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CONTENTS

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L. **ABSTRACT:**

ATROPHY (NECROSIS) OF LIVER.

Abstr. W. P. Ritchie.

References:

1. Roman, B.:
Acute yellow atrophy of the liver.
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Historical:

Legg (for ref., see 3), 1880 made a thorough historical survey which indicated that the disease was probably recognized as early as the year 1600, the first case being reported by Ballonius in that year. In 1842, Rokitansky (for ref. see 4) accurately described the disease anatomically in its earliest or yellow stage.

Thirty years later Zenker (1872) described a case in which the liver instead of being yellow showed a bluish-red color. It was thought, and subsequently substantiated, that this was a later stage of the disease.

Twenty-three years following this, Marchand (1895) showed a further change characteristic of the longer standing cases--i.e., regeneration of the liver tissue.

Synonyms:

The term "acute yellow atrophy of the liver" was first used by Rokitansky in 1842. The unfitness of the name is universally recognized for frequently the condition is neither "yellow" or "acute" and occasionally it may not even justify the term "atrophy". Although it is no longer taken literally, its use is generally continued.

Disease referred to as "icterus

gravis", "acute parenchymatous hepatitis"; "parenchymatous degeneration of the liver" and "malignant jaundice." The name "acute necrosis of the liver" might be used as being more characteristic (3).

Literature:

Roman (1927) has one of best surveys in last 6 years. He reviews all important work up to that time. Since then, there has been comparatively little. Reports of cases following the use of cincophen predominate. There are many other reports of acute yellow atrophy following arsphenamine, chloroform, etc. In the last few years, there have been several good articles - one by Judd and Beaver (2) reviewing 22 cases, another by S. Weiss (3) reviewing the subject as a whole. There are cases and series of reviews but the work of Roman in 1927 appears to be the most informative work on this subject.

General comment:

(1) (2). There are 3 features of the anatomic picture which represent the important steps in the course of the pathological picture; namely, yellow atrophy, red atrophy and nodular hyperplasia. It has generally been considered that in acute fulminating cases we would find the yellow type, in more chronic cases the red type, and in longer standing cases the nodular hyperplastic type. Judd and Beaver have found it extremely difficult however to correlate the clinical course with the anatomic changes in the liver. In one of their 22 cases in which the jaundice was of 16 days duration, the lesion was anatomically acute, whereas in another case, with 3 days of jaundice, the lesion was by the same criteria of a late subacute type.

"Inability to correlate the symptomatic age of the lesion with the anatomic age emphasizes that even in this form of hepatic atrophy considerable destructive change may occur in the liver before clinical evidence is seen."

"Although it is impossible accurately to foretell the exact state of the liver as judged by the duration and severity of symptoms, nevertheless, a clinical classification should exist. The only approach to this must be on the basis of duration and severity of symptoms." Although it may not be in accord with anatomic findings it does give a relatively useful indication to the clinician of the stage of the disease.

Since jaundice is the most constant symptom of this disease, it is perhaps the best clinical guide. Ascites is relatively late and denotes a chronic stage.

Incidence:

Incidence on whole may be regarded as variable. Only 6 cases were found among 28,000 patients during a span of 23 years (3) at the Johns Hopkins Hospital. Only 1 case is found in the cross index of the Minnesota General Hospital since July 1928.

There has been a definite increase in the incidence in the last 10 years, according to Wood (14). Roman had 7 cases from Buffalo from 1921-23 with none in the several years previously. Wood (4) reports 14 cases coming to necropsy in 1928-30, in Dallas with only 4 in the previous 10 years. Good-pasture, Symmers and others report a similar experience. A similar increase in incidence occurred in Germany shortly following the war and later in Sweden and England. There has been no satisfactory explanation of this increase (4). In England, Germany and France and in several parts of this country, particularly New York State, the recent increase in incidence has apparently been associated with epidemic jaundice in which the bacteriological studies have been negative (4).

Age-Sex:

Majority of cases seem to occur between the 10th and 40th years and roughly about 50% of these between 20 and 30 years. Judd's 22 cases do not concur with this for the ages varied between 7 to 60 years, the average being 48 years. Only 2 patients in this group were under

30 years of age.

