CALIFORNIA TUMOR TISSUE REGISTRY

FIFTIETH SEMI-ANNUAL SLIDE SEMINAR

ON

TUMORS OF GENERAL PATHOLOGY

MODERATORS:

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SUNDAY, DECEMBER 6, 1970
9:00 A.M. - 5:30 P.M.

REGISTRATION: 7:00 A.M.
MARK HOPKINS
SAN FRANCISCO, CALIFORNIA

Please bring your protocol, but do not bring slides or microscopes to the meeting.

CLASSIFICATION OF NEOPLASMS:

AN OPERATIONAL ANALYSIS

PREFACE TO A CALIFORNIA TUMOR TISSUE REGISTRY SEMINAR

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The twin themes of this seminar are the huge, almost unanalyzable personal element in tumor diagnosis and the incoherencies in tumor classification. These problems relate to broad general issues. In a personal struggle with these issues, the greatest single source of help has been a volume which is not new and has not a word about neoplasms. Bridgman's Reflections of a Physicist. (5) It seems well to say something about the relevance of the Reflections to tumor pathology.

Bridgman, Harvard Department Head and Nobel laureate, did not regard physics as the only true science. In fact, he foresaw much more scope for science among polyatomic and obviously complex systems, such as the biological and even the sociological, than in atomic physics, where the unknowable loomed large and the end of the discoverable might be at hand. (5,8,35) In the midst of the resurgent fashionable hope for prompt resolution of all biological enigmas in terms of chemistry and ultimately of physics, it may be well to note that the shadow of the unknowable still looms over current physics. The principle theme of the Reflections is the operational approach, which deprecates abstractions, insists on stating measurements and conclusions in terms of how they were derived, and emphasizes the frequent importance of attention to details of that derivation. Thus Bridgman finds no satisfaction in a concept of length which does not tell how length is measured. He speaks of optical length and tactual length, noting the discrepancy between the two which, as the special theory of relativity acknowledges, is to be anticipated at high velocities. He is not concerned over which is nearer to the true length or what, if anything is meant by true length. Even he, we may note, finds it difficult to avoid the use of language which presumes such concepts as true length. It is hard for human minds to stop struggling with the question of what actuality actually is: i.e., how it would look to a being (such as the Deity) able to view it totally and without distortion, yet Bridgman finds that question unprofitable since operations relevant to its solution are not at hand. He disliked purely mental operations, sometimes denigrating them with epithets such as verbalism, while acknowledging that one cannot altogether dispense with them. His preference is for pointer-reading operations (measurements) and paper and pencil operations (mathematics) which, as he says, can be performed unambiguously. This preference did not attenuate his conviction that science was an individual adventure. Though he did not relish projects involving large teams of scientists, he conceded that for some problems they were appropriate. He knew that a group of colleagues was often useful in spotting an error which the original student had missed. Still he insisted that the collective, and, if you will, objective aspect of science had been emphasized too much and the individual aspect too little. One should not suppress his own doubts in deference to consensus of colleagues. A proof was not a proof unless it convinced one personally. Acceptance of a reported experimental result was willingness to assume that if one did the same experiment he would get the same result, and the report should have enough detail to make it easy to repeat procedures with exactitude.

Bridgman preferred "operation" to techniques or procedure because it implied an operator. Operator, of course, was used in a broad and novel sense neither surgical, telephonic, political, nor entrepreneurial. If "performance" and "performer" had been considered as alternatives, possibly their association

with theater and circus might have been regarded with disfavor. Just as to Holmes(19) the law was not a numinous presence in the sky; but simply what the courts had done and would do so to Bridgman science was not a mysterious collective something-or-other, but the sciencing of individual scientists.

An operational analysis of what we pathologists do when we diagnose, name or classify neoplasms(1,2) should lead to a more appropriate evaluation of the operations of tumor pathology and to suggestions for making them more relevant and helpful. That analysis will have to start with a quick general inquiry as to what scientists and other intelligent people do when they classify and why they do it. This inquiry which should help toward understanding both the necessity and the impermanence of classifications; with necessity involving both communication and individual exploration,(15) will have to start with a quick glance at the major features of the process of finding things out. This glance, alas, comes from one almost totally lacking in sophistication with respect either to traditional epistemology or to modern psycho-physiological studies of perception and learning.(15)

Epistemology, of course, deals with the nature and limitations of human knowledge, i.e., with the questions as to whether we know anything and if so, how, and what. Since the operationalist disclaims ultimate insight, I suppose he would have to define knowledge as information based upon acquaintance with events which, if properly used, should facilitate wise reactions to them. The concept of wisdom has traditionally been more pragmatic and operational than that of knowledge. It might be defined as propensity, (inclination plus ability) for relevant and appropriate reaction to events. If challenged to define relevant and appropriate, I suspect that the operationlist, after several attempts along the lines of Santayana's attempts to distinguish wise myths from myths which were not so wise,(29) might give up and concede that these were basic and undefinable operational concepts. Finding out, or learning, may be thought of as the acquisition either of knowledge or of wisdom.

The hope of acquiring knowledge, to the extent that it disclaims dependence on mystical intuition or authoritative revelation, will have to rest on analysis of experience.(29) Scientific or practical knowledge about anything involves comparing it with something else. The hope of learning from experience anticipates the discernment of recurrent patterns amid the welter of events; it depends upon comparison of one item or event with others. Analysis of experience consists of comparisons and contrasts. It concentrates on a few items at a time in the hope of discerning important similarities among some of them. Since we have attempted to refrain from implications about the inner and ultimate nature of things, by similarity we refer to the outcomes of appropriate investigative operations. In the more useful analyses, for example, those in the formal sciences, the selection of items for further study will have been made on the basis of previously discerned or suspected similarity, and the study will probe the extent and depth of that similarity. Thus characteristically such a study will have started from a classification and will result in a reclassification. As successive analyses become more detailed, extensive and profound similarities which originally looked important may look

less so, and previously unsuspected similarities may come to be of major concern. Yet at all stages the cognitive process demands assertion of comparisons and contrasts, i.e., classification. As assertion of knowledge about (the capacity to react appropriately to) an oncoming item of experience is an assertion that in some aspects that item resembles previously studied items. Analysis of even the rarest and most monstrous of items is essentially comparison (and contrast) with other items.

In the attempt to sharpen our perception of the cognitive process one may visualize the hypothetical (and perhaps mythical) situation of an early attempt by emerging humanity or by developing individual to sort out and make sense of some aspects of experience with very little guidance from previous classification. Our hypothetical untutored student may be aware of a great many items which he might study, but if he is going to study effectively he will have to concentrate on a few at a time and ignore the rest. How is he going to select those few? Perhaps by a hopeful hunch, based on quick glance or vague memory, that among those few there may be at least two which will still look alike after his first comparative analysis. Such a preliminary selection is appropriately regarded as a tentative classification. On later critical review it might appear to have been hasty and presumptuous. Still, it enabled him to get started, and without some sort of selection (whatever that is) might have been better than none. Since classification (or selection) is a preliminary, and perhaps a necessary one, to comparative analysis, almost any scheme of classification was immutable.

The hope of learning through classification of experience, when prudent, will be modest and patient. It will not assume total similarity among items in even the smallest category. It will be content to accept groupings as tentative and will not stifle the suspicion that some items may be unique, or may possess unique components. The faith that a new classification is a worthwhile advance is sometimes difficult to sustain when the ultimate looks infinitely far off and while a cyclic pattern of intellectual fashions, even in the sciences, is so painfully apparent. One may therefore readily sympathize with some of the boisterous alternatives to such meekness. The most patient investigator may suffer spasms of irritation over the time and effort which he has to give to classifying and reclassifying. A mystical mind avid for direct contact with reality may scorn classification as a crutch appropriate to the less gifted. A confident scholastic mind may remain hopeful of achieving a permanent classification which will accurately correspond to the structure of actuality. Yet sone of these positions can be regarded as realistic or operational.

We cannot expect things to classify themselves. In the growing, breathing, feeding, hunting world of living things, the taxonomist cannot demand that the various plant and animal species segregate themselves for his convenience. Classification is the work of the arranging mind, and a mind capable of arranging without distortion from antecedent bias or incomplete knowledge could only be that of the Deity. Many obviously artificial classifications are useful and perhaps indispensable. A large heap of letters will nt arrange

itself, and no method of arrangement has been suggested by "nature." Yet a crassly artifactual arrangement based on names of writers and addresses in alphabetical order may be very useful if one wishes to locate a particular letter.

The position of the impatient scientist, the mystic, and the scholastic Aristotelian seem readily refuted in contrast with that of the Pyrrhonist who to the question, "Can any assertion of human knowledge be deemed valid?" replies, "Probably not." Pyrrhonism, or radical skepticism, which regards any specific assertion as probably neither more nor less likely than its opposite, is an old and consistently recurring theme in human intellectual history. In many important respects the pyrrhonist and operationalist positions are not far apart. It is perhaps not surprising that Bridgman, after challenging all approaches other than the operational by means of pyrrhonistic analysis, failed to confront operationalism and Pyrrhonism with one another. Perhaps the orthodox operationalist line would emphasize the apparent intrinsic biologic (and operational) commitment of the human race to analyses of experience in the hope of learning to respond more appropriately to it. In the face of this commitment, speculation and logical analysis as to the substaniality of that hope may appear irrelevant and non-operational.

Orthodox operationalism, though deaf to questions about the congruence between classification and actuality. might be sympathetic with inquiry as to the degree to which various categories could be aligned with unambiguous operations, and with guesses as to the likelihood of their persistence without merger or further subdivision. On that basis, the category of hydrogen atoms (as distinguished from helium atoms) might be adjudged rather secure, that of Indian (as distinguished from African) species of elephant as hardly less so, and that of Ewing's sarcoma of bone (as distinguished from Reticulum cell sarcoma of bone) as definitely less so. (34,1,2)

With reference to neoplasms, I suppose that by derivation diagnosis means knowing through and through, hence implying a degree of familiarity greater than that asserted by the terms naming and classification. As we have seen, diagnosis implies classification, i.e., comparison of this item with others previously catalogued. Neoplasms do not name themselves; names are given by human students, and, to be useful, require a degree of consensus Operationally, diagnosis, classification, and naming of a tumor are all much the same thing, and the central operation is that of a pathologist looking through a microscope and interpreting what he sees. It is of interest to compare and contrast the professional observation and interpretation of a section with the technological preparation. Both sets of operations are intensely personal. All the good tissue technologists and all the good tumor pathologists I have known have been people of decided non-compliant individuality. The pathologists' personality patterns have been variegated, while those of the technologists have uniformly included a meticulous and rigid perfectionalism. The technological operations are gratifyingly unambiguous, but the pathologic operations are distressingly ambiguous.

The difficulty which one experiences in study of sections of problem cases from other good laboratories is seldom due to uncertainty about fixation, imbedding, cutting, staining, and mounting. There is appropriate attention to identification of the tissue throughout the processing. A well-prepared permanent section is not appreciably altered by ordinary observation or by the lapse of a good deal of time, and there is no question of the identity of a properly labelled slide taken from and replaced in a suitable file on a number of occasions. Unless the lesion is "typical," however, differences in interpretation may be anticipated when such a slide is reviewed by several observers or even on several occasions by one observer. Different blocks from the same lesion, and different cuts from the same block may show decided differences in pattern, yet the divergencies of opinion which occur when a large number of slides from an interesting lesion are sent to a large number of pathologists are for the most part attributable to the observers rather than to the sections.

Actual micrometer measurements of cells and nuclei are seldom recorded in histopathological descriptions or cited as bases for histopathologic diagnoses. The only mathematical operation commonly used in tumor diagnosis is the simple arithmetic of mitotic counts. My own mental operations begin with a hunch as to what the lesion should be called. If, after checking details such as size, shape, and distribution of cells and nuclei, I decide that my first hunch won't do, I have to wait for another and start over again. I don't think I have ever caught myself using the inductive procedure. Do we not all lean heavily on mental images? Is not the acuity of a tumor pathologist largely dependent on his stock of mental images and his skill amd judgment in their use? Mental images, skill, and judgment are alike highly personal, fluctuating, and hard to estimate or analyze.

Attempts at discussion of divergent diagnostic interpretations are quite often uninstructive. They may get no further than "It looks like A to me." "No, sorry, it looks like B to me." More diverting, if perhaps even less instructive are the polemics which sometimes ensue, with fervor quite disproportionate to either party's basis for assurance. Such debates may recall the farcical violence of a Punch-and-Judy show, or even those bitter lines about a tale told by an idiot.

At least as disturbing, and perhaps more so, are some of the hasty agreements. The assembled monthly minutes of our Registry's Regional Study groups are particularly instructive here. If a given tumor might plausibly be called A or B, the total state vote may work out to about 50 - 50. However, one study group will be all for A while another will be unanimous for B. Clearly each group has been in a hurry to find and follow a leader.

Evidently the warmth of controversy or the fellowship and anonymity of consensus sometimes encourage expression of an assurance which could not be supported merely by individual dispassionate critical analysis. The appropriateness of Bridgman's warning against sciencing by consensus seems particularly clear.(5) I, at least, have found it appropriate to keep recollecting

the example which Dr. Hazard gave us last spring.(16) Here was a master in the area of thyroid pathology who, when he found a histologic pattern equivocal, called it equivocal, and refused to budge off the fence unless he had solid histologic justification for doing so. An example to be admired and followed!

Naturally we would prefer not to think that the status of tumor pathology was as unsatisfactory as these monthly registry minutes suggest. Their relevance had been challenged on the ground, first, that pathologists give more careful attention to their own daily work than to slide sets, and second, that the general run of hospital material is much less controversial and confusing than the Registry material. Along this same line the Registry is criticized for including too much controversial stuff and too few good teaching cases. The relevance of these challenges is quantitative rather than qualitative. They leave us with the feeling that the status of tumor pathology, if not as quite as bad as the minutes indicate, is still not good. I find that a problem in tumor diagnosis which puzzles me after fifteen minutes will usually puzzle me after fifteen days. Of course we do not send our "easy stuff" to the registry unless it happens to be that rare thing, a typical textbook case of an unusual entity. Still, a good deal that I don't get around to sending to the registry is just about as puzzling as what I do. Material which at least to me is puzzling and controversial is not at all rare in my practice. How about the rest of you?

The "good teaching material" complaint calls for a little further analysis. To put it very bluntly, I will have to suggest that by "good teaching material" some of us mean typical textbook cases of uncommon entities. Are such cases as unusual in everyone else's experience, as they are in mine? If so, since it is idle to carp at general experience, such disparity has to be regarded as a criticism of the textbooks. The critical comment that textbooks are often out of date is hardly novel. Surely good teaching is not synonymous with crass oversimplification.

Diagnostic conclusion from examination of a lesion suspected of being neoplastic requires first of all a decision on neoplastic versus non-neoplastic. If the decision is neoplastic, one then has to decide on benign versus malignant and on further classification. Even on neoplastic versus non, the pathologist may be troubled by the poor fit between the Procrustean bed of classification and the variegated actuality, and by the personal and subjective character of his decision and the possibility of error. In most classifications Letterer-Siwe disease is not grouped with neoplasms, but how many of us can convincingly explain why not?(1) In Von Recklinghausen's neurofibromatosis, just where does one draw the line between maldevelopment and neoplasm?(32) When the possibility of a mixture of neoplastic and inflammatory elements has to be considered, how does one decide whether the section is adequately representative of the lesion?

With awe and affection your moderator recalls correspondence with our late beloved mentor Arthur Purdy Stout over a lesion which proved to be embryonal

rhabdomyosarcoma but which A.P.S. had at first insisted was granulomatous pseudotumor. (34)

Stout, although his tissue culture studies (32) revealed deep concern with the fundamental biology of neoplasia, had, like Ewing, (11) concluded that current approaches should be practical, logical, and clinical. Although both these patriarchal saints had become wary of generalizations about cancer, I suspect that they might have sympathized with an effort to state the basic worries with clarity. After A.P.S. had received the final autopsy material from the case just mentioned, he urged that it be reported, characteristically volunteering to be quoted by name as having missed the diagnosis completely at first. A lesser man in his position might have become a stuffed shirt. He never did. He remained always the student among students. There was simply no false front to him. Surely in the next world he has been assigned a celestial laboratory which provides opportunity to resolve the fundamental biology of neoplasia. One might wonder whether that laboratory also included a slide file, perhaps one containing sections of tissues sent up following pit side surgery. One would presume that angels of heaven would be free of neoplasms. If imps of the pit suffer neoplasms as part of a process of expiation and redemption, one would suspect A.P.S. might be keeping his eye in practice by a review of sections, and playing a wise and sympathetic part in the care of these regrettable patients.

