepithelia neoplasia, and that the CIN divisions are represented by dotted lines indicating that the grade is less important and that debate as to where the dotted line is placed is a relatively minor issue.

Cured by electrocoagulation cryotherapy cone histerectomy

References

"Natural History of Cervical Intraepithelial Neoplasia", R.M. Richart. Clin. Obstet. & Gynec. 5:748-784, 1968.

End two are near - diploid
Nm " " Eye aneuploid

"A Follow-Up Study of Patients with Cervical Dysplasia", R.M. Richart and B.A. Barron. Amer. J. Obstet. & Gynec. 105:386-393, 1969.

"A Statistical Model of the Natural History of Cervical Carcinoma Based on a Prospective Study of 557 Cases", B.A. Barron and R.M. Richart. J. Nat. Cancer Inst. 41:1343-1353, 1968.

"Cervical Intraepithelial Neoplasia: A Review", R.M. Richart. Pathology Annual 1973, edited by S.C. Sommers, Published by Appleton Century Crofts.

The translation of the conceptual view of cervix cancer precursors as CIN into wide-spread clinical practice has been made possible by the utilization of colposcopy, directed punch biopsies, and endocervical curettage as a follow-up and triage procedure for the patient with an abnormal papanicolaou smear.

The colposcope is little more than an expensive magnifying glass with a bright light, but its use in examining the cervix which has been treated with 3% acetic acid makes it possible to define reliably the distribution of intraepithelia neoplasia, to distinguish those patients with CIN from those with invasive cancer and to treat most intraepithelia diseases on an out-patient basis, using biopsy, electrocoagulation, cryotherapy, or a combination of these.

In the most experienced programs, less than 5% of patients with abnormal smears are admitted to the hospital; the remainder are treated on an out-patient basis. It must be emphasized, however, that the use of colposcopy in an out-patient management protocol relies upon the absolute ability of the clinician, or management team, to rule out invasive cancer before treatment is instituted. This requires a degree of clinical, cytological, and histological skills which are not available to most practitioners and a significant investment in equipment which has generally been confined to center-based or large-group-based programs. Without the appropriate equipment and requisite skills, the traditional methods of management, including conization and hysterectomy, are more appropriate.

The remainder of this series consists of colpophotographs, kindly reproduced with the permission of Dr. Duane Townsend of the University of Southern California School of Medicine, with accompanying photomicrographs of removed tissue representing the lesions illustrated.

Microfiche

E-3 A patient with a "normal" cervix with an IUD string protruding from the os. The classical "normal cervix" has native squamous epithelium extending to a squamocolumnar junction which is at the anatomical external os. One rarely sees a normal cervix, however. This cervix has been restored to its "normal" state by the use of cryotherapy.

E-4 Photomicrograph of a biopsy taken from the native squamous epithelium of a normal cervix. The basal layer is regular. The cells mature in a regular fashion, and there is no cytological atypia.

E-5 A cervix with severe cervico-vaginitis and multiple small erosions. This picture is most commonly seen in patients with severe trichomonal vaginitis. Most erosions are due to traumatic avulsion of the epithelium at the time of speculum insertion.

E-6 Biopsy of a clinical erosion. The lesion has all the features of an ulcer with granulation tissue.

E-7 The so-called transformation zone is the key to understanding cervical neoplasia and is defined as that portion of the exposed cervix previously covered by columnar epithelium and reepithelialized by squamous epithelium through a combination of centripetal ingrowth and squamous epithelium through a combination of centripetal ingrowth and squamous metaplasia. There are two junctions which are important - the squamo columnar junction and the junction between the transformation zone and the native squamous epithelium. All cervical neoplasia begins at the squamo columnar junction in the transformation zone with native squamous epithelium. CIN occurs most commonly on the anterior and posterior lips and coincides with the distribution of the transformation zone.

E-8 Biopsy taken from edge of the transformation zone with a tongue of squamous epithelium centripetally growing beneath the columnar epithelium.

E-9 Large fields of native columnar epithelium on the exposed portion of the cervix with islands of squamous metaplasia seen as whitish areas with coalescence of the grape-like fronds of the mucus-secreting cells.

E-10 Biopsy of transformation zone with metaplastic epithelium proliferating beneath the columnar endocervical-type cells.

E-11 Transformation zone with clearly defined junction between area of transformation and native squamous epithelium in the upper portion of the photograph.

E-12 Biopsy showing regularly irregular epithelium associated with the transformation zone. Note that there is virtually no glycogenization, that although the cells do not mature in a normal fashion, they are not pleomorphic, that the cell borders are well defined, and that most nuclei have a single large nucleolus. This is a normal finding in the transformation zone, represents a physiological reparative process and, although frequently confused with CIN and diagnosed as mild dysplasia, is totally benign and bears no proximate relationship to cervical neoplasia.

E-13 Mature transformation zone in which the process of squamous ingrowth is complete and the epithelium has fully matured. The white, dome-shaped areas represent Nabothian cysts which have large but regular vessels overlying their apices.