Skornin (3) refers to 7 instances in which it was reported in newly born infants and Rolleston (3) collected 42 cases in which it occurred during the 1st decade. The sex incidence is about 8 to 5 in favor of females.

Pathology:

(1) (2): Ordinarily the liver is greatly decreased in size but many authors speak of an enlargement in the earliest period of the disease. Average weight is about 955 gms. As in all atrophic processes of the liver, the anterior border is thin and sharp often consisting of nothing more than 2 layers of the capsule. Of interest is the fact that the left lobe is usually more severely affected than the right. Rarely the process is in same stage of development. In Judd's cases the color in the earlier cases was variable. Usually a mottled red and yellow appearance. This is in accord with other authors. The red regions represented the zones of total parenchymal destruction with the detritus of the necrotic hepatic cells cleared away. The red was due to blood still circulating in the skeletonized areas. In the later stages, the bulk of liver is red or grayish-red, often described as splenization but scattered in its substance as gross evidence of regeneration grayish-yellow, a grayish-green, well circumscribed, nodular masses.

Earliest microscopic changes in yellow areas, in which the lobular structure is macroscopically still recognizable, consist of cloudy swelling and hydropic and fatty degeneration in the cells. Other areas (red) show loss of liver cells leaving a shrunken lobule with much granular detritus and dilated sinusoids filled with blood. As process advances, round cell infiltration usually appears in the portal spaces and numerous small bile ducts became prominent.

As to mode of regeneration whether from pre-existing liver cells, or from bile ducts or both, the opinion is divided. Opinion is also divided as to zonal necrosis, some authors describe central, others peripheral and others describe intermediate zonal necrosis. General pathological changes are described as follows. Judd states that in general the initial toxic substances exerted but little effect on other organs than the liver. Degenerative changes occurred in them, probably because of metabolic toxins that accumulated as a result of hepatic dysfunction.

Spleen: All authors found an increase in size with free blood and hemosiderin in the pulp.

Bone Marrow: Hyperplasia noted.

Pancreas: Not infrequently small foci of fat necrosis are found.

Ascites: Most authors state 6th week it is the rule - rarely before then.

Heart - usually seat of moderately severe fatty degenerative change.

Kidneys - In Judd's studies usually were the seat of an acute diffuse toxic type of degenerative change characterized by swelling and intensive bile staining. Glomeruli were apparently not involved. Sometimes, except for bile staining, kidneys appeared normal. Other authors concur.

Other observations - fatty degeneration of skeletal muscles, fatty degeneration of the glandular cells of the stomach and those of intestinal villi; retinal hemorrhages with fatty degeneration and incrustations with tyrosin crystals; atrophy of thyroid (not so in any of Judd's cases).

Laboratory studies:

A. Urine: Quantity usually diminished towards end with increase in specific gravity. Bilirubin is usually present but it tends to diminish in quantity towards the end. Of interest are leucin and tyrosin crystals. Frerichs who discovered them claimed that they were present in all cases. However, other authors do not substantiate this. Some

authors (Weiss) state that biliary cirrhosis can be differentiated by absence of leucin and tyrosin in urine. Inasmuch as these are variable in yellow atrophy and when they are present are difficult to differentiate from crystals of ammonium urate and also from bilirubin needles, it does not seem that they can be of much aid in the diagnosis.

B. Blood: Estimations of urea do not as a rule offer much help in estimating degree of hepatic degeneration. However often in severe cases, the urea nitrogen may fall as low as 24 mg. per 100 cc. (Judd's case). Sugar values are said to be first increased and later diminished. Anemia never an alarming feature. Coaguability of blood is delayed and bleeding time is increased.

In acute and subacute yellow atrophy, high fixed curves of serum bilirubin are common. In this group, very high levels may be encountered, in fact, any value of 25 mg. for each 100 cc. or more should lead to a suspicion of extensive hepatic degeneration (5). This is in contrast to the early high curves of infections or catarrhal jaundice gradually subsiding to normal and the relatively lower, non-fluctuating serum bilirubin curves of portal and biliary cirrhosis.

C. Feces: Considerable variation. Most often described as clay-colored, but they are not altogether free from bile pigment, especially on chemical examination.