The decision on benign versus malignant, so important to clinician and patient, is not altogether separable from the decision on further classification. The benign-malignant decision is one on potentiality; it is a hedged prediction, and one which is sometimes corrected by future events. When one says that a lesion is malignant, he implies that if there are cells still in the patient like those now fixed and stained on the slide, they are likely to give the patient further trouble. By further trouble we sometimes mean metastatis; sometimes we include local recurrence as well. There are semantic as well as biological uncertainties. In some instances the cellular pattern on the slide may suggest strongly that the process was not localized. Such is the inference, for example, from diagnoses such as high-grade lymphoma, sympathicoblastoma, and oat cell carcinoma. When one considers the variables both in neoplasms and in hosts, (30) it is not surprising that our predictions are sometimes unfulfilled. Rather it is perhaps surprising that we do as well as we do. Is it not possible that the benign-malignant decision, with all its difficulties, is on the whole better managed than the decision of further classification? If such is the case, might not the difference reflect a difference in the availability of follow-up control? At least, some, though by no means all errors in the benign-malignant decision will come to light on follow-up. To be pulled up short by subsequent developments is a disturbing experience to a pathologist but it may be salutary and instructive one. Thus if one has called a lesion benign and it metastasizes, the original call was wrong. If, on the other hand, an incompletely excised lesion which one has called highly malignant shrivels up and disappears and is not heard from again during prolonged follow-up, and several senior reviewers, reexamining the sections, call it benign, they are probably right and the original call was probably wrong. Clearly it behooves pathologists to become expert not only in the histology of neoplasms but in their natural history and in the correlation between them.

Further classification of neoplasms presents a maze of problems. The scheme, which was devised when almost nothing was known of the biochemistry and etiology of neoplasms, in fact when "of unknown etiology" was part of the definition of neoplasm, is based on comparison of the neoplasm with a normal tissue which it is thought to resemble or from which it was believed to have arisen. It was easier and more "economical" to assume that the utterly mysterious neoplastic transformation would only involve one cell line at a time than to entertain the possibility of multiclonal transformation.

The majority of names of benign tumors were based on a notion of close similarity to differentiated non-neoplastic forbears. Thus a benign tumor of fibrous tissue is a fibroma, of smooth muscle, leiomyoma, of bone, osteoma, of glandular epithelium, adenoma, and of nerve sheath, neurilemmoma.

Some confusion was introduced with the use of the suffix-blastoma for benign tumor compared to partially differentiated cells, as in chondroblastoma, for in glioblastoma or sympathicoblastoma, for example, this suffix had implied malignancy. It may be discreet to say as little as possible about the myoblastoma scandal. Has anyone seen cells resembling so-called granular cell myoblasts in any structure, adult or embryonal, other than a so-called granular cell myoblastoma?

Broader categories were used for many of the malignant neoplasms, thus those thought to be epithelial are carcinomas while those thought to be mesenchymal are sarcomas. Here again there are frequent inconsistencies. Thus while lymphosarcoma implies a malignant tumor, lymphoma does not specify a benign one. On the other hand, on the whole the so-called cystosarcoma phylloides is rather benign, the tautologic phrase malignant cystosarcoma being necessary to specify a malignant one. Some of the designations of subdivisions are susceptible to more than one interpretation. Thus squamous carcinoma may mean a malignancy derived from squamous epithelium or merely one which resembles it. Adenocarcinoma may mean a malignancy derived from glandular epithelium, or one which exhibits a glandular pattern.

To name malignant neoplasms after normal tissues is to overlook the basic biological differences between malignant and normal structure which are after all, the heart of the problem of malignancy. Usually, though not invariably, morphologic differences between malignant neoplasm and adjacent normal tissue are not difficult to spot. If this were not the case, we would have great difficulty in recognizing carcinoma in situ. It is often assumed that malignant cells, however bizarre they may become, will look and act more like their normal cell forbears than like cells of other lines of differentiation. Comparison and analogy between degree of malignancy and degree of loss of differentiation are suggested. Thus the monumental study of Cushing and Bailey on the gliomas compared the cells of relatively benign examples to relatively mature glial cells, while those of the more malignant gliomas were compared to indifferentiated glial cells. (13) One objection to that analogy is the obvious one that the cellular progeny of

embryonal "glioblasts" mature slow down and differentiate completely while those of malignant glioblasts remain malignant. The high malignancy of "malignant trophoblast" fits with the attempt to correlate degree of malignancy with primitiveness or totipotency of the anlage; the indolence of so many of the tridermal teratomas does not. (9, 18 37, 38)

Under this set of assumptions some mixed patterns were readily accepted while others were not. Thus a few or many malignant fusiform cells in a malignant tumor of adult renal cortex did not bother anyone particularly since renal tubular "epithelium" was believed to be derived from mesenchyme and just a touch of dedifferentiation seemed a good enough explanation for these cells. (1, 34) To be sure if such cells were predominant, dispute over whether the neoplasm should be called carcinoma or sarcoma might appeal to those who relish such logomachy. The dedifferentiation analogy did not fit the so-called polypoid carcinomas with pseudosarcoma, of esophagus tongue, and larynx (33) in which it would seem necessary to assume either 1) transformation of both epithelium and stroma; 2) "stromal metaplasia" of malignant epithelium or 3) "pseudosarcomatomas metaplasia" of stroma somehow associated with the epithelial malignancy. These neoplasms have caused much consternation to the learned and attempts to explain them or explain them away have beeen numerous, fervent, and ingenious. (12, 33, 34)

Recent trends in embryology have not made the mystery of differentiation look less mysterious. Whatever the mechanism of differentiation, it does not appear to involve loss of chromosomes. In fact, among differentiated mammalian cell lines it is only mature erythrocytes and post-meiotic germ cells which lack any of the "chromosomal information" of the original zygote. Thus if the chromosomes are the persistent and essential governors of cell potentialities, it would be rash to presume that a differentiated cell would be incapable of transformation into something quite different-epithelium into mesenchyme, mesenchyme into epithelium, neurectoderm into connective tissue, or any of these into something quite embryoid.

Some malignant cell lines exhibit a remarkable polyploidy (36) It has become increasingly evident that an extraordinary range of changes in cellular structure and function may accompany malignant transformation; such changes may make identification of the anlage of a malignancy both difficult and of minor relevance. While squamous carcinomas of skin and squamous mucosae are readily ascribed to malignant transformation of squamous epithelium, the normal epithelium of bronchi is columnar and in the vast majority of squamous cell bronchial carcinomas one must assume that the squamous change was intimately associated with the malignant change. It is not altogether obvious why "stromal metaphasia" during malignant transformation whould be deemed so much less likely than "squamous metaphasia." When one comes to squamous bronchial carcinomas with gonadatropin-like or parathormone-like (6,7,25,26) activity-well, clearly there is no use searching normal ontogeny for an analogy to this sort of thing; we have a combination of structure and function

entirely unparalleled in normal cell lines. Clearly the possibilities of repression and derepression seem almost limitless. Finally, there seems no reason whatever to assume that an oncogenic stimulus could not localize at a junction between two or more divergent cell lines and transform any or all of them.

A continually recurring suggestion, which seems to have more lives than a hydra ascribes cancers to transformation, not of differentiated cell groups but of undifferentiated rests. This suggestion, which may well prove pertinent to some of the "embryoid" malignancies of early life, (17,23,27,37,38,39) seems less so for the general run of adult cancers. It has been suggested, for example, that squamous differentiation of buccal cancers might represent organizer action on a previously undifferentiated cell clone after malignant transformation. The squamous pattern of such cancers persists on distant metastasis, and it is a little difficult to visualize a mechanism which would make a cell line susceptible to organizer action after but not before malignant transformation. With regard to teratomas, benign or malignant, tumors with malignant trophoblast or malignant yolk sac, and the somewhat poorly defined group of "embryonal carcinomas," (3,9,17,18,39) there has been furious debate over whether the tumors arose from neoplastic transformation of primordial germ cells, non primordial germ cells, non-germinal cells which had somehow eluded organizer activity, differentiated cells which could revert, or what. It is a little difficult to see how any of these suggestions could be ruled out, and one might hope for a little more patient study and a little less heat in the study of these lesions.

In the past year or two there has been a spate of papers from colleagues whose names and words carry weight on the use of electron microscopy as an aid in selecting names for tumors. (1) Such studies have concentrated on tumors with distinctive patterns, for which the choice of a normal tissue to name them after remained uncertain. In several instances, while the pattern on light microscopy was equally close to A or B, the electron microscopic comparison definitely favored one or the other. One entirely without experience in this fascinating technique may perhaps wonder to what extent the selection of cells for comparison and the comparison itself can be made entirely objective. One might meekly question whether, until much more is known about the organelles revealable by electron microscopy and about factors which influence them, electron microscopic comparisons could be regarded as much safer clues to histogenesis than light microscopy comparisons.

The logical dehiscences now so obvious in the scheme of tumor classification have not, in the past, prevented the accumulation around it of considerable information about tumor natural history. One of the greatest of the great classic classifiers was James Ewing. (11) A pupil of his who was a teacher of mine used to say that while Ewing's notions of histogenesis were absurd, his experience and authority in histological-clinical correlation were peerless. Evidently Ewing, like Stout, influenced younger fellow-students profoundly and evoked great affection from them through his gracious generosity and unpretentious learning, I rather suspect that Ewing himself would have

given more weight to his experience with histologic-clinical correlation than to his histogenetic surmises.

I think we would agree that a major aim--perhaps the major one--of tumor pathologists would be furtherance of study of histologic-clinical correlation with particular reference both to natural history and to therapy. I would hope that this aim might be furthered if it were possible to squeeze some of the excessive ambiguity out of the operations of tumor classification. One way of trying to do this would be to remold our tumor classification so that it could be based more upon an attempt at objective analysis of tumor patterns as they actually are and less upon vague and often quite indefensible guesses as to how they got that way. (24) Recognition that the histogenetic Ewing scheme has not in the past prevented study of histological-clinical correlation does not blunt my suspicions that that scheme may be a substantial obstacle to clinico-histologic studies at the present time.

Such generalizations come much more easily than specific suggestions for emendation. Perhaps, in a good many instances, if the terms were interpreted in a descriptive-analytical rather than in a histogenetic sense, the terms themselves could be continued. Classic eponyms such as Hodgkin's disease and Wilms' tumor convey a vivid notion of a definite pattern. Choriocarcinoma has definite morphologic and endocrinologic implications, and the use of this term need not involve us in the divergence of opinion between Arthur Hertig (17,18) and Rupert Willis (37,38,39) on the migration of primordial germ cells. I have a degree of personal prejudice in favor of the term yolk sac carcinoma, while recognizing that unlike choriocarcinoma (3) it lacks endocrinologic criteria. (20,21,23,27) However, if a more descriptive term such as the mixed papillary and a solid embryoid carcinoma with the Schiller du Val bodies were to be preferred, I should be willing to acquiesce.

Many other terms seem to me to require change, though I am not very happy about the suggestions for replacement which have occurred to me. I shall mention two notions I have toyed with merely to encourage some of my perspicuous colleagues to do better. The Very Bad Cancer with the Small Cells might include what we now call oat-cell carcinoma of the lung, small cell carcinoma of the thyroid, and perhaps other organs, rapidly progressive lymphoma (including reticulum cell sarcoma), sympathicoblastoma, medulloblastoma, embryonal rhabdomysarcoma, and Ewing's tumor. Subdivisions in this large group could be made later as deemed appropriate. The Bad Cancer with the giant cells would include giant cell glioblastoma, gourdcell rhabdomysarcoma, anaplastic liposarcoma, giant cell carcinomas of lung and thyroid, some of the more anaplastic osteosarcomas, and perhaps some cases of Hodgkin's with lymphocytic depletion.

Eventually, and perhaps sooner than we anticipate, etiology will have to be introduced into classification of human neoplasms. (23) Perhaps some morphologico-etiological correlations may become discermible.

Such hopes are suggested by experimental studies. Thus in a recent study of malignant transformation of a rodent cell line by a hybrid virus, the morphology of the neoplasm was found to depend on which part of the hybrid happened to predominate. (10) One might also hope that exploration of the intimate chemistry of neoplastic change might lead, not only to better understanding and control but to histo-and-cytochemical techniques which would introduce solidly unambiguous elements into diagnosis.

Of course we should not just sit on our hands and moon while waiting for new knowledge, new techniques, and a new nomenclature. If appropriately used with tongue in cheek, perhaps the old nomenclature need not be excessively handicapping. Much is to be gained from full use of old techniques, and particularly of one of the oldest, the necropsy. We have all of us seen instances in which what had been assumed to be metastatic malignancy proved at autopsy to be something else. I recall with particular chagrin a case of a patient, who, following pneumonectomy for squamous carcinoma, had what was presumed to be massive metastases to the other lung. At autopsy these lesions were found to be massive caseating coccidioidomas. On the other hand, clinically unsuspected neoplasms, silent or lethal, not infrequently turn up at autopsy. (4,21) Just as one small example, your moderator might cite his own experience with primary intracranial neoplasms (21) as the entirely unanticipated solution to medico-legal problems. Problems of classifying widespread metastatic malignancy are sometimes resolved by demonstration of small clinically unsuspected primary lesions at autopsy. Recently, I was consulted on an interestingly undifferentiated tumor involving both bone and soft tissue of the upper arm. Selection of a name for that tumor was settled by the demonstration in a pulmonary metastasis (but not elsewhere) of unmistakable tumor bone. I have had similar experience with several other quite undifferentiated mesenchymal tumors, which could readily be labelled rhabdomyosarcoma after examination of pulmonary metastases, which showed just an extra touch of differentiation as compared with other foci. It is interesting to speculate on whether higher oxygen tension might encourage a little extra differentiation.

To be sure, there are many puzzling neoplasms that remain just as puzzling after autopsy. However, the chance of learning something is substantial. The statement at the end of so many interesting registry histories "the patient died at such-and-such a date. No autopsy was done," calls for regret that is more than perfunctory and a resolve to do something about it. Although there are obdurate families, these have been found to be few upon approach by someone with the resolution and perspicuity of a Harvey Cushing. (13) In most of the instances just cited, one has to guess that no one really displayed much interest in doing the autopsy or obtaining the consent.

While we are, I believe, doing not too badly at incubating clinical pathologists, I wonder whether we are doing what is appropriate to foster the development of pathologic anatomists. I suggest that there is a great and continued need for anatomic pathology, in both the surgical and postmortem areas, and in the correlation between the two. I think we are

obligated to strive for a greater degree of unambiguousness in the operations of tumor pathology. This means, among other things, not quite so total a reliance upon individual personal interpretation. However, even if we succeed beyond our expectations, the role of individual skill, knowledge, and judgment will continue to be huge, I think, therefore, that we are bound to try to encourage the development, not only of good run-of-the mill working pathologic anatomists, but of the Ewings and Stouts and Willises of the next generation.

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SEMINAR ON TUMORS OF GENERAL PATHOLOGY

MODERATOR: ROBERT W. HUNTINGTON JR., M. D.

DECEMBER 6, 1970

DIAGNOSTIC INDEX

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(3.	14946	Fred Preuss, M. D.	Tubal (gestational) choriocarcinoma
(4.	15998	E. R. Jennings, M. D.	Testicular choriocarcinoma
5.	18369	R. Peters, M. D. & F. Hirose, M. D.	Chordoma of the sphenoid-clivus region
(6.	18260	Jerome Heard, M. D.	Sacrococcygeal yolk sac tumor (embryonal adenocarcinoma)
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(18.	18213	William Winchell, M.D.	Juvenile secretory breast carcinoma (McDivitt-Stewart)
(19.	18566	W. H. Davis, M. D.	Probable nodular lymphoma of breast
(20.	18631	R. F. Martin, M. D.	Hemangiosarcoma of breast
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NAME: G. E. W.