E-14 Biopsy from a mature transformation zone with well-differentiated squamous epithelium overlying glands consistent with a histological diagnosis of epidermidization. The gland mouths frequently become blocked, the mucus material is inspisated and a Nabothian cyst is formed.

E-15 A cervix with an atypical transformation zone consisting of white epithelium extending superiorly from the transformation zone and approaching the fornix. This is one of the abnormalities seen in patients with CIN using colposcopy when 3% acetic acid has been applied to the cervical epithelium.

E-16 Biopsy with CIN grade 1. Note that the epithelium is mature, but that the maturation is abnormal and that there are large numbers of pleomorphic cells.

E-17 Atypical transformation zone on the posterior lip consisting of white epithelium. In the triage of patients with CIN, it is important that no patient be treated unless the entire

limits of the lesion can be seen using colposcopy. In this patient, the lesion extends to the squamo columnar junction, and it is difficult to see whether it extends into the endocervical canal.

E-18 An endocervical speculum is utilized to open the external os and to permit the observer to examine the canal following the application of acetic acid. In this cervix the entire squamo-columnar junction can be seen. No neoplastic epithelium extends into the canal, and the patient can be managed on an out-patient basis.

E-19 A biopsy showing CIN grade 11.

E-20 All patients whose management is contemplated to be on an out-patient basis should have a thorough endocervical curettage (ECC) performed by a clinician skilled in this technique as part of their evaluation. The ECC is an additional triage procedure which confirms the colposcopic finding of no disease in the canal. In this photomicrograph there are fragments of negative endocervical epithelium. This rich sample is obtained by instructing the clinician to save all the blood, mucus and tissue fragments which he obtains at the time of endocervical curettage, placing them on a dry cork or piece of paper towel and fixing the material as a block. A specimen such as this should not be reported as "quantity insufficient for diagnosis", but as "fragments of negative endocervix", since it is an important negative finding to be considered in planning the patient's management.

E-21 An atypical transformation zone consisting of extensive areas of white epithelium with mosaic structure and punctation. Although these features are not diagnostic of intraepithelial neoplasia, when they are this coarse, the vessels are this wide apart, and the epithelium this white and thick, it is unusual for the lesion to be benign.

E-22 Biopsy from area of punctation containing CIN grade 111.

E-23 Pregnant patient with extremely coarse grape-like structure in a regular contour consistent with pregnancy, and an atypical transformation zone with mosaic structure. Colposcopy has proven particularly useful in the management of pregnant patients with abnormal Pap smears

since, under appropriate circumstances, the patient need not have a conization or be biopsied during pregnancy, but may be followed during the course of gestation and treated post-partum.

E-24 CIN grade 11 involving the widely dilated and closely packed glands associated with pregnancy. It is important to differentiate the massive glandular involvement sometimes seen during pregnancy from invasive or microinvasive carcinoma.

E-25 Patient with extensive white epithelium, mosaic structure, and punctation on the posterior lip, extending into the canal, beneath an endocervical polyp.

E-26 Biopsy containing CIN grade 111.

E-27 Endocervical curettage with strips of neoplastic epithelium confirming the presence of squamous neoplasia in the endocervical canal. A patient in whom the limits of the lesion cannot be seen and who has a positive ECC should not be managed on an out-patient basis, but should undergo diagnostic conization prior to other therapy.

E-28 Invasive carcinoma with highly atypical vessels coarsing over the surface. The distinction between CIN and invasion is made based on an examination of vascular structures on the surface which have been correlated with penetration of the basal membrane. This is the most important and most difficult aspect of colposcopy. The ability to distinguish between the intraepithelial and invasive stages of the disease requires a great deal of experience.

E-29 Biopsy with poorly differentiated invasive squamous cell carcinoma.

E-30 Summary of 170 patients managed with electrocoagulation. It will be noted that the failure rate after the first electrocoagulation treatment was 11%, but that 15 of these initial 19 failures were recycled through the program, and only 2.5% of the series required hospitalization for management. Similar results are obtained using cryotherapy. In neither the electrocoagulation nor cryotherapy treated groups have recurrences been noted in follow-up periods which extend past five years.

References

"Cervical Neoplasia in Pregnancy: A Series of Pregnant and Postpartum Patients Followed with Biopsy or Therapy", R.M. Richart. Amer. J. Obstet. & Gynec. 87:474-477, 1963.

"The Handling of Small Tissue Samples for Pathologic Examination", R.M. Richart. Bulletin, Sloane Hospital for Women 9:113-117, Winter 1963.

"Colpomicroscopic Studies of the Distribution of Dysplasia and Carcinoma in situ on the Exposed Portion of the Human Uterine Cervix", R.M. Richart. Cancer 18:950-954, 1965.

"Influence of Cell Collection Techniques Upon Cytological Diagnosis", R.M. Richart and H.W. Vaillant. Cancer 18:1474-1478, 1965.

"Treatment of Cervical Dysplasia by Outpatient Electrocauterization", R.M. Richart, and J.J. Sciarra. Amer. J. Obstet. & Gynec. 101:200-205, 1968.

"An Evaluation of a One-Slide Cervical Cytology Method for the Detection of Cervical Intraepithelial Neoplasia", G.D. Wilbanks, E. Ikomi, R.B. Prado, and R.M. Richart. Acta Cytol. 12:157-158, 1968.