Nature of process - Roman: Generally speaking the process is spoken of as necrosis but the picture does not conform to that of ordinary necrosis either in the liver or elsewhere. One sometimes gains the impression that both the disintegration and the removal of the debris is so rapid that cells had not had time to develop characteristic picture of necrosis. At one time, the initial process was thought to be inflammatory but Salkowsky and Jacoby threw light on the situation by research which gradually brought about the recognition of the fact that the process was an autolysis. Regarding the agency that brings about the autolysis of the liver cells, acute yellow atrophy or conditions simulating it closely had been observed for a long time in cases of poisoning such as phosphorus, chloroform, etc. It could therefore be assumed on the basis of what amounted to human experiments that in idiopathic atrophy of the liver the injury of the liver cells leading to their autolysis is due to some form of poison either bacterial or metabolic. It goes without saying that the poison while injuring the cell does not at the same time destroy the autolytic enzymes (1).

Judd states that it is apparent in a careful analysis of cases, especially those due to a known agent, in addition to the toxic factor some fundamentally unknown constitutional state perhaps transient and of metabolic character also enters into the etiology and pathogenesis.

Of the substances reported to produce hepatic changes may be mentioned cincophen, chloroform, mercury, arsphenamine, arsenic, phosphorus, trinitophenol, tetrachlorethane, dinitrobenzene, aspidum, carbon tetrachloride, toxic hyperthyroid states, toxic products of pregnancy, bacterial toxins, alcohol in large quantities, hemagglutinative serums and cystine (2).

A toxic substance as an etiological factor could be found in only 7 of Judd's 22 cases.

Alcohol does not seem to be as prominent a predisposing cause as the older authors thought.

That pregnancy is a predisposing factor is certain. More than one-half the cases are said to have occurred in pregnancy. Disease usually occurs in second half of pregnancy although many cases have occurred in the puerperium and a few in the earliest periods. Hofbauer has described anatomic changes in the form of a central fatty degeneration, a loss of glycogen in the cells and certain vascular changes in normal pregnancy. Since it is generally recognized that previous damage to the liver such as repeated

attacks of jaundice and fatty liver due to alcohol or cirrhosis predispose to acute yellow atrophy it may be the changes described by Hofbauer in normal pregnancy influence the onset of acute necrosis.

Bacterial infection - attempts to establish specific organism for etiology have failed. Many cases are sterile, others show variation of organisms.

Syphilis - the association of acute atrophy with syphilis is prominent and of importance.

Roman (1) states that altogether there are about 700 cases of acute yellow atrophy published in the literature to date (1927). About 130 to 150 of these were combined with syphilis and almost always in the secondary stage.

In the cases in recent years many of the patients had been treated with arsphenamine. Fischer had collected 50 cases, Weber 53 and Herzheimer 69. In 1914, Michael (1) states that 10% of cases in literature were associated with syphilis.

Infectious or epidemic jaundice - seems to have been a predisposing cause at times. In recent years, waves of jaundice have occurred in Germany, Holland, Sweden and U. S. and the increase in incidence of acute yellow atrophy has been marked. The belief is gradually gaining ground in this country as well as abroad that it is merely the sporadic type of infectious jaundice and both may develop into acute yellow atrophy.

Phosphorus poisoning: Phosphorus in man may bring about a disease strikingly similar to that of acute yellow atrophy.

Chloroform poisoning: In 1924, Herxheimer found 70 cases reported in the literature to which he added 12 of his own. Note that the deaths from chloroform have occurred mostly after abdominal operations, especially in regions drained by the portal vein--that alcoholism, previous liver disease and repeated chloroform narcosis predispose to the accident and that most often it occurs in young individuals (1). The pathological picture is identical with that of an idiopathic acute yellow atrophy.

Mushroom poisoning: has long been one of the outstanding causes of acute hepatic necrosis.

Ford (1) estimates the total number of cases reported in the literature to be more than 300. An active principle called phallin is found which is harmless to man unless it is insufficiently boiled. Must be a temperature of more than 70° C. Changes are identical with phosphorus poisoning.