DECEMBER 6, 1970 - CASE NO. 1

AGE: 39 SEX: Male RACE: Unknown

ACCESSION NO. 18519

CONTRIBUTOR: Richard F. Folkes, M. D.
Chapman General Laboratory
Orange, California

Outside No. 70-R-582

TISSUE FROM: Appendix

CLINICAL ABSTRACT:

History: The patient complained of progressive abdominal pain, 10 hour duration, first situated in the epigastrium and radiated to the right lower quadrant of the abdomen for several months. He had previous history of similar attacks of abdominal pain, the last occurring 5 weeks previously. Excision of anal fissure and fistula was performed 1 1/2 years ago.

Physical examination indicated tenderness in the right lower quadrant.

Laboratory report: Complete blood count - hemoglobin 14.1, WBC 22,700, 72 segs, 2 bands, 16 lymphocytes, 10 monocytes. Urinalysis and sedimentation rate were within normal limits.

Radiograph: Barium enema and upper gastro-intestinal series were negative.

SURGERY:

On April 22, 1970, the patient underwent an exploratory laparotomy with appendectomy. Findings were a high cecum in the right upper quadrant with a retrocecal appendix which was suppurative, but apparently not ruptured. There were also rope-like adhesions of the omentum over the region of the cecum and the ileum. Otherwise, the small bowel was of usual appearance. There was no palpable ulceration of the duodenum and stomach. The abdomen was closed without drainage.

GROSS PATHOLOGY:

The specimen labeled "appendix and omentum" consisted of a J-shaped tubular organ, measuring 8 x 1.2 x 1.2 cm. and a fringe of turgid mesoappendix up to 1.5 cm. in greatest dimension. The appendix had an opalescent exudate over its tip. On sectioning, the appendix revealed great thickening of its wall near the base resulting in narrowing of the lumen.

Also submitted was a piece of lobulated adipose tissue.

FOLLOW-UP:

Postoperative wound culture grew E. coli but satisfactory healing occurred.

The patient was last seen in October 1970 and at that time an upper gastro-intestinal series and barium enema was performed which showed no abnormality. The patient is now symptomless.

NAME: G. E. W. DECEMBER 6, 1970 - CASE NO. 1

AGE: 39 SEX: Male RACE: Unknown ACCESSION NO. 18519

CONTRIBUTOR: Richard F. Folkes,M.D. Outside No. 70-R-582
Chapman General Laboratory
Orange, California

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Moderator's diagnosis: Carcinoma of Appendix, largely mucinous adenocarcinoma but with carcinoid elements.

DISCUSSION:

Slides were shown of this case and of a similar case of Dr. Wybel's.

This inflamed appendix has a neoplasm which is largely mucinous. Pure primary mucinous carcinomas of the appendix are unusual; Mel Black volunteers the interesting information that of several he has studied, none have metastasized. The history does not support a suggestion of secondary carcinoma. Tumor is abundant at the periphery of the appendix, more sparse toward the center. The mucosa which has escaped the inflammatory process looks normal and non-muciferous. In respects other than mucus production, this tumor resembles the common appendiceal tumor, the carcinoid. Aggregates of non-mucus producing cells can be found which, if they stood alone, would be entirely compatible with a diagnosis of carcinoid, and I call this a mixed adenocarcinoma-carcinoid tumor of the appendix similar to one which Dr. Russell Fisher studied several years ago and to another recently submitted by Dr. Wybel. Many cells have a lot of mucus, some have none, and others are betwixst in between. It seems profitless to speculate as to what cell properties correspond to those of the anlage, what represent modification during transformation, and whether the tumor pattern results from convergent transformation of two originally distinct cell lines or divergent transformation of one line. As Hernandez and Reid said, "The usual hypothesis that carcinoids arise from Kulchitsky cells did not appear valid. The morphology and function of cells are determined by genetic information systems. Unexpected variations may result in derepression of latent information in neoplasia . . . It would appear that tumors should be described by the morphologic and histochemical features which they actually possess, without reference to their possible cell origin."

CONTINUED - Case No. 1

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NAME: L. A. B. DECEMBER 6, 1970 - CASE NO. 2

AGE: 26 SEX: Female RACE: Caucasian ACCESSION NO. 15609

CONTRIBUTOR: Harlan F. Fulmer, M. D. Outside No. S67-1804
St. Agnes Hospital
Fresno, California

TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: The patient was gravida II, para II (children - 3 1/2 years and 18 months of age). Beginning in November 1966, she noted the onset of intermittent vaginal spotting which had never been previously noted. This persisted at intervals of two to three weeks up to the time of hospital admission on April 9, 1967. Also, she noted increasing lower abdominal girth and bloating. She had an apparently normal menstrual period on April 7, 1967, superimposed on three to four weeks of continuous vaginal spotting.

Physical examination revealed a 7 cm. fairly firm discrete right lower quadrant pelvic mass which was slightly tender on palpation. This had been present for two months and was noted to be rapidly enlarging.

Laboratory report: A cervical smear done on January 20, 1967 was reported as Class I.

SURGERY:

On April 10, 1967 a panhysterectomy and appendectomy was performed.

GROSS PATHOLOGY:

The tumor weighed 205 grams, was ovoid and measured 9.5 x 8 x 6 cm. in overall dimensions. The serosal surface was smooth, glistening, pink-gray and faintly yellow-tan. On cut surface, there was a capsule-like remnant of ovarian tissue, measuring 0.1 to 0.3 cm. in thickness. The entire remainder was a firm dark-red hemorrhagic solid mass with a cobweb-like or chickenwire-like network of gray-tan trabeculae throughout. Compressed to one end of the ovoid mass was a residual or grossly normal ovary, measuring 2 x 1.5 x 1 cm.

COURSE:

On the third postoperative day, a 24-hour urine specimen revealed 17,920 international units of chorionic gonadotropin per 24 hours. On the sixteenth postoperative day, a 24-hour urine specimen was negative for chorionic gonadotropin.

FOLLOW-UP:

She received post-operative radiation over the entire abdomen and the pelvis.

Patient is well and there is no clinical evidence of recurrence or metastasis. Xrays of lungs have always been negative.

NAME: L. A. B. DECEMBER 6, 1970 - Case No. 2

AGE: 26 SEX: Female RACE: Caucasian ACCESSION NO. 15609

CONTRIBUTOR: Harlan F. Fulmer, M.D.
St. Agnes Hospital
Fresno, California
Outside No. S67-1804

TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: The patient was gravida II, para II (children - 3-1/2 years and 18 months of age). Beginning in November 1966, she noted the onset of intermittent vaginal spotting which had never been previously noted. This persisted at intervals of two to three weeks up to the time of hospital admission on April 9, 1967. Also, she noted increasing lower abdominal girth and bloating. She had an apparently normal menstrual period on April 7, 1967, superimposed on three to four weeks of continuous vaginal spotting.

Moderator's diagnosis: Embryonal Carcinoma of Ovary with Embryoid Bodies.

Gross photographs of the tumor, and numerous microphotographs including some from the placental lactogen study by Beck et al (1).

DISCUSSION:

The transworld cooperation embodied in the admirable report of this case by Beck, Fulmer and Lee came about through awareness on my part of Willis' distaste for the term embryonal carcinoma and of a just slightly malicious interest in finding out what he would make of this one, and in Willis' characteristically magnanimous reply, which included a suggestion that tissue be sent to Prof. Currie's department at Aberdeen, of which Dr. Beck is a leading member. My correspondence file provides convincing evidence that Willis' bark is much worse than his bite. The thundering didactic tone of some of his publications does him less than justice, making it easy to overlook the numerous modifications of his opinions and the candor with which they have been recorded. His views have been consistantly based on considerable personal study and cogitation, and they have not been ambiguous; thus, whether one agreed or diaagreed, they have constituted admirable points of departure.

I put this tumor in the general group of embryoid tumors and in the specific category of embryonal carcinoma with embryoid bodies. It contains a large number of structures resembling early embryos and a good many cells which look like trophoblast--some of which do contain placental lactogen. The rather nondescript microcysts lined by flattened cuboidal epithelium are of interest since Gaillard has suggested that these may be the parent tissue of such tumors.

Embryoid is suggested as a general term for tumors with information systems showing some resemblance to those of early embryogenesis. The question as to whether the tumors arise from cells whose embryoid mechanisms had never been repressed or from transformation of cells whose embryoid mechanisms previously repressed were derepressed during transformation seems remote, complex and not too important. The embryoid tumor category covers a wide range of differentiation and aggressiveness; it would include tumors with a good deal of teratoid differentiation, and tumors with trophoblastic or other structures reminiscent of early embryogenesis. It would certainly have to include tumors such as this, and would probably have to take in some uncouth anaplastic tumors which could not be put anywhere else.

Noting with satisfaction Willis' increasing awareness that the malignancy of embryoid tumors is often embryoid or total, I sympathize with his unhappiness over the term embryonal carcinoma, which is vague in its morphologic implications and does tend to embody and foster a fallacious comparison of embryonic and malignant tissues which runs through a good deal of tumor nomenclature. Other things being equal, embryonic and malignant cell clones may resemble one another in undifferentiation or dedifferentiation, and in rapidity of proliferation. Yet it is characteristic of normal embryonic clones to slow down and differentiate; it is characteristic of malignant clones to do neither. The differences between normal and malignant trophoblast, or between normal embryo and this tumor, are quite as profound as those between normal squamous epithelium and squamous carcinoma. In normal ontogeny differentiations with appropriate repressions are the rule; in embryoid malignancy along with continued proliferation, there is failure to repress an embryoid information system. With regard to this patient's present state of health, I can only comment that she has had excellent treatment and has also been very lucky.

I should not apply the term embryonal carcinoma to tumors with distinctive teratoid differentiation or to tumors largely trophoblastic or vitelline. I don't suppose that it really matters a great deal whether one calls this teratocarcinoma with embryoid bodies or embryonal carcinoma with embryoid bodies. The term embryonal carcinoma has, despite Willis' objections, been around for quite a while, and I am unwilling to discard it without being certain that I shall have no further use for it. It is readily applicable to this particular tumor. I am not going to try to generalize about other patterns to which it might be applicable.

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NAME: M. W. DECEMBER 6, 1970 - CASE NO. 3

AGE: 27 SEX: Female RACE: Caucasian ACCESSION NO. 14946

CONTRIBUTOR: Fred S. Preuss, M. D. Outside No. 65-18849
Dr. Preuss Pathology Laboratory
Dallas, Texas

TISSUE FROM: Fallopian tube

CLINICAL ABSTRACT:

History: The patient was first seen in the office of her physician on November 16, 1965, with a history of two bleeding episodes since her last regular menstrual period on October 15, 1965. Physical examination at that time revealed mild tenderness of the uterus without enlargement. Treatment consisted of hormones "to regulate her periods". During the following months she was seen three times, complaining of intermittent vaginal bleeding and increasing pelvic tenderness and pain. She was treated with hormones and antibiotics. On December 15, 1965 she was admitted to the hospital for a laparotomy.

Physical examination at the time of admission to the hospital was essentially normal except for marked tenderness and a palpable mass the size of a small lemon in the area of the left adnexa.

SURGERY:

Laparotomy on December 15, 1965 revealed what appeared to be an unruptured left tubal pregnancy. The omentum was plastered to the tube and the tube was adherent to the urinary bladder. The fallopian tube and the adherent piece of omentum were removed.

GROSS PATHOLOGY:

The specimen consisted of one fallopian tube. The proximal two thirds were markedly dilated, up to a diameter of about 5.0 cm. The wall was hemorrhagic and showed multiple areas of perfor tion. Cut section showed the lumen to be filled with partially clotted blood and there were areas suggestive of placental tissue. The distal one third showed an average diameter. The abdominal ostium was patent.

Presented separately were two pieces of omental fat tissue, the larger one measuring about 8.0 cm. in diameter. The tissue showed extensive areas of hemorrhage near one surface.

COURSE AND FOLLOW-UP:

Two days following surgery, a U C G pregnancy test was performed with serial dilutions positive up to a dilution of 1 to 128. She received a course of Methotrexate consisting of 2.5 mg. injections every five hours for five days. Following this, the U C G test became negative. During the next three

months, she received four additional courses of Methotrexate with the U C G titer rising several times to 1 to 256. After the last course the titer had remained negative. Repeat chest xrays remained negative.

On April 22, 1966, a total hysterectomy with right salpingectomy and bilateral oophorectomy was performed. A few small peritoneal implants were observed which on histological examination were described as containing inactive and nonviable tumor tissue.

On last examination the patient felt well and had no complaints. (May 1966)

FOLLOW-UP: (Report dated 11-2-70)

On May 31, 1966, she was admitted to the hospital and at that time her gonadotrophin was 20,000,000 mouse units per 24 hours. Her chest xray appeared to be negative for disease. On June 29, 1966, she developed severe abdominal pain, nausea and vomiting. Subsequent tests revealed abnormal liver function and liver scan done on July 6 revealed multiple defects compatible with metastatic disease. Intravenous fluids were given for most of her hospital stay and she also received a total of 13 units of whole blood. On August 31, 1966, bilateral lung lesions appeared. Her therapy consisted of Actinomycin D, Methotrexate, Duanomycin, and a combination of Methotrexate and Duanomycin. All these were without response. Despite constant care and therapy, her gonadotrophin continued to rise to over 100,000,000 mouse units per 24 hours and she expired on November 11, 1966.

Autopsy revealed metastases to lungs and liver. The pelvis was clean.

NAME: M.W.

DECEMBER 6, 1970 - CASE NO. 3

AGE: 27 SEX: Female RACE: Caucasian

ACCESSION No. 14946

CONTRIBUTOR: Fred S. Preuss, M.D.
Dr. Preuss Pathology Laboratory
Dallas, Texas

Outside No. 65-18849

TISSUE FROM: Fallopian Tube

CLINICAL ABSTRACT:

History: The patient was first seen in the office of her physician on November 16, 1965, with a history of two bleeding episodes since her last regular menstrual period on October 15, 1965. Physical examination at that time revealed mild tenderness of the uterus without enlargement. Treatment consisted of hormones "to regulate her periods". During the following months she was seen three times, complaining of intermittent vaginal bleeding and increasing pelvic tenderness and pain. She was treated with hormones and antibiotics. On December 15, 1965 she was admitted to the hospital for a laparotomy.

NAME: R.H.

DECEMBER 6, 1970 - CASE NO. 4

AGE: 20 SEX: Male RACE: Caucasian

ACCESSION NO. 15998

CONTRIBUTOR: E. R. Jennings, M.D.
Memorial Hospital of Long Beach
Long Beach, California

Outside No. 6329-67

TISSUE FROM: Left testicle

CLINICAL ABSTRACT:

History: The patient was hospitalized complaining of gradual enlargement of the left testicle during the past 4-1/2 months. He was afebrile and had no history of trauma.

Moderator's Diagnoses: CASE 3 - Tubal (Gestational) Choriocarcinoma

CASE 4 - Testicular Choriocarcinoma

NAME: R. H. DECEMBER 6, 1970 - CASE NO. 4

AGE: 20 SEX: Male RACE: Caucasian ACCESSION NO. 15998

CONTRIBUTOR: E. R. Jennings, M. D. Outside No. 6329-67
Memorial Hospital of Long Beach
Long Beach, California

TISSUE FROM: Left testicle

CLINICAL ABSTRACT:

History: The patient was hospitalized complaining of gradual enlargement of the left testicle during the past 4 1/2 months. He was afebrile and had no history of trauma.

Physical examination: There was a 2 x 3 inch mass in the left scrotum which was soft and slightly tender.

SURGERY:

On October 28, 1967, the scrotum was explored. The testicle and cord were excised. The abdomen was explored and a lymph node from the level of the renal pedicle was excised.

GROSS PATHOLOGY:

The specimen was a testicular mass with an attached 10 cm. segment of spermatic cord. The mass appeared to be completely encapsulated by smooth pink glistening tissue. The cut surface of the mass was a mosaic of dark and medium red. The background was pale red with dark red areas which tended to be round or oval. The mass was spongy, but particularly in the dark areas, firm. It measured 4.5 x 3.0 x 3.0 cm. It appeared to arise within the testicle and to replace all but a 1 cm. border of testicular tissue.