"Techniques for the Detection and Diagnosis of Cervical Neoplasia", R.M. Richart. In: Proceedings of Alexander Brunschwig Symposium; Gynecological Oncology. Excerpta Med. Internat. Congress Series No. 203: 71-79, 1969.

Atlas of Colposcopy, Per Kolstad and Adolf Stafl. University Park Press, Inc.: Baltimore, Md., 1972.

Colposcopy: A Scientific and Practical Approach to the Cervix in Health and Disease, Malcolm Coppleson, Ellis Pixley, Bevan Reid. Charles C. Thomas: Springfield, Ill, 1971.

"The Application of Cryosurgery to Gynecologic Malignancy", edited by R.W. Rand, AP Rinfret, H. von Leden. Symposium on Cryosurgery, Los Angeles, March, 1967. Springfield, Illinois, Charles C. Thomas, 1968, pp. 334-347.

"Cryosurgical treatment of neoplasia of the uterine cervix", W.E. Crisp. Obstet. Gynecol. 39:495-499, 1972.

"Cryocauterization for preinvasive cervical neoplasia", D.E. Townsend and D.R. Ostergard. J. Reprod. Med. 6:1710175, 1971.

THE SEARCH FOR EVIDENCE IMPLICATING RNA TUMOR VIRUSES IN HUMAN LEUKEMIAS AND LYMPHOMAS

We have over the past few years focused our efforts on an attempt to determine whether the knowledge gained from animal viral oncology is relevant to the etiology of human cancer. We first searched in human tumors for RNA molecules related in sequence to those found in the RNA tumor viruses known to cause corresponding cancers in experimental animals. Radioactive DNAs synthesized on the appropriate viral RNA templates with RNA-directed DNA polymerase were used as probes. The data obtained revealed a pattern of specificities that agreed remarkably with what was known from the animal experimental systems. Thus, human leukemias and lymphomas were found to contain RNA homologous to that of the Rauscher leukemia virus, an agent related to a group that causes similar neoplasias in mice.

More informative for a viral involvement was the demonstration with the simultaneous detection test that the RNA detected in these human cancers was 70S in size and encapsulated with RNA-directed DNA polymerase in a particle possessing a density between 1.16 and 1.19 gm/ml. Furthermore, DNA synthesized endogenously by these RNA enzyme complexes in human leukemias and lymphomas exhibited evidence of complementarity to the RNA of the Rauscher leukemia virus. Thus, the experiments have documented in these human neoplasias the presence of particulate elements possessing four features diagnostic of animal RNA tumor viruses.

These experiments and the subsequent utilization of the particulate elements to demonstrate the specificity of the viral-related sequences will be discussed.

References:

1. Hehlmann, R., Kufe, D. and Spiegelman, S.: RNA in human leukemic cells related to the RNA of a mouse leukemia virus. Proc. Nat. Acad. Sci. USA, 69:435, 1972.

2. Spiegelman, S., Kufe, D., Hehlmann, R. and Peters, W.P.: Evidence for RNA tumor viruses in human lymphomas including Burkitt's disease. Cancer Research, 33:1515, 1972.

3. Baxt, W.G. and Spiegelman, S.: Nuclear DNA sequences present in human leukemic cells and absent in normal leukocytes. Proc. Nat. Acad. Sci. USA, 69:3737, 1972.

4. Kufe, D.W., Peters, W.P. and Spiegelman, S.: Unique nuclear DNA sequences in the involved tissues of Hodgkin's and Burkitt's lymphomas. Proc. Nat. Acad. Sci. USA, 70:3810, 1973.

NEW YORK PATHOLOGICAL SOCIETY

I hereby make application for membership in the New York Pathological Society, and agree to abide by all the rules and regulations of the Constitution and By-laws.

1 Name .....

2 Address .....

3 Education: Collegiate and University

School ..... Years ..... to ..... incl.

School ..... Years ..... to ..... incl.

School ..... Years ..... to ..... incl.

School ..... Years ..... to ..... incl.

Academic Degrees ..... School ..... Year .....

Medical Degree ..... School ..... Year .....

4 Internship: (If a graduate in medicine)

Hospital ..... Years ..... to ..... incl.

Hospital ..... Years ..... to ..... incl.

5 Special Training, giving dates and under whose direction work was done:

.....

.....

.....

.....

Other Experience:

.....

.....

6. Hospital and Teaching Appointments past and present:

_____ Exact date ____ to ____

_____ Exact date ____ to ____

_____ Exact date ____ to ____

7. Publications: Author and co-authors, exact title of article, name of journal, volume number, page and year of publication must be listed. In case space is not sufficient use another sheet.

_____

_____

_____

_____

8. I HEREBY PLEDGE MYSELF TO THE HIGHEST PROFESSIONAL STANDARD IN MY PROFESSIONAL ACTIVITIES

Signed _____

Date _____

9. Application must be signed by two members of the New York Pathological Society.

Proposed by _____

Seconded by _____

10. Action by Committee on Admission and Ethics

Approved	Disapproved