COURSE:

A chest xray, 10-30-67, showed 3 coin lesions measuring up to 1.5 cm. in diameter. He was discharged from the hospital on November 7, 1967 and placed on actinomycin D.

FOLLOW-UP:

The patient was re-admitted to the hospital on January 8, 1968 with severe pain. On examination there was a huge epigastric mass and xray revealed pulmonary metastasis. He died on January 15, 1968 of metastatic disease. Autopsy was not performed.

Slides shown included microphotographs of cases 3 and 4 and of a recent KGH case in which the neoplasm in the tests all looked differentiated and mature while the metastasis was choriocarcinoma.

DISCUSSION:

Choriocarcinoma may be circularly defined as tumor exhibiting the properties of malignant trophoblast. Prominent among these properties are the endocrine functions of trophoblast. There are, alas, plenty of cases of choriocarcinoma in which relevant endocrine studies were not done, but I know of none in which the results of such studies were consistently negative. Although by analogy one might anticipate the occurrence of non-functioning choriocarcinomas, it has not been established and might be difficult to recognize. Appropriate endocrine disturbance, though a major factor in the diagnosis of choriocarcinoma, is not a sufficient one; similar disturbances have been recorded with primary bronchial neoplasms. Obviously, a choriocarcinoma is a malignancy acting on information systems which resemble those of trophoblast. The big difference, of course, is that normal trophoblast decorously comes to a dead end. Gestational choriocarcinomas which arise occasionally in hydatiform mole, less frequently in other types of pregnancy, clearly are derived from transformation of trophoblastic anlage. The cellular ancestry of testicular choriocarcinoma is less clear; I don't recall ever having seen chorionic villi or benign trophoblast in testicular tumors.

Case 3 is one of tubal choriocarcinoma, undoubtedly gestational; Case 4 is one of testicular choriocarcinoma. One notes that both cases ended fatally. Such termination is the rule for testicular choriocarcinomas; in this post-methotrexate era it is rather the exception for gestational choriocarcinomas. As case 3 shows, young women are still dying of gestational choriocarcinomas; such a result seems particularly likely when there has been delay in diagnosis. The diagnosis of tubal choriocarcinoma would be a difficult one prior to exploration. I don't believe that enough of them have been studied to indicate how their prognosis compares with that of intrauterine choriocarcinomas. I don't see any basis for criticism of the clinical management of the case.

The apparent efficacy of chemotherapy in gestational choriocarcinomas, as contrasted with its inefficacy in testicular choriocarcinomas, has been attributed to reinforcement of drug action by histo-incompatibility. Although much work has been devoted to attempts to actualize this highly plausible and indeed almost inevitable model, the results to date have been meagre; the problem of placental antegenicity is a turbid one. It may be well to keep an open mind as to the possibility of other biological differences between gestational and testicular choriocarcinomas.

CONTINUED - Case No. 3 and No. 4

We should say just a word about apparently primary ovarian and extragenital choriocarcinomas. These raise questions about the possibility of disappearance of a primary choriocarcinoma while a metastases is flourishing. I recall with painful vividness the discovery at autopsy of intracranial choriocarcinoma in a young women whose curettings, even on hindsight, had shown only potentially malignant mole and whose uterus had no tumor at autopsy. The intracranial tumor certainly was metastatic; such a sequence is not extremely rare. Yet since other primary extragenital embryoid tumors occur, why not extragenital choriocarcinoma? Dr. Hertig, with characteristic gynecologic cynecism toward assertions of virginity, believes that practically all so-called ovarian choriocarcinomas are in fact metastatic gestational choriocarcinomas. Yet, "pure" choriocarcinoma of the testis (as in Case 4), though less common than mixture of choriocarcinoma and teratoma, does occur and sweeping denial of the possibility of "pure" ovarian choriocarcinoma looks hasty. If, in an ovarian tumor like that of case 2, the trophoblastic element were to become more lurid and outgrow everything else, it would seem that ovarian choriocarcinoma might ensue. My gynecologic colleague, Roy Smale, and I have studied a case which we classify as one of primary ovarian (non-gestational) choriocarcinoma.

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NAME: M. R. DECEMBER 6, 1970 - CASE NO. 5

AGE: 12 SEX: Male RACE: Mexican ACCESSION NO. 18369

CONTRIBUTORS: R. W. Peters, M. D. Outside No. A-69-464
F. W. Hirose, M. D.
Harbor General Hospital
Torrance, California

TISSUE FROM: The clivus surrounding the lower brainstem

CLINICAL ABSTRACT:

History: The patient presented at the age of five with complaints of head and neck pain which was not relieved by aspirin or therapy from a local chiropractor. Workup revealed a lesion in the posterior clinoid region. Biopsy and decompression at age six revealed the present tumor. He was given xray therapy.

He did fairly well until age nine when a second decompression was performed and an internal shunt was placed. He had attended school up until this time and was maintained on phenobarbital for grand mal seizures. Over the next two years he developed progressive cranial nerve palsies and finally, quadriplegia. He died at age 12 of brainstem compression.

GROSS PATHOLOGY: (Autopsy)

There was moderate muscle wasting. Remarkable findings were otherwise limited to the brain.

Brain: A rubber drain extended into the posterior horn of the left lateral ventricle. The optic nerves and third and fourth cranial nerves were free of tumor. The other cranial nerves were incorporated in a large tumor. The mass presented on the anterior surface of the brainstem and encircled the lateral margins. The cerebral peduncles were displaced laterally by the mass. The inferior three quarters of the pons was obscured and displaced posteriorly by it. The lower end of the medulla was also displaced posteriorly and laterally. The anterior portions of the cerebellum were also compressed. The tumor was extremely firm and was gray white. It cut with a gristle-like consistency. There was marked dilatation of the left inferior horn of the lateral ventricle with marked thinning of the overlying brain. The other horns of the lateral ventricles were slightly dilated. The fourth ventricle was almost obliterated.

NAME: M.R. DECEMBER 6, 1970 - CASE NO. 5

AGE: 12 SEX: Male RACE: Mexican ACCESSION NO. 18369

CONTRIBUTORS: R. W. Peters, M.D.
F. W. Hirose, M.D.
Harbor General Hospital
Torrance, California

Outside No. A-69-464

TISSUE FROM: The clivus surrounding the lower brainstem

CLINICAL ABSTRACT:

History: The patient presented at the age of five with complaints of head and neck pain which was not relieved by aspirin or therapy from a local chiropractor. Workup revealed a lesion in the posterior clinoid region. Biopsy and decompression at age six revealed the present tumor. He was given X-Ray therapy.

He did fairly well until age nine when a second decompression was performed and an internal shunt was placed. He had attended school up until this time and was maintained on phenobarbital for grand mal seizures. Over the next two years he developed progressive cranial nerve palsies and finally, quadriplegia. He died at age 12 of brainstem compression.

Moderator's diagnosis: Chordoma of the Sphenoid-Clivus Region

Slides shown included x-rays and gross specimen of a similar case, and microphotographs of this case.

DISCUSSION:

Chordoma may be characterized as a tumor acting on information systems resembling those of notochord, and may perhaps be considered as another embryoid tumor. It has a fairly characteristic histology and a fairly characteristic location. Although extrachordal chordomas are recorded, the great majority of chordomas do arrive close to the spine and may plausibly be ascribed to neoplastic transformation of notochordal rests. Interestingly enough, they show up in yough less commonly than in middle or old age, and the exceedingly tragic history of this particular child subject is, therefore, a bit unusual.

To this erudite group it would be superfluous to dwell on the phylogenetic and ontogenetic significance of the notochord. Since it arises at the front end of the archenteron, your moderator will call it a vitelline structure. There are notochordal remnants in the nucleus pulposus of intervertebral discs; somewhat larger "ecchordoses" may occur at either end of the vertebral column. Willis has provided an interesting summary of the history of knowledge of chordomas. Those in the cranial cavity were the first to be recognized; they were originally confused with chondrosarcomas. Recent studies emphasize that appropriate surgery and radiation may both prolong and improve life for these patients, and that the diagnosis of chordoma does not justify therapeutic despair. Metastases, especially in long-standing cases, are not as rare as we used to think. A recent ultrastructural study records the finding of virus-like objects.

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NAME: N. M. E. DECEMBER 6, 1970 - CASE NO. 6

AGE: 2 SEX: Female RACE: Mexican ACCESSION NO. 18260

CONTRIBUTOR: Jerome J. Heard, M. D. Outside No. 6773-69
Mercy Hospital & Medical Center
San Diego, California

TISSUE FROM: Sacrococcygeal area

CLINICAL ABSTRACT:

History: This two year old Mexican female was seen by her physician because of a rapidly growing large tumor in the sacrococcygeal area.

Physical examination: The tumor extended into the presacral soft tissue.

Radiograph: A barium enema study showed displacement of the rectum and colon to the right and anteriorly.

SURGERY:

On October 3, 1969, all visible tumor was excised.

GROSS PATHOLOGY:

The specimen measured 10 x 6 x 7 cm. and weighed 204 grams. The surface was irregular, moderately bosselated and covered by a fibrous transparent membrane in part and in part by thick fibrous tissue. One surface was ragged showing a pale tan pink tumor surface. The fixed tumor was firm. The cut surface was variegated. A portion was granular and pale gray white. There were cystic areas. Some of the cysts contained genatinous brownish material. Bands of fibrous appearing tissue traversed the tumor in many directions. There was a cartilaginous area and a dark reddish brown area.

FOLLOW-UP:

The postoperative course was uneventful and wound healing was prompt. A postoperative chest xray was reported as normal.

NAME: M. E. DECEMBER 6, 1970 - CASE NO. 7

AGE: 12 SEX: Female RACE: Caucasian ACCESSION NO. 17430

CONTRIBUTOR: Geraldine Pace, M. D. Outside No. 68-D-605
Anatomical and Clinical Pathology
Modesto, California

TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: This 12 year old white female was hospitalized with symptoms and signs thought to represent intestinal obstruction. A large mass was noted in the right pelvic area.

The child had not yet menstruated or shown signs of secondary sexual development.

SURGERY:

A very large right ovarian tumor was excised with a portion of the right fallopian tube. There was about 300 cc. of clear serous fluid within the abdomen.

GROSS PATHOLOGY:

The mass measured about 18 x 12 x 8 cm. Its cut surface was bright yellow in some areas, and, in others, marbled light gray and tan. It had degenerated cystic changes and foci of hemorrhage. A thin rim of ovarian tissue remained in some areas. The tumor had cysts ranging from a few millimeters up to 3 cms. in diameter. Some were multiloculated. They contained yellowish serous fluid.

FOLLOW-UP:

Follow-up information not available.

NAME: W. G.

DECEMBER 6, 1970 - CASE NO. 8

AGE: 41 SEX: Male RACE: Negro

ACCESSION NO. 18156

CONTRIBUTOR: Weldon K. Bullock, M. D.
R. F. Martin, M. D.
LAC-USC Medical Center
Los Angeles, California

Outside No. 69-10134

TISSUE FROM: Testis

CLINICAL ABSTRACT:

History: The patient, a 41 year old Negro male, was admitted to the hospital on July 9, 1969 with a three-month history of left inguinal swelling and pain. The pain was more pronounced on standing and was relieved by lying down. The patient had noted a recent increase in the pain up to the time of admission. This was accentuated by coughing. The pain was described as sharp and stabbing, with radiation across the entire lower abdomen on coughing.

At the time of admission, the patient gave a history of a 12-lb. weight loss over the prior three months with a normal food intake. He had a life long history of a left undescended testis. Careful review of systems was negative, including an entirely negative review of urinary tract symptoms. There was a past history of alcoholism, but the patient stated he had not been drinking for the past three months. The remainder of the review of systems and past medical history was noncontributory. The patient's libido was normal and he had not noted any recent decrease in libido.

The positive physical findings at the time of admission were a 1 x 2 cm. pear-shaped mass over the opening of the left external inguinal ring and a large suprapubic mass extending from the symphysis to 1.5 cm. below the umbilicus. The right testis was felt to be atrophic but was not measured.

Abdominal aortography and intravenous pyelography were negative except for the presence of the mass which was also seen on KUB. Barium enema study showed displacement of the bowel posteriorly by the mass.

SURGERY:

On July 30, 1969, the patient underwent an exploratory laparotomy, at which time a large tumor was noted in a suprapubic position attached to the small bowel. Numerous metastases were noted to a large segment of bowel which was impacted. The liver was grossly free of metastasis. The tumor, which was encapsulated, was removed with approximately 15 cm. of small bowel. The tumor extended into the left inguinal canal where an undescended testis was found.

GROSS PATHOLOGY:

The specimen consisted of a tumor and attached segment of bowel. The entire specimen measured 30 x 6 x 15 cm. The tumor mass measured 15 x 11 x 10 cm. Attached to the lateral margin was a cord-like structure and spherical piece of purplish tissue. The cord measured 5 x 1.5 cm. and the attached spherical tissue measured 2 x 1.5 cm. The bowel was opened in its entirety and the tumor was attached to the external surface of the bowel entirely. Cut section of the tumor appeared focally necrotic and hemorrhagic and in places cystic. The surface was covered by a thin capsule. The outer portion of the tumor was yellowish except for focal necrotic or hemorrhagic areas. The tumor was adherent to the bowel which was matted together. Along some of the free intestinal surfaces were nodules, the largest of which measured 1.5 x 0.75 cm.

COURSE:

It was decided at Tumor Board to treat the patient with chemotherapy and radiation. Subsequently he was given five doses of Actinomycin-D, followed by a course of oral Methotrexate and Cytoxan. He did well until September 3, 1969 when he developed generalized malaise and associated anorexia with diffuse lower abdominal aching. Subsequently he developed nausea and vomiting, but no diarrhea, and he was again admitted to the hospital. At the time of admission his hematocrit was 31, white count 600, and he was felt to be clinically septic. Chemotherapy was discontinued and he was started on Keflin, Kanamycin, and Polymyxin-B. His white count rose to 800. He expired on November 26, 1969 of metastatic disease. Autopsy was not performed.

NAME: D. S. DECEMBER 6, 1970 - CASE NO. 9

AGE: 17 SEX: Male RACE: Caucasian ACCESSION NO. 14585

CONTRIBUTOR: K. W. Falconer, M. D. Outside No. P-26-65
Washoe Medical Center
Reno, Nevada

TISSUE FROM: Anterior mediastinum

CLINICAL ABSTRACT:

History: This boy started having difficulty in swallowing and complained of upper abdominal pain. On routine chest films, a mass was identified in the anterior-superior mediastinum. The patient followed a rapid downhill course in spite of radiation therapy and died on September 12, 1965.

Biopsy of scalene lymph nodes was performed. Frozen section was reported as malignant lesion.

GROSS PATHOLOGY: (Autopsy)

At autopsy, the superior portion of the anterior mediastinum was involved by a large mass of nodular tumor which extended over the superior portion of the heart and great vessels, and extended up into the neck to just within the lower borders of the thyroid gland. The tumor also projected to the left and superior to the left clavicle. In the portion of the tumor between the right and left main stem bronchi was an irregular cyst, measuring 10 x 8 x 7 cm. It was yellowish-tan and somewhat more firm than the vascular appearing moist red tissue found on the pleurae and in the left supraclavicular area. Portions of the cyst contained keratin debris and hair. The pericardium was studded by tumor nodules. The liver contained numerous nodules of metastatic tumor. Additional nodules of metastatic tumor were present in the subcutaneous tissue of the neck.

CASES NO. 6,7,8, & 9 - HISTORIES AND DISCUSSIONS

NAME: N. M. E. DECEMBER 6, 1970 - CASE NO. 6

AGE: 2 SEX: Female RACE: Mexican ACCESSION NO. 18260

CONTRIBUTOR: Jerome J. Heard, M.D. Outside No. 6773-69
Mercy Hospital & Medical Center
San Diego, California

TISSUE FROM: Sacrococcygeal area

CLINICAL ABSTRACT:

History: This two year old Mexican female was seen by her physician because of a rapidly growing large tumor in the sacrococcygeal area.

NAME: M. E. DECEMBER 6, 1970 - CASE No. 7

AGE: 12 SEX: Female RACE: Caucasian ACCESSION NO. 17430

CONTRIBUTOR: Geraldine Pace, M.D. Outside No. 68-D-605
Anatomical and Clinical Pathology
Modesto, California

TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: This 12 year old white female was hospitalized with symptoms and signs thought to represent intestinal obstruction. A large mass was noted in the right pelvic area.

The child had not yet menstruated or shown signs of secondary sexual development.

NAME: E. D. DECEMBER 6, 1970 - CASE NO. 24

AGE: 55 SEX: Male RACE: Negro ACCESSION NO. 13805

CONTRIBUTOR: Charles Rolle, M. D. Outside No. S-64-1296
Brookside Hospital
San Pablo, California

TISSUE FROM: Retroperitoneum

CLINICAL ABSTRACT:

History: This 55 year old Negro patient had been in excellent health until January 1964, when he developed lower abdominal pain without bowel symptoms or digestive system symptoms. He had a feeling of "close"pressure in the bladder, but did not have any difficulty in voiding.

Familial history: This man had two daughters. The first daughter, a 33 year old female, had a massive retroperitoneal tumor resected in 1962. The tumor weighed 1480 grams and was diagnosed as a malignant lymphoma. She died almost exactly one year later in 1963 with widespread metastases involving retroperitoneum, ovary, pericardial and pleural linings, lung, liver, lymph nodes, and bone marrow. The autopsy prosector interpreted the tumor as a "small cell carcinoma." The second daughter, a 31 year old female, had a retroperitoneal leiomyosarcoma, measuring 16 cm. in diameter, removed in 1962. Follow-up data not available. On review there is a strong resemblance between the retroperitoneal neoplasms seen in the two daughters and the father.

Physical examination: A large intra-abdominal tumor was palpable, located at the suprapubic region. The tumor seemed to extend up toward the right lower abdominal quadrant. It was movable and not fixed to the anterior abdominal wall. It was minimally tender to palpation. Aside from the tumor, the other aspects of the examination were essentially negative.

Radiograph: The chest was normal fluoroscopically. Barium enema revealed extensive deformity of the sigmoid colon and of the cecum by the large lower abdominal and principally right sided tumor.

SURGERY: (4-24-64)

A large retroperitoneal tumor was found. The tumor extended to the urinary bladder and to the jejunum and its mesentery, as well as forming multiple peritoneal implants. Excision of the retroperitoneal tumor with attached jejunal segments was performed.

GROSS PATHOLOGY:

The tumor was a large bosselated mass which weighed 1296 grams and measured 22 x 17 cm. in maximal diameters. The greater portion of the external surface was covered by membrane which appeared to be peritoneum. On

the superior-anterior aspect of the tumor there was a segment of jejunum attached which measured 15 cm. in length and 6 cm. in circumference. The tumor apparently invaded the serosa and musculature, but there was no evidence of any lesion in the mucosa of the bowel. Section through the tumor revealed the presence of a central cavity produced by necrosis of the tissue. This cavity measured 8 cm. in diameter and was filled with coagulated blood. The remainder of the tumor was composed of a mottled, granular, viable tissue which was yellow and red, and in some areas appeared gray and cephaloid.

FOLLOW-UP:

Patient was readmitted to the hospital on April 18, 1966 in a semi-comatose condition of 6 hours duration. Since surgery in 1964, patient returned to work and had worked regularly as a truck driver until 2 months ago. At that time he began to notice weakness, abdominal cramping pain and moderate abdominal distention. On examination in physician's office, it was found that he had a moderate amount of ascitic fluid in his abdomen and there was nodularity and enlargement of the liver.

He died without regaining consciousness. Autopsy was not performed.

NAME: E.D. DECEMBER 6, 1970 - CASE NO. 24

AGE: 55 SEX: Male RACE: Negro ACCESSION NO. 13805

CONTRIBUTOR: Charles Rolle, M.D.
Brookside Hospital
San Pablo, California
Outside No. S-64-1296

TISSUE FROM: Retroperitoneum

CLINICAL ABSTRACT:

History: This 55 year old Negro patient had been in excellent health until January 1964, when he developed lower abdominal pain without bowel symptoms or digestive system symptoms. He had a feeling of "close" pressure in the bladder, but did not have any difficulty in voiding.

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Moderator's diagnosis: Unnameable Retroperitoneal Tumor, Familial, Inducing Hypoglycemia

Slides: Microphotograph of tumor.

DISCUSSION:

This is another of those retroperitoneal things; in fact, it could be quite temperately be characterized as a retroperitoneal outrage. The man died in hypoglycemia and the daughter who is still being is said to have hypoglycemic episodes. When this case was presented to the Study Groups in November 1969, the majority vote was for leiomyosarcoma; that is as good a morphologic diagnosis as I can make. Leiomyosarcomas associated with hypoglycemia have been reported but as for familial leiomyosarcomas with hypoglycemia! Well, if Roger Terry can run this down a little further, let's name it Terry's Syndrome.

CONTINUED - CASE NO. 24

A glance at the Cumulative Index reveals extraordinary recent interest in tumor-induced or tumor-associated hypoglycemia. Thus the "monthly cumulative indices" for 1970 up to November reveal a total of 18 entries, in only four of which was the tumor thought to be pancreatic. A variety of mechanisms appear to be involved. Of particular interest are the insulin-producing mesenchymal tumors reported by Saeed, Fine and Horn.

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NAME: R. G. DECEMBER 6, 1970 - CASE NO. 25

AGE: 73 SEX: Male RACE: Caucasian ACCESSION NO. 18605

CONTRIBUTOR: Harlan Fulmer, M. D.
St. Agnes Hospital
Fresno, California
Outside No. S70-2460

TISSUE FROM: Left testicle

CLINICAL ABSTRACT:

History: In March of 1969, the patiant was first seen and found to have a nodular prostate. At that time he was also found to have marked induration of the left testicle which was only slightly enlarged. He was seen again in March of 1970 complaining of further increase in the size of the left testis during the month prior to re-examination. Throughout the course of his history he had no urinary tract symptoms or pain or tenderness of the left testicle.

Physical examination: The left testicle was enlarged to twice normal size and was hard and nodular throughout.

SURGERY:

On April 29, 1970, a left orchiectomy was performed.

GROSS PATHOLOGY:

The specimen was a 7 x 5 x 4 cm. testicle with an attached cord, measuring 12 cm. in length and 1.5 cm. in diameter. On section, the normal testicular parenchyma was replaced by a gray homogeneous infiltrate, except for a 3 x 1 cm. area of remaining yellow testicular parenchyma in the lower pole. The tumor was hard. In the superior pole, the epididymis appeared to be infiltrated by tumor. No tumor masses were noted in the cord. The tunica was smooth, gray, and shiny.

FOLLOW-UP:

Follow information not available.

NAME: R.G. DECEMBER 6, 1970 - CASE No. 25

AGE: 73 SEX: Male RACE: Caucasian ACCESSION NO. 18605

CONTRIBUTOR: Harlan Fulmer, M.D.
St. Agnes Hospital
Fresno, California
Outside No. S70-2460

TISSUE FROM: Left testicle

CLINICAL ABSTRACT:

History: In March of 1969, the patient was first seen and found to have a nodular prostate. At that time he was also found to have marked induration of the left testicle which was only slightly enlarged. He was seen again in March of 1970 complaining of further increase in the size of the left testis during the month prior to re-examination. Throughout the course of his history he had no urinary tract symptoms or pain or tenderness of the left testicle.

Moderator's diagnosis: Lymphoma (Reticulum Cell Sarcoma) of Testis

Slides - Microphotographs.

DISCUSSION:

Harlan Fulmer originally tried to make this a seminoma with histiocytic reaction, and Weldon Bullock a granulomatous orchitis. I cannot buy either, and in my non-buying I have the concurrence of Harlan Spjut who is the real expert on granulomatous orchitis and of Mostofi at AFIP. If this is not a lymphoma of the testis and specifically a reticulum cell sarcoma, then I am never going to be able to make that diagnosis. You will recall that at the conference our good lymphoma scholar, Ron Dorfman, concurred in the diagnosis of reticulum cell sarcoma. Involvement of the testis occurs in disseminated lymphomatosis, however, in primary testicular lymphoma, which is what this appears to be, the outlook is not bad. We shall await follow-up with interest.

References:

Kieley, J., et al, Lymphoma of the Testis. Cancer 26, pp. 847-852, 1970.

NAME: W. G.

DECEMBER 6, 1970 - CASE NO. 8

AGE: 41 SEX: Male RACE: Negro

ACCESSION NO. 18156

CONTRIBUTOR: Weldon K. Bullock, M.D.
R. F. Martin, M.D.
LAC-USC Medical Center
Los Angeles, California

Outside No. 69-10134

TISSUE FROM: Testis

CLINICAL ABSTRACT:

History: The patient, a 41 year old Negro male, was admitted to the hospital on July 9, 1969 with a three-month history of left inguinal swelling and pain. The pain was more pronounced on standing and was relieved by lying down. The patient had noted a recent increase in the pain up to the time of admission. This was accentuated by coughing. The pain was described as sharp and stabbing, with radiation across the entire lower abdomen on coughing. He had a life long history of a left undescended testes.

NAME: D.S.

DECEMBER 6, 1970 - CASE NO. 9

AGE: 17 SEX: Male RACE: Caucasian

ACCESSION No. 14585

CONTRIBUTOR: K. W. Falconer, M.D.
Washoe Medical Center
Reno, Nevada

Outside No. P-26-65

TISSUE FROM: Anterior mediastinum

CLINICAL ABSTRACT:

History: This boy started having difficulty in swallowing and complained of upper abdominal pain. On routine chest films, a mass was identified in the anterior-superior mediastinum. The patient followed a rapid downhill course in spite of radiation therapy and died on September 12, 1965.

Biopsy of scalene lymph nodes was performed. Frozen section was reported as malignant lesion.

CONTINUED - CASES No. 6,7,8,& 9

Moderator's diagnoses: CASE 6 - Sacrococcygeal Yolk Sac Tumor
(Embryonal adenocarcinoma)

CASE 7 - Ovarian Yolk Sac Tumor

CASE 8 - Testicular Yolk Sac Tumor
(Embryonal adenocarcinoma)

CASE 9 - Mediastinal Teratoma, largely Yolk Sac Tumor.

Slides: Microphotographs of these and similar tumors.

DISCUSSION:

The pattern of these tumors has been characterized by an erudite colleague as at once embryoid and mesonephric. Usually one will find areas of featureless epithelium, stroma in varying degrees of differentiation, frankly glandular epithelium and papillary and other epithelial-stromal combinations, among them those which Schiller compared to mesonephric glomeruli and Teilun to endodermal sinuses of Du Val, Hyalin membrane, as emphasized by Pierce, is often conspicuous. Alpha-feto-protein studies on these tumors will be awaited with great interest. They do not have the endocrinologic properties of trophoblast. I know of no other biochemical features which facilitate their recognition.

Concurrence in the recognition of a variegated, yet distinctive, pattern common to these tumors of various sites, though widespread is not unanimous. Some students, unimpressed by the distinctiveness of the pattern, have preferred to lump it with that of "embryonal carcinoma", or "neoplasm of germ cell origin". Others have been unaware of, or have elected, to disregard the histologic similarity among tumors of various sites. Although the pattern occurs in the testes of adults (Our Case #8), for example, it has been characterized as that of the "distinctive adenocarcinoma of the infant testis". Ovarian tumors of similar pattern have been called "Schiller Mesonephromas" and the diagnosis of extraspinal ependymoma has been suggested for some extragonadal examples.

These tumors have attracted a good deal of current interest. Your moderator's notions are adequately represented in his published studies. Other recent studies are by more authoritative students. The Memorial Hospital group has suggested "embryonal adenocarcinoma" as a designation both for sacrococcygeal and for testicular examples. Their notions about these tumors are not far from ours; their term seems to me to invite confusion with embryonal adenocarcinoma without the adeno. Norris, Bagley, and Taylor, in their study of infantile vaginal tumors, adhere to Teilum's term "Endodermal Sinus Tumor".

This was the term which we ourselves first used. Later it seemed that the term "yolk sac tumor" was preferable as more general and more self-explanatory. We agree with the Memorial group that the malignancy of these tumors should be definitely stated, and on that basis the term "yolk sac carcinoma" would be preferable. In our concept of these tumors we rely heavily both on Teilum's studies and on those of Pierce. Some have deprecated the importance of these studies because of unwillingness to compare mice and men. Rodent material does happen to be particularly convenient for study both of normal and of neoplastic yolk sac; nevertheless, yolk sac does play a large role in human embryogenesis.

We find that the pattern of these tumors resembles that of yolk sac, and conclude that this resemblence must reflect a similarity in functioning information systems. I disclaim any knowledge of just how these information systems are activated or reactivated and maintained. With sacrococcygeal, testicular, ovarian, and mediastinal examples, and with a pineal example recently sent me from the Netherlands by Dr. Van Unnik, it is easy to speculate on the possibility of primordial germ cell anlage if one chooses to do so. Such a guess is less attractive for the infantile vaginal tumors of Norris and his colleagues. Dr. Van Unnik has recently sent me one of these also.

The original material in Case No. 9 showed mature teratoid elements in addition to the vitelline pattern; there were no mature elements in the material available for these sets. The occurrence of yolk sac pattern in a tumor of an undescended testis (case No. 8) is interesting but not surprising. Follow-up on patient No. 6 will be awaiting with interest; there were no survivors among the Memorial Hospital patients with sacrococcygeal tumors, but in one instance there was an interval of 26 months between original surgery and recurrence. Patient No. 7 with the ovarian tumor has died, Dr. Pace tells me; we had only two survivors in our group of ovarian tumor patients. The surprisingly hopeful outlook for boys under 2 with testicular tumors merits continued emphasis. Norris et al record cures in two of their six patients with vaginal tumors, and recommend that such tumors be approached with a degree of resolute optimism.

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NAME: R. M.

DECEMBER 6, 1970 - CASE NO. 10

AGE: 5 SEX: Female RACE: Caucasian

ACCESSION NO. 15261

CONTRIBUTORS: J. R. McGrath, M. D.
T. J. Bassler, M. D.
Redondo Beach, California

Outside No. SB-2652-66

TISSUE FROM: Right kidney

CLINICAL ABSTRACT:

History: Patient fell while playing, striking right upper abdomen, followed by progressive pain. A right flank mass was noticed after trauma. Pulse 120.

Laboratory report: Hemoglobin 10.6 gm.

Radiograph revealed a large intrarenal mass on right. Chest xray was clear.

SURGERY:

Transperitoneal exploration and right nephrectomy was performed.

GROSS PATHOLOGY:

A 500 gram, gray, soft, tumor mass partially replaced the right kidney.

FOLLOW-UP:

The patient received chemotherapy for 12 months. She was alive and well without evidence of disease 18 months after nephrectomy (left the State).

NAME: R.M. DECEMBER 6, 1970 - CASE NO. 10

AGE: 5 SEX: Female RACE: Caucasian ACCESSION NO. 15261

CONTRIBUTORS: J.R. McGrath, M.D. Outside No. SB-2652-66
T.J. Bassler, M.D.
Redondo Beach, California

TISSUE FROM: Right kidney

CLINICAL ABSTRACT:

History: Patient fell while playing, striking right upper abdomen, followed by progressive pain. A right flank mass was noted after trauma. Pulse 120.

Moderator's diagnosis: Wilms Tumor (Neuroblastoid Variant)

Slides - Microphotographs of this case and of a case with a more typical pattern.

DISCUSSION:

I do not share the broad prejudice against eponyms on the ground that they are not analytical! That defect can be a positive virtue when there isn't much to analyze. We have to call this one Wilms' tumor or nephroblastoma, and I have a further prejudice against the blastoma suffix on account of its ambivalence. Sympathicoblastoma, glioblastoma, and medulloblastoma are malignant; chondroblastoma is benign. I would not say anything at all about myoblastoma if I were not in a position to pass on a substantial hope that Morrie Blumenfeld is about to resolve the status of that entity.

The pattern here is that of a variant of Wilms' tumor in which it is particularly easy to accept Masson's suggestion of a conspicuous role of neural elements. Of course, Masson did not suggest that there was a distinctive neuroblastoid variant of Wilms' tumor; what he said was that there were neuroblastic elements in all Wilms' tumors. I do not believe that any suggestion of Pierre Masson's merits scorn--even from Rupert Willis. It is interesting that Wilms' tumor and sympathicoblastoma, common solid malignancies of childhood, often arise in the same general area and require exploration for differential diagnosis. At times that differential may be a little difficult even after microscopic examination.

This child, like the majority of children with Wilms' tumor, did not allow any obvious non-neoplastic anomalies. However, an interesting and

important group does have such anomalies. Anomalies of the G-U tract are not particularly surprising; the significant association of Wilms' tumor with hemihypertrophy and with aniridia is considerably more so. The aniridia differs from the usual familial variety; if a mutation, it must be a recent one. Such observations have led to the concept of a "Wilms' tumor syndrome" with varying degrees of completeness. They also lend considerable interest to the recent demonstration of "a small virus" in tissue culture from a Wilms' tumor.

The standard surgery-radiation-chemotherapy procedure for the management of Wilms' tumor is successful enough so that it has to be used boldly when indicated and also sufficiently perilous to be shortened and simplified when it is safe to do so. Thus, considerable recent study has been devoted to attempts to discern morphologic patterns which have been lumped with Wilms' tumor in the past but which carry a more hopeful prognosis and do not require so drastic a therapy. Some of these variants appear to be particularly common in the neonatal period, and it is uncertain how far their removal from the Wilms' category would modify the present concept of age-prognosis relationship in Wilms' tumor. Certainly the cystic-hamartomatous pattern which Ben Landing discussed in 1967, despite the very worrisome mesenchymal masses, does not belong in the Wilms' category. About some of the other so-called variants, I am not so sure. I believe that the neuroblastoid variant, which this tumor represents, is fully malignant and should be left in the Wilms' group. I am glad to be able to pass on the news that Ben Landing and his group are buckling down to the question "When is a Wilms' tumor not a Wilms' tumor?" In a year or two they should have a lot of help to give us.

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NAME: A. W. DECEMBER 6, 1970 - CASE NO. 11

AGE: 61 SEX: Female RACE: Caucasian ACCESSION NO. 17604

CONTRIBUTOR: Milton L. Bassis, M. D. Outside No. SF 67-5118
San Francisco, California

TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: This 61 year old Caucasian female was hospitalized for an exploratory laparotomy and a transabdominal polypectomy. Many benign polyps had been excised from her colon by sigmoidoscopy. A barium enema revealed additional polyps beyond the reach of the sigmoidoscope. She had a history of hypertension. A hysterectomy had been performed in the past for fibroid tumors.

SURGERY:

On June 5, 1967, a laparotomy was performed and sigmoid colon polyps were excised. A right ovarian cyst was discovered and this was also removed.

GROSS PATHOLOGY:

A previously opened cystic tumor of the ovary when reconstructed measured about 8 cm. in greatest dimension. The inner surface was roughened and irregular. Variegated tan-gray to white tissue was adherent to the interior. The thickness varied from 0.1 to 0.8 cm. At one end of the tumor there was a nodular, glistening yellow to gray-white-thickening, measuring 2.5 cm. in greatest dimension. Within the wall was a 0.2 cm. cystic focus.

FOLLOW-UP:

The patient was readmitted to the hospital in February 1969 with complaint of right lower quadrant pain of six weeks' duration. Shortly after admission a left lower quadrant paracentesis was performed with removal of 40 cc. of straw-colored fluid. The pathology report showed metastatic tumor cells. The chemotherapist suggested repeated paracentesis with instillation of Thio-Tepa in the peritoneal cavity and the initiation of oral Chlorambucil. The pelvic examination performed by a gynecologic consultant demonstrated a tumor mass arising in the pelvis and extending almost to the umbilicus. There was repeated accumulation of fluid during the hospital stay and repeated paracenteses with removal of over three liters of fluid on each occasion. Patient was discharged on Chlorambucil, 2 milligrams q.i.d.

The patient died at home on October 9, 1969 of terminal cancer and was not biopsied.

NAME: A.W. DECEMBER 6, 1970 - CASE NO. 11

AGE: 61 SEX: Female RACE: Caucasian ACCESSION NO. 17604

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TISSUE FROM: Right ovary

CLINICAL ABSTRACT:

History: This 61 year old Caucasian female was hospitalized for an exploratory laparotomy and a transabdominal polypectomy. Many benign polyps had been excised from her colon by sigmoidscopy. A barium enema revealed additional polyps beyond the reach of the sigmoidscope. She had a history of hypertension. A hysterectomy had been performed in the past for fibroid tumors.

Moderator's diagnosis: Clear Cell Carcinoma of Ovary

Slides - Microphotographs of this case.

DISCUSSION:

This case illustrates a pattern of ovarian carcinoma agreed to be readily recognizable and readily definable. These clear-cell carcinomas tend to be less malignant than the common ovarian carcinomas; this patient, however, evidently died from this neoplasm. There has been considerable debate about the cellular ancestry of this tumor. Your moderator trusts that he has made it clear by this time that he lacks enthusiasm for debates about cellular ancestry. However, these debates have resulted in nomenclatural suggestions which we shall have to list and try to explain.

In its tubular and clear-cell pattern this tumor does resemble kidney and the common renal clear-cell carcinoma. Many of those who attribute it to a renal rest anlage call it clear-cell mesonephroma. "Clear-cell" serves to distinguish it from the so-called Schiller mesonephroma which is what I have called yolk sac carcinoma. If there are renal rests in the ovary which give rise to tumors, one wonders on what basis they are called mesonephric rather than pronephric or metanephric. Mesonephric ducts do persist, but I am unaware of studies of persistent mesonephric cortex or of just how it would differ from metanephric cortex.

Scully, whose opinions in this and other areas I find very weighty, regards these tumors as Muellerian (endometrioid). The tumors of similar pattern in the adolescent vagina invite a similar designation.

It is a little disconcerting, therefore, to learn that in a recent study the ultrastructural pattern of a clear-cell ovarian carcinoma similar to the present one was found to resemble neither that of a clear-cell carcinoma of the kidney, nor that of endometrioid carcinoma. In fact, about the only pattern it did resemble was that of mesothelium or coelom.

Teilum has been insistent on the distinction between this tumor, which he was willing to accept as mesonephric, and the so-called Schiller mesonephroma which he regards as yolk sac or "endodermal sinus" tumor. Scully and I have been equally eager to keep these two patterns separate, since we have assumed that the yolk sac tumors were germinal and these tumors Muellerian. We have already alluded to the yolk sac tumors of the infant vagina and the difficulty of ascribing them to germ cells. So far, I have not seen neoplasms which I regard as intermediate in pattern between "yolk sac carcinomas" and "clear-cell carcinomas". Of course, clear cell masses do occur in yolk sac carcinomas, but the overall yolk sac pattern is uncouth and embryoid in contrast to the relatively orderly pattern of the "clear-cell carcinoma". Still, I suspect that if I live long enough, I may see intermediate patterns, and I am not entirely certain that these two distinct patterns are not just opposite sides of the same coin.

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NAME: M. R. DECEMBER 6, 1970 - CASE NO. 12

AGE: 70 SEX: Female RACE: Caucasian ACCESSION NO. 18553

CONTRIBUTOR: J. N. Carberry, M. D.
St. Francis Hospital
Lynwood, California
Outside No. S-2970-70

TISSUE FROM: Left renal area

CLINICAL ABSTRACT:

History: The patient was hospitalized on May 19, 1970 complaining of gas and bloating. She had gone to the doctor one week prior to admission and was found to have a palpable left abdominal mass. An IVP showed a large left renal shadow, non-functioning.

The patient was hypertensive and took diuretics. The admission blood pressure was 150/80. Routine laboratory studies were within normal limits.

Radiograph: Retrograde pyelogram and a renal angiogram showed a mass, thought to be renal, and prominent hydronephrosis.

SURGERY:

On May 22, 1970, upon exploration, a mass was encountered which was thought to be an inoperable hydronephroma. However when the mass was biopsied, it proved to be cystic. It collapsed and then became resectable. It did not include the kidney.

GROSS PATHOLOGY:

The specimen was a 520 gram, 18 x 11 x 8 cm. ovoid mass. Its surface was in part hemorrhagic fatty tissue, and on one side a collapsed 10 cm. cyst. The cyst lining had gray, glistening areas as well as hemorrhagic apparently necrotic areas. The wall incorporated mottled yellow orange tissue resembling degenerated fat. The collapsed cyst did not appear to communicate with the rest of the mass which consisted of what seemed to be largely fat and fibrous tissue with cysts. The cysts ranged in size up to a diameter of 8 cm. They contained straw-colored fluid which was sometimes cloudy having floating crystalline bodies and inspissated proteinaceous appearing material.

FOLLOW-UP:

A post-operative chest film showed bilateral pleural effusion but no tumor.

Follow-up information received 10-21-70: "Patient made an uneventful recovery. She is doing well, and there is no evidence of recurrent disease."

NAME: M.R. DECEMBER 6, 1970 - CASE NO. 12

AGE: 70 SEX: Female RACE: Caucasian ACCESSION NO. 18553

CONTRIBUTOR: J. N. Carberry, M.D. Outside No. S-2970-70
St. Francis Hospital
Lynwood, California

TISSUE FROM: Left renal area

CLINICAL ABSTRACT:

History: The patient was hospitalized on May 19, 1970 complaining of gas and bloating. She had gone to the doctor one week prior to admission and was found to have a palpable left abdominal mass. An IVP showed a large left renal shadow, non-functioning.

The patient was hypertensive and took diuretics. The admission blood pressure was 150/80. Routine laboratory studies were within normal limits.

Radiograph: Retrograde pyelogram and a renal angiogram showed a mass, thought to be renal, and prominent hydronephrosis.

Moderator's diagnosis; Neurilemoma

Slides: Pyelogram and renal arteriograms of this case.

Gross specimen, and microscopic sections

DISCUSSION:

This was a tumor adjacent to kidney, and apparently after the operation the radiologist and the pathologist had to go to some trouble to convince the surgeon that what he had removed was not kidney. The occurrence of a nerve sheath tumor in this area recalls the story of the Masson-Willis controversy over neural elements in Wilms' tumor.

I think we will agree that the pattern is in all respects that of a benign nerve sheath tumor, encapsulated, with checkerboard mixture of loose myxoid and firm fibrocellular tissue, microcystic degeneration, and palisading. I don't gather that it was obviously attached to a large nerve trunk. However, there are plenty of nerves everywhere and its elements, whatever their cellular ancestry, are acting like nerve sheath elements. Stout called these benign tumors neurilemomas, reserving Schwannoma for the malignant counterpart; other students have spoken of benign and malignant Schwannomas.

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NAME: N. J. G. DECEMBER 6, 1970 - CASE NO. 13

AGE: 5 SEX: Male RACE: Unknown ACCESSION NO. 18451

CONTRIBUTOR: R. W. Purvis, M. D. Outside No. 70-P-255
Memorial Hospital
Modesto, California

TISSUE FROM: Scrotal mass

CLINICAL ABSTRACT:

History: The patient noted development of a scrotal mass 2 weeks before admission. He thought he had been hit on the testicle a few days before. The past history and development were not remarkable.

Physical examination: The scrotal mass measured 2 1/2 x 2 1/2 cm. whereas the opposite testicle measured 1 1/2 x 1 cm. The upper pole of the mass was irregular and it appeared to transilluminate. A second examination showed the mass to be somewhat larger and nodular.

SURGERY:

The testicle and adjacent mass were removed.

GROSS PATHOLOGY:

The testicle and the mass were separate and did not appear to be related. The mass measured 4 x 3 x 4 cm. It was bosselated and focally cystic. It was largely solid and tan and pinkish gray.

FOLLOW-UP:

Tomograms in February 1970 revealed metastatic nodules in the lower lobe and perihilar area of the left lung. Intravenous pyelography demonstrated displacement of the distal ureter presumably by enlarged lymph nodes. Bone survey and liver scan were reported as negative. The pulmonary metastases were treated by 1300 rads. Chemotherapy has included 3 pulsed doses of Actinomycin-D, 13 doses of Vincristine and daily maintenance on Cytoxan. By September 1970 all evidence of metastatic disease had disappeared. The next follow-up visit is scheduled to coincide with this seminar.

NAME: N.J.G. DECEMBER 6, 1970 - CASE NO. 13

AGE: 5 SEX: Male RACE: Unknown ACCESSION NO. 18451

CONTRIBUTOR: R.W. Purvis, M.D. Outside No. 70-P-255
Memorial Hospital
Modesto, California

TISSUE FROM: Scrotal mass

CLINICAL ABSTRACT:

History: The patient noted development of a scrotal mass 2 weeks before admission. He thought he had been hit on the testicle a few days before. The past history and development were not remarkable.

Moderator's diagnosis; Intrascrotal Rhabdomyosarcoma.

TABLE I

RHABDOMYOSARCOMA*

SITE	ADULT		JUVENILE	
Upper extremity	38)		15	
Lower extremity	90)	76%	27	
Anterior torso	28)		5	
Posterior torso	26)		11	
Retroperitoneum, omentum, mesentery	15		11	
Mediastinum	4		1	
Orbit	0		26)	
Rest of head and neck	12		67)	67%
Urogenital tract	16		64)	
Viscera and unknown	9		9	
TOTAL	238		236	

* 474 cases recorded in the Laboratory of Surgical Pathology of Columbia University, November, 1906 - November, 1964.

Slides - Table from Stout (Ref. 12) on sites of origin of adult and juvenile rhabdomyosarcomas. Gross photo of present specimen. Microphotographs of various fields.

DISCUSSION:

This case, like the last one, shows that despite what the hasty and pessimistic may feel, there really is progress in the histopathology of neoplasms. Twenty years ago there would probably have been a good deal of dispute over the correct label for this tumor; now there would be massive consensus.

Stout's figures on the primary sites of adult and juvenile rhabdomyosarcomas are of considerable interest. (vide supra) 182, or 76% of the 238 adult tumors arose in areas with considerable muscle mass. However, among the 236 juvenile cases, in 157 or 67%, the primary site was in an area where voluntary muscle was sparse, i.e., head and neck or urogenital tract. In a recent study of 42 cases of childhood rhabdomyosarcoma, the primary site was arm in two, leg in five, chest wall in three, head in ten (several of these in the orbit), neck in three, pelvic in ten, perineal in seven and intra-abdominal and bronchial in one each.

The gross photograph shows this intrascrotal tumor to be separate from the testis. The microphotographs show the variegated histologic pattern. In some areas the cells are crowded and nondescript; elsewhere, they tend to be fusiform. In one of the photographs there are a couple of cells with cross-striation. This is a fairly characteristic childhood type rhabdomyosarcoma; of course, one must realize that the childhood type may occur in adults and the adult type in children.

The response of this child's metastases to chemotherapy is interesting, and we shall be eager to have further follow-up.

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NAME: C. H. DECEMBER 6, 1970 - CASE NO. 14

AGE: 4 mos. SEX: Female RACE: Unknown ACCESSION NO. 18331

CONTRIBUTOR: Gilbert Gersenfish, M. D.
Grossmont Hospital
La Mesa, California
Outside No. 69-4711

TISSUE FROM: Liver

CLINICAL ABSTRACT:

History: On October 5, 1969, this infant was seen because of abdominal distention of 1 month's duration. Her mother thought that she had been fussy and crying too much.

Physical examination revealed a protuberant tense abdomen. The liver and spleen appeared enlarged by xray. She was thought to have peculiar facies and was underweight. The pulse was rapid and there was a questionable systolic murmur at the base.

Laboratory studies showed anemia with target cells. Chromosome and metabolic studies proved to be normal.

SURGERY:

The liver was biopsied on October 22, 1969. It was enlarged, but otherwise grossly appeared normal. The spleen was also enlarged.

COURSE:

The infant failed to respond to radiation therapy or prednisone. She developed congestive heart failure. To relieve her congestive failure, hepatic artery ligation was undertaken on November 12, 1969. Upon exploration, she was found to have an anomalous hepatic artery arising from the superior mesenteric artery to supply the right lobe of the liver. The usual hepatic artery supplied only the left lobe. Both were ligated. Postoperatively her congestive failure immediately improved.

She died on December 10, 1969.

GROSS PATHOLOGY: (Autopsy)

The liver extended 4-5 cm. below the costal margin. Large umbilicated masses were visible over its surface. The cut surface of the nodules was tan. The heart was enlarged weighing 60 grams. There was chronic passive congestion of the lungs, liver, spleen, and kidneys. There were bilateral terminal bronchopneumonia.

NAME: C.H. DECEMBER 6, 1970 - CASE NO. 14

AGE: 4 mos. SEX: Female RACE: Unknown ACCESSION NO. 18331

CONTRIBUTOR: Gilbert Gersenfish, M.D. Outside No. 69-4711
Grossmont Hospital
La Mesa, California

TISSUE FROM: Liver

CLINICAL ABSTRACT:

History: On October 5, 1969, this infant was seen because of abdominal distention of 1 month's duration. Her mother thought that she had been fussy and crying too much.

Physical examination revealed a protuberant tense abdomen. The liver and spleen appeared enlarged by x-ray. She was thought to have peculiar facies and was underweight. The pulse was rapid and there was a questionable systolic murmur at the base.

Moderator's diagnosis: Infantile Hepatic Hemangioblastoma
(or Hemangio-endothelioma)

Slides - Two microphotographs.

DISCUSSION:

The literature leaves no doubt that this is an entity, and that it has to be called infantile hepatic hemangio-endothelioma or hemangioblastoma. About the character of this entity, there is less assurance. At the moment the best opinion seems to be that despite its lurid histology and its occasional multifocal distribution, the lesion is hamartomatous rather than neoplastic. As in the present case, its physiologic role appears to be that of arteriovenous fistula precipitating heart failure. Some of the children who survive manage to contain the lesion. The history of improvement in this patient's status after hepatic artery ligation, and of subsequent relapse, is of great interest.

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NAME: K. B. R.

DECEMBER 6, 1970 - CASE NO. 15

AGE: 65 SEX: Male RACE: Caucasian

ACCESSION NO. 18480

CONTRIBUTOR: R. Mihata, M. D.
LAC-USC Medical Center
Los Angeles, California

Outside No. A-83250

TISSUE FROM: Mediastinum

CLINICAL ABSTRACT:

History: This 65 year old white male was admitted to the hospital on February 10, 1970 in a comatose state.

Physical examination: The left pupil was larger than the right and both unreactive. A bilateral marked gynecomastia was present and his body was flaccid and without neurological reflexes.

The patient expired before a complete diagnostic workup on February 11, 1970.

Past history: Suprapubic prostatectomy for carcinoma of the prostate (date not given) and had been on estrogen therapy. His acid phosphatases had been rising concommitantly with increase in bone pain.

GROSS PATHOLOGY: (Autopsy)

The central nervous system examination revealed a cerebral infarction due to cerebral arteriosclerosis and metastatic prostatic adenocarcinoma to vertebral bones (only bones examined).

The mediastinum revealed a lobulated, rubbery, gray-white tumor, measuring 8 x 5 x 4 cm. This was attached to the superior aspect of the pericardium just below the attachment to the aorta. Surfaces made by cutting were multinodular, glistening gray white fleshy appearing. No thymus was recognized.

NAME: K.B.R. DECEMBER 6, 1970 - CASE NO. 15

AGE: 65 SEX: Male RACE: Caucasian ACCESSION NO. 18480

CONTRIBUTOR: R. Mihata, M.D. Outside No. A-83250
LAC-USC Medical Center
Los Angeles, California

TISSUE FROM: Mediastinum

CLINICAL ABSTRACT:

History: This 65 year old white male was admitted to the hospital on February 10, 1970 in a comatose state.

Physical examination: The left pupil was larger than the right and both unreactive. A bilateral marked gynecomastia was present and his body was flaccid and without neurological reflexes.

The patient expired before a complete diagnostic workup on February 11, 1970.

Moderator's diagnosis: Small cell epithelial tumor of thymus.

Slides - Microphotographs of this case.

DISCUSSION:

The recent proliferation of thymology, though breath-takingly rapid, cannot be called malignant, for indeed it has been orderly and guided, and well-integrated with other topics such as comparative immunology and embryology. One might hazard a guess that the present set of notions about the cellular ancestry of components of the thymus will not be the final one. One might further guess that later notions will prove no less elaborate and complex.

We have been brought up to assume that the thymus contained both epithelial and lymphoid elements and to acknowledge that it was sometimes difficult to demarcate one from the other. Perhaps the less said about the scandal of "granulomatous thymoma" the better, since we are now inclined to acknowledge that granulomatous thymoma is really old-fashioned Hodgkin's Disease. The recurrent suggestion that thymic lymphocytes are of epithelial

origin recently received some support from electron microscopic observations, which were thought to suggest transition forms neither obviously epithelial nor obviously lymphocytic. It is perhaps fair to comment that electron microscopy of the thymus has been confusion; thus, in another study of a non-lymphoid thymic tumor resembling normal thymus in its immunity-producing role, the ultrastructure of the tumor was quite at variance with that of non-neoplastic thymic epithelium. The most sophisticated techniques for embryologic study indicate that the ultimate procursors of thymiclymphocytes have migrated from the bone marrow, to be profoundly modified in the thymus, which, though not their parent, is the school where they learn all they know.

Since the pattern of this tumor does not resemble that of any prostatic carcinoma with which I am familiar, I am willing to accept the statement that the man's prostatic cancer and this mediastinal tumor looked entirely different and are unrelated. I think we may further agree that the arrangement of the small cells of this tumor is not lymphoid but epithelial. The pattern has enough suggestion of carcinoid so that appropriate biochemical study would have been of interest.

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NAME: E. B. DECEMBER 6, 1970 - CASE NO. 16

AGE: 68 SEX: Male RACE: Unknown ACCESSION NO. 4785

CONTRIBUTOR: Reuben Straus, M. D.
St. Joseph Hospital
Burbank, California
Outside No. 1709-52

TISSUE FROM: Parotid

CLINICAL ABSTRACT:

History: The patient was admitted to the hospital on June 3, 1952 with a lump below the angle of the right jaw which had been present for three years. It had been increasing in size for the past 1 1/2 months. It was firm and painless.

The history and physical examination essentially negative otherwise. Blood count and urine examination not contributory.

SURGERY:

At surgery on June 4, 1952, there was a tumor apparently in the right parotid gland which appeared to be irregular but encapsulated and measured 3 x 2 x 2.5 cm. On section, the tissue was firm, grayish-white, with streaks of yellow and hemorrhagic discoloration.

The overlying skin presented an elevated sessile nodule, 2.5 x 1.8 cm. On section it was smooth and gray flecked with yellow which was interpreted as a benign, nonpigmented nevus.

FOLLOW-UP:

Patient lost to follow-up. The surgeon has long since died.

NAME: E.B. DECEMBER 6, 1970 - CASE NO. 16

AGE: 68 SEX: Male RACE: Unknown ACCESSION NO. 4785

CONTRIBUTOR: Reuben Straus, M.D.
St. Joseph Hospital
Burbank, California
Outside No. 1709-52

TISSUE FROM: Parotid

CLINICAL ABSTRACT:

History: The patient was admitted to the hospital on June 3, 1952 with a lump below the angle of the right jaw which had been present for three years. It had been increasing in size for the past 1-1/2 months. It was firm and painless.

The history and physical examination essentially negative otherwise. Blood count and urine examination not contributory.

Moderator's diagnosis: Spindle-cell melanocarcinoma of parotid gland.

Slides - Microphotographs of H & E and Fontana-stained sections.

DISCUSSION:

In evaluating and labelling this very remarkable tumor, I think we have to rely on its actual characteristics rather than on the presence or absence of precedents in the literature. It contains a good deal of pigment which looks like melanin and stains like melanin in the Fontana procedure. Its largely spindle-cell pattern would, if the tumor had arisen in a pigmented nevus, have been regarded as that of perfectly good spindle-cell melanocarcinoma. There is nothing in the history to suggest metastasis to the parotid from somewhere else, and in some of the sections, I find persuasive evidence of transition from normal parotid or neoplasm.

One cannot, of course, deny the possibility of development of melanin stains more specific than the Fontana or of re-evaluation of the pigment in this tumor when such stains become available. One must also concede that large metastatic melanomas do arise from tiny primaries, and that one can be fooled in evaluating what looks like step-wise neoplastic transformation. One must further concede the possibility of ultimate biochemical differentiation between these spindle-cell melanoblasts (if that is what they are) and others of similar shape. However, on the basis of the evidence now before us, I am forced to call this primary spindle-cell melanocarcinoma

of the parotid gland, and I am not outraged at the suggestion that such things may occur. The production of melanin pigment is a talent shared by a variety of cell lines. Whatever the totality of cellular information upon which melanocarcinomas act, I don't doubt that it is potentially present in a good many cells which are not normal melanocytes. I simply cannot accept the no-melanocyte, no-melanoma dictum.

In the present continuing controversy over the cellular ancestry of melanomas, one may recognize three principal gangs: 1.) The almost any dammed kind of epithelial cell boys, 2.) the specialized epithelial melanocyte boys, and 3.) the neuralist boys. My own prejudice with regard to the majority of melanomas and to this one in particular, is that of position (1).

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NAME: K. H. DECEMBER 6, 1970 - CASE NO. 17

AGE: 11 SEX: Male RACE: Caucasian ACCESSION NO. 17885

CONTRIBUTOR: Roger Terry, M. D. Outside No. 69-1539
LAC-USC Medical Center
Los Angeles, California

TISSUE FROM:

CLINICAL ABSTRACT:

History: This 11 year old white male was referred to the LAC-USC Medical Center because of four episodes of rectal bleeding during the previous 3-4 months on December 5, 1968.

Physical examination: A vigorous, well hydrated, well nourished boy with normal vital signs.

Proctoscopic examination revealed multiple small polyps as did sigmoidoscopy. Biopsies revealed incipient polyposis (congenital).

Radiographs: Barium enema revealed multiple polyposis of the large bowel. Numerous skeletal (including skull and jaws) radiographs revealed no abnormalities.

SURGERY: (2-4-69)

A subtotal colectomy with ileoproctostomy was performed leaving the rectum. An epidermal inclusion cyst (left cheek) removed on April 9, 1968.

GROSS PATHOLOGY:

The specimen consisted of a running segment of ileum, cecum, and remaining colon to the sigmoid, measuring 9.0 cm. in length and 6 cm. in circumference. The mucosal surfaces were diffusely involved with small 1 to 3 cm. polyps except the distal portion of the cecum. The distal 4 cm. of the ileum was simiarly involved. The appendix was not involved.

FOLLOW-UP:

He has continued to have problems with bleeding from the polyps that remain in the rectum. He has undergone several fulguration and each time he has done well. When examined, 3-23-70, he had a few polypoid lesions posteriorly in the rectum. On June 8, 1970, the polyps appeared to be less and patient was to be admitted for examination and fulguration on October 19, 1970 but failed to keep his appointment.

NAME: K.H. DECEMBER 6, 1970 - CASE NO. 17

AGE: 11 SEX: Male RACE: Caucasian ACCESSION NO. 17885

CONTRIBUTOR: Roger Terry, M.D. Outside No. 69-1539
LAC-USC Medical Center
Los Angeles, California

TISSUE FROM:

CLINICAL ABSTRACT:

History: This 11 year old white male was referred to the LAC-USC Medical Center because of four episodes of rectal bleeding during the previous 3-4 months on December 5, 1968.

Moderator's diagnosis: Congenital Polyposis of Colon. Gardner's syndrome.

Slides - Microphotograph

DISCUSSION:

This is a unique case of congenital polyposis in that all of the polyps are not fully developed and they begin at the surface and not in the crypts. For years we followed Dulses who believed that the glandular adenomatous polyps started in the crypts where mitotic activity was known to occur. However, with the intravenous administration of tritiated thymidine, Cole and McKalen found that the radioactive labelled nuclei are confined to the lower portion of the crypts of Lieberkühn in the normal colon, but in the adenomatous polyps there was "a shift" in the normal zone of the cell regeneration and proliferation from the base of the crypts to the more superficial position in the epithelium. This is exactly what the case at hand shows. There is an exocentric growth pattern which, if we could view the lesions further along in this boy's disease, the continuing epithelial growth of the surface epithelium would no doubt result in full-blown adenomatous polyps.

Perhaps the epidermal inclusion cyst is sufficient basis for the narrower diagnosis of Gardner's syndrome, though the skeletal changes of complete "Gardner's Syndrome" are absent. Let us hope that the prompt colectomy will have prevented the development of carcinoma.

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NAME: M. P. DECEMBER 6, 1970 - CASE NO. 18

AGE: 28 SEX: Female RACE: Caucasian ACCESSION NO. 18213

CONTRIBUTOR: William H. Winchell, M. D. Outside No. SC 68-2018
Dominican Santa Cruz Hospital
Santa Cruz, California

TISSUE FROM: Left breast

CLINICAL ABSTRACT:

History: The patient was hospitalized for excision and drainage of a galactocele of the left breast.

She had delivered a normal female infant in March 1968. The left breast remained swollen 2-3 months after delivery. One month before this hospitalization she had been seen by a physician because of a mass in the left breast which was thought to be an abscess. Incision had yielded only what appeared to be inspissated milk.

Physical examination: The left breast was twice as large as the right. Its upper inner quadrant was firm, red and tender. There was induration of the periareolar area.

On October 29, 1968, the left breast was explored. There was a 10 x 10 cm. cavity. Necrotic fat and what appeared to be curdled milk infiltrating the tissue were debrided.

SURGERY:

A left radical mastectomy was performed on November 1, 1968.

GROSS PATHOLOGY:

The specimen consisted of 180 grams of tissue received in multiple fragments which were pink-tan, soft and rubbery.

FOLLOW-UP:

Follow-up information not available.

NAME: A. G. DECEMBER 6, 1970 - CASE NO. 19

AGE: 71 SEX: Female RACE: Caucasian ACCESSION NO. 18566

CONTRIBUTOR: W. Harriett Davis, M. D. Outside No. 1593-70
Burbank Community Hospital
Burbank, California

TISSUE FROM: Right breast

CLINICAL ABSTRACT:

History: Six months prior to admission, the patient fell and injured her right breast but had no apparent sequelae. Two months before admission she noted a cord-like thickening in the right axilla. This failed to respond to diathermy and ultrasound and a month later she was found to have a definite right axillary mass. Several days prior to admission she suddenly discovered a very large right breast mass. A complete blood count was normal and radiographs of the chest and bones showed no metastases.

Physical examination: There was a 6 cm. mass in the medial lower quadrant of the right breast with equivocal fixation to the underlying tissue. The skin was normal. Right axillary nodes were enlarged up to 3 cm. in greatest dimension.

SURGERY:

On May 25, 1970, a modified right radical mastectomy was performed after frozen section diagnosis of malignancy. The breast tumor was found to be fixed to the pectoral fascia.

GROSS PATHOLOGY:

The biopsy included fatty tissue and a 2.2 x 2.0 x 1.5 cm. hard, homogeneous, pale tan mass.

The residual tumor in the mastectomy specimen measured 5.0 cm. in greatest dimension. It extended to the muscle. All but two of 10 axillary lymph nodes showed gross features of metastatic tumor. They ranged from 0.3 to 3.0 cm. in diameter.

FOLLOW-UP:

The patient received radiation therapy to supraclavicular and para-mediastinal areas.

Follow-up information received 10-28-70: Post-operative chest film, taken 9-1-70, was clear. Liver panel - everything normal, except prolonged prothrombin time. CBC normal. Patient doing well clinically; no evidence of recurrence or other lesions.

NAME: G. O. DECEMBER 6, 1970 - CASE NO. 20

AGE: 24 SEX: Female RACE: Caucasian ACCESSION NO. 18631

CONTRIBUTOR: R. F. Martin, M. D. Outside No.70-7115
LAC-USC Medical Center
Los Angeles, California

TISSUE FROM: Right breast

CLINICAL ABSTRACT:

History: This 24 year old white female was first seen in the LAC-USC Medical Center Tumor Clinic on April 27, 1970. She was 4 month pregnant and gave a history of noting a mass in her right breast 9 months previosly that had tripled in size.

Physical examination: The right breast was three times the size of the left breast. It was tense with markedly dilated veins coursing through the entire surface of the breast. No palpable axillary nodes. Left breast was normal. The examining physician's impression was that the tumor was a cystosarcoma phyllodes.

Radiograph: Chest film was normal.

SURGERY: (4-30-70)

An incisional biopsy (RFS) revealed an angiosarcoma and a total mastectomy was done with both the deep and superficial regions being cleaned. No axillary nodes were found.

GROSS PATHOLOGY:

The specimen consisted of the entire right breast weighing 1680 gm. There was a sutured incision superior and medial to the nipple. Within the substance of the breast was a large space occupying lesion roughly 17 cm. in length and 11 cm. in depth. On the deep margin were several fragments of pectoralis muscle. All margins appeared clear. When surfaces made by sectioning were examined, they were markedly hemorrhagic with gray septae dividing it into lobules. There was no capsule but the tumor was circumscribed.

FOLLOW-UP:

Follow-up information not available.

NAME: M.P. DECEMBER 6, 1970 - CASE NO. 18

AGE: 28 SEX: Female RACE: Caucasian ACCESSION NO. 18213

CONTRIBUTOR: William H. Winchell, M.D. Outside No. SC 68-2018
Dominican Santa Cruz Hospital
Santa Cruz, California

TISSUE FROM: Left breast

CLINICAL ABSTRACT:

History: The patient was hospitalized for excision and drainage of a galactocele of the left breast.

She had delivered a normal female infant in March 1968. The left breast remained swollen 2-3 months after delivery. One month beforethis hospitalization she had been seen by a physician because of a mass in the left breast which was thought to be an abscess. Incision had yielded only what appeared to be inspissated milk.

NAME: A.G. DECEMBER 6, 1970 - CASE NO. 19

AGE: 71 SEX: Female RACE: Caucasian ACCESSION NO. 18566

CONTRIBUTOR: W. Harriett Davis, M.D. Outside No. 1593-70
Burbank Community Hospital
Burbank, California

TISSUE FROM: Right breast

CLINICAL ABSTRACT:

History: Six months prior to admission, the patient fell and injured her right breast but had no apparent sequelae. Two months before admission she noted a cord-like thickening in the right axilla. This failed to respond to diathermy and ultrasound and a month later she was found to have a definite right axillary mass. Several days prior to admission she suddenly discovered a very large mass in the right breast. A complete blood count was normal and radiographs of the chest and bones showed no metastases.

NAME: G. O. DECEMBER 6, 1970 - CASE NO. 20

AGE: 24 SEX: Female RACE: Caucasian ACCESSION NO. 18631

CONTRIBUTOR: R. F. Martin, M.D.
LAC-USC Medical Center
Los Angeles, California
Outside No. 70-7115

TISSUE FROM: Right breast

CLINICAL ABSTRACT:

History: This 24 year old white female was first seen in the LAC-USC Medical Center Tumor Clinic on April 27, 1970. She was 4 months pregnant and gave a history of noting a mass in her right breast 9 months previously that had tripled in size.

Moderator's diagnoses: Case 18 - Juvenile Secretory braast carcinoma (McDivitt-Stewart)

Case 19 - Probable nodular lymphoma of breast

Case 20 - Hemangiosarcoma of breast.

Slides - Microphotographs of cases 18 and 19. Gross and microscopic photos of case 20. Microphotographs of a case of Dr. DeSanto's in which a benign-looking breast angioma was followed by angiosarcoma a year later

DISCUSSION:

These three interesting breast lesions can conveniently be discussed together. Case 18 forces us to think about breast carcinomas in young femals, and about this specific pattern. There has been a recent re-surgence of interest in breast carcinomas in young subjects and it seems that these are neither as rare nor as balful as Ewing had believe. Of the 135 subjects studied by Norris and Taylor, one was 10, the others between 20 and 30. In pregnancy and lactation, in the presence of axillary metastases, the outlook is bad; otherwise, it is not unfavorable.

The "juvenile secretory" pattern of this case, while it does occur in young adults (such as this one), is, if there is such a thing, the "char-acteristic" breast carcinoma of children. The basic study is that of McDivitt and Stewart. Most of us doubtless could not recall having seen

this particular pattern before, but found it distinctive enough so that we should be able to recognize it if we saw it again. We were probably correct in believing that we had not seen it before, and we may have to wait quite awhile before we see it again, for McDivitt, who established the entity, has seen only 17 cases. To date the prognostic implications appear excellent. Many of the children whose surgery was nothing more than a lumpectomy have done perfectly well.

With regard to Case 19, I can't call it anything but nodular lymphoma. The prognosis of such breast lesions is evidently not too unfavorable. Ronald Dorfman, whom I am quite willing to lean on in the lymphoma area, tells me that he has just a few misgivings on this one, based on the high-magnification appearance of the cells. In other words, he is not entirely certain that this is not some sort of bizarre non-neoplastic reaction.

In Case 20 the gross photo looks much worse than the microscopics. The learned all emphasize the discrepancy between the rather well-differantiated appearance of the vascular channels and the baleful biologic character of the lesion. Under the microscope these channels do not really look as bad as those of the infantile hepatic hemangioblastoma (Case 14). Dr. DeSanto's case is of the sort that gives one nightmares. The original impression of benign character of the vascular proliferation is so sadly at variance with the later pattern and the clinical course.

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NAME: M. J. A. DECEMBER 6, 1970 - CASE NO. 21

AGE: 14: SEX: Female RACE: Caucasian ACCESSION NO. 18389

CONTRIBUTOR: E. R. Jennings, M. D. Outside No. 6795-69
Memorial Hospital of Long Beach
Long Beach, California

TISSUE FROM: Small intestine

CLINICAL ABSTRACT:

History: The patient had a history of epigastric pain of several hours' duration with nausea and vomiting. Abdominal xrays were typical of small bowel obstruction in the mid-jejunal region.

Physical examination: The abdomen was soft and distended primarily in the upper abdomen and most of the right flank. The abdomen was quiet on auscultation with no rushes or peristaltic activity noted.

SURGERY:

On October 29, 1969, an exploratory laparotomy was performed with a partial small bowel resection.

GROSS PATHOLOGY:

The specimen consisted of an 8 x 7 x 1.5 cm. segment of small bowel. Protruding above the mucosal surface was a cauliflower-like lobulated gray-tan lesion measuring 5 x 6 x 1.5 cm. Its cut surface was gray-white and gelatinous. It involved the mucosa and submucosa only.

FOLLOW-UP:

Patient is doing well, no sequelae.

NAME: M.J.A. DECEMBER 6, 1970 - CASE NO. 21

AGE: 14 SEX: Female RACE: Caucasian ACCESSION NO. 18389

CONTRIBUTOR: E.R. Jennings, M.D. Outside No. 6795-69
Memorial Hospital of
Long Beach
Long Beach, California

TISSUE FROM: Small intestine

CLINICAL ABSTRACT:

History: The patient had a history of epigastric pain of several hours' duration with nausea and vomiting. Abdominal x-rays were typical of small bowel obstruction in the mid-jejunal region.

Moderator's diagnosis: Lymphangioma, small bowel.

Slides - X-Ray (GI Series), Gross photos, Microphotograph.

DISCUSSION:

Handy literature on this interesting lesion is dishearteningly meagre. The process known as lymphangioma can present as diffuse or scattered lymphangiectasia which in the intestine may show up as "protein-wasting enteropathy"; it may also occur as unilocular "cystic hygroma" or as almost any stage in between If we are to be punctilious in differentiating between neoplasms and hamartomas, we shall have to call this hamartoma. The abrupt onset of "acute abdomen" is fairly typical The exact mechanisms involved are not entirely clear.

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NAME: S. E. J. DECEMRER 6, 1970 · CASE NO. 22

AGE: 43 SEX: Female RACE: Unknown ACCESSION NO. 18619

CONTRIBUTOR: Reuben Straus, M. D. Outside No. 3146-70
St. Joseph Hospital
Burbank, California

TISSUE FROM: Peritoneum

CLINICAL ABSTRACT:

History: The patient was admitted to the hospital on January 1, 1962 with dysfunctional uterine bleeding, fibroid uterus and possible right ovarian cyst. A total hysterectomy and bilateral salpingo-oophorectomy was performed on January 2, 1962. Surgical findings: Uterus was anterior, approximately two times average size. A right ovarian cyst was present measuring approximately 10+ cm., containing numerous pseudomucinous areas. The left ovary was normal in size but contained small pseudomucinous areas on its surface. Multiple pseudomucinous implants were present in the greater omentum and various areas of the regional peritoneal surfaces posterior to the uterus. Gross pathology: The right ovary measured 9 x 6 cm. and revealed many cysts measuring up to 1.2 cm. and filled with amber-clear fluid. The ovary appeared to consist of multilocular cysts on section. These ranged from 0.2 to 2.0 cm. in diameter. The inner surface was smooth. The left ovary was not remarkable. Additionally received was a mass of omental tissue with many pedunculated cystic structures also up to 3.0 cm. in diameter. These were filled with amber-colored fluid similar to that noted in the ovaries. The cysts were smooth and glistening.

Patient was again admitted on May 8, 1970. About six months prior to this she was found to have an enterocele with a palpable cystic structure in the pelvis "because of the previous diagnosis of cystadenocarcinoma this was watched." The cystic structure persisted but did not enlarge. Because the enterocele was getting larger, it was felt the patient should be explored for possible metastatic disease as well as enterocele repair.

SURGERY: (5-8-70)

On opening the abdomen, there were numerous cysts, measuring up to 8.0 cm. in largest diameter. There appeared to be hundreds in number. They involved the omentum, mesentery of the bowel and throughout the pelvis. Some appeared to be pedunculated, others were unattached. It was not possible to remove all of them. Grossly, the specimen submitted consisted of numerous thin-walled translucent cysts filled with clear fluid and measured from 5 mm. to 7 cm. in diameter.

COURSE:

The patient recovered well from the surgery and was discharged on May 14, 1970.

FOLLOW-UP:

The patient is being followed carefully with rectal examinations and chest xrays. She is on no present medication or therapy. Her last visit to the doctor's office was on October 13, 1970 and everything was fine. He believed this was a low grade malignancy.

NAME: S.E.J. DECEMBER 6, 1970 - CASE NO. 22

AGE: 43 SEX: Female RACE: Unknown ACCESSION NO. 18619

CONTRIBUTOR: Reuben Straus, M.D.
St. Joseph Hospital
Burbank, California

Outside No. 3146-70

TISSUE FROM: Peritoneum

CLINICAL ABSTRACT:

History: The patient was admitted to the hospital on January 1, 1962 with dysfunctional uterine bleeding, fibroid uterus and possible right ovarian cyst. A total hysterectomy and bilateral salpingo-oophorectomy was performed on January 2, 1962. Surgical findings: Uterus was anterior, approximately two times average size. A right ovarian cyst was present measuring approximately 10+ cm., containing numerous pseudomucinous areas. The left ovary was normal in size but contained small "pseudomucinous areas" on its surface. Multiple "pseudomucinous implants" were present in the greater omentum and various areas of the regional peritoneal surfaces posterior to the uterus. Gross Pathology: The right ovary measured 9 x 6 cm. and revealed many cysts measuring up to 1.2 cm. and filled with amber-clear fluid. The ovary appeared to consist of multilocular cysts on section. These ranged from 0.2 to 2.0 cm. in diameter. The inner surface was smooth. The left ovary was not remarkable. Additionally received was a mass of omental tissue with many pedunculated cystic structures also up to 3.0 cm. in diameter. These were filled with amber-colored fluid similar to that noted in the ovaries. The cysts were smooth and glistening.

Moderator's diagnosis: Inflammatory Hyperplasia of Peritoneum (Foreign Body Reaction)

Slide: Microphotograph

DISCUSSION:

This is another unique case with "cystification" of the peritoneum in which the thin fibrous walls are lined by flattened mesothelial cells. I regard it as a foreign body reaction in the peritoneum although this cannot be identified. It is a striking example of how proliferative such reactions can be. Once again, we must thank Dr. Straus for a particularly interesting case.

Reference:

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NAME: J. L. G. DECEMBER 6, 1970 - CASE NO. 23

AGE: 23 SEX: Female RACE: Caucasian ACCESSION NO. 12945

CONTRIBUTOR: J. McGrath, M. D. Outside No. C-1633-63
Centinella Valley Community Hospital
Inglewood, California

TISSUE FROM: Retroperitoneum

CLINICAL ABSTRACT:

History: This young woman noted a lump in the left side of her abdomen about 2 or 3 months previous. She noted pain when overtired. She denied weight loss and indigestion.

Past history: Patient had toxemia of pregnancy with hematuria and albuminuria six months prior to this hospitalization. Both father and paternal grandfather died of cancer (liver and lung, respectively)

Physical examination (April 3, 1963): A large, nontender, slightly movable mass was palpated in the left upper quadrant and questionably attached to the kidney.

Radiograph: UGI and BE showed only extrinsic pressure defect in the left upper abdominal quadrant.

Course: The patient was readmitted on May 11, 1963 when she developed a sudden onset of severe left upper abdominal pain with emesis. A large pulsatile tender mass was palpable in the left upper quadrant. IVP showed good function bilaterally. She underwent an exploratory laparotomy.

SURGERY:

A lacerated retroperitoneal tumor was found adjacent to the left kidney. There was over 1000 cc. of blood in the peritoneal cavity and bleeding was considerable. The adrenal glands were normal. The tumor and kidney were removed. The kidney was found to be normal after the surgery.

GROSS PATHOLOGY:

A hemorrhagic lobulated mass (15 x 12 x 10 cm; 750 gms.) had a fish-flesh appearance with prominent blood vessels and areas of new and old hemorrhage. Towards one tumor margin there was a structure grossly resembling a segment of ureter. The kidney was essentially normal.

FOLLOW-UP:

The patient received postoperative radiation therapy. When seen on December 23, 1963, her hemoglobin was 9.0 gm. There was no evidence of recurrent tumor.

NAME: J.L.G. DECEMBER 6, 1970 - CASE NO. 23

AGE: 23 SEX: Female RACE: Caucasian ACCESSION NO. 12945

CONTRIBUTOR: J. McGrath, M.D. Outside No. C-1633-63
Centinella Valley Community Hospital
Inglewood, California

TISSUE FROM: Retroperitoneum

CLINICAL ABSTRACT:

History: This young women noted a lump in the left side of her abdomen about 2 or 3 months previous. She noted pain when overtired. She denied weight loss and indigestion. This proved to be a large, non-tender, slightly moveable mass located in the LUQ.

Moderator's Diagnosis: Retroperitoneal Neoplasm, unclassified.

Slides - Microphotographs.

DISCUSSION:

I do not know what this tumor is; I do not even know what label should be attached to it. It got into the set through some haste on my part and Weldon's. We wanted to include a "sarcomatoid" variant of renal cortical carcinoma, and, from a hastily transmitted history (later found to be erroneous) and quick examination of the first slide (later found to be not representative) we thought this might fill the bill. This is a retroperitoneal tumor which does not involve the kidney, and from examination of a good many representative sections, I do not find the histology very suggestive of kidney tumor. Of course, retroperitoneal clear cell tumors do occur; we recently had one which Dr. Ackerman assured us was renal while Dr. Spjut was equally convinced that it was suprarenal. In the discussion of the present case at the meeting, one singularly learned and judicious colleague called it sarcoma unclassified; after the meeting was over, another was equally emphatic in asserting its epithelial character. There are areas which look epithelial; there are areas which look sarcomatoid. In his fascicle Ackerman starts off by saying "There has never been a satisfactory classification of the Retroperitoneal Tumors. The following is suggested as a tentative classification." He then goes on to give a page and a half of titles. When faced with a problem of this sort, Dr. Stout would often begin with the mild comment, "Well, this is another of those retroperitoneal things".

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