Cincophen (6): Since the introduction of cincophen (phenyl, quinoline-carboxylic acid) in 1908 its use as an analgesic has been widely used particularly for rheumatism. The drugs variously named quinophan, atophan contain quinoline mucleus which is basis of toxicity. In 1930 Rabinowitz collected 41 cases in literature and added 9. Toxic manifestations have no relation to the amount of drug ingested. Rabinowitz suggests there must be a predisposing cause. The conclusion of most authors is that the extensive use of cincophen compounds for "arthritis" should be discontinued.

Clinical Aspects: As illustrated by 22 cases of Judd-Beaver (2, 3, 4).

1. Initial symptoms: Jaundice is often the only symptom present at first, sometimes accompanied by pruritis, acholic stools, etc. Malaise often at first without jaundice.

Abdominal distress is usually a vague, mild abdominal pain, fullness in the epigastrium, flatulence, nausea or vomiting. In 4 of 22 cases pain over the liver was definitely mentioned. There is nothing characteristic of the onset (2).

No suggestion of the seriousness of the patient's condition is presented in the initial stage, the disorder being usually regarded as an ordinary catarrhal jaundice. This may last from a few days to 2 or 3 weeks (3).

Progressive symptoms: Although jaundice was present in 12 of Judd's cases at the onset, it became universal as the case progressed. In the cases in which it was delayed it became evident between 1 - 35 days after onset of illness. In some cases, there is a fluctuation of the jaundice but the icteric tinge never totally leaves the skin or sclera.

Weiss states that the jaundice may not appear in very rare, extremely rapid cases.

Vomiting is present but not universally. Occasionally, hematemesis is observed. Interesting that in 7 of Judd's cases pain approaching the nature of colic, typical of intraductal occlusion by calculus, was observed with the appearance of jaundice. Usually there was only 1 attack of pain which disappeared without marked improvement in the jaundice and without leaving marked residual soreness. In only 1 case were stones present in the gall-bladder at autopsy.

Weakness, progressing eventually to a state of exhaustion was a significant part of the clinical state.

The temperature is variable. There may be a slight fever but generally it is subnormal. In one of Judd's cases, there was initial chill and fever for one day. The pulse is usually rapid, feeble and of low tension. Tenderness over the liver occurs (Judd 10 out of 22 cases).

The terminal stage: For a variable period, the condition may remain constant with some tendency to temporary remission or exacerbation. The turn is gradual. Weakness becomes more pronounced, jaundice increases and all the aforementioned symptoms are exaggerated. Finally, mental changes occur and coma sets in. According to Judd the mean duration of this stage from time of onset was 12½ days, ranging from 1 - 33 days. After the development of the more profound mental changes, duration of life was a matter of only a few days. Weiss stresses dilation of pupils.

Diagnosis:

It is of prime importance to differentiate between intrahepatic and extrahepatic lesions, and of the former whether the condition is a cirrhosis, catarrhal jaundice or acute yellow atrophy. In addition to the history and laboratory findings previously mentioned (progressive jaundice not always painless) weakness, etc; diminished urine, presence of leucin and tyrosin crystals in urine (of doubtful significance); continued high curve of serum bilirubin in contrast to early high with rather slow but smooth fall in catarrhal jaundice, and relatively low curve of nodular cirrhosis; direct van den Bergh, high icterus index - usually in direct proportion to severity of condition, etc., there have been other laboratory procedures which have been instituted.

The different liver function tests present a problem about which there is a great diversity of opinion.

Vanzant says (in personal communication) that at the Mayo Clinic they have been using 3 procedures in all the cases of jaundice: 1. galactose tolerance test; 2. serum bilirubin curve; 3. biliary drainage.

The use of the galactose tolerance test is an example of the widespread diversity of opinion. In the European clinics, it is used with a great deal of faith. Briefly, 40 gm. galactose are given after an overnight fast. Five hourly urine specimens are collected. Total quantity mixed and quantitative sugar is found. Normal range of excretion is from 0 - 3 gm. A 3 gm. excretion is suggestive of hepatic insufficiency--anything above is diagnostic. In experience of Schay and Schloss (7), it is only means of identifying toxic or infectious jaundice early in its course.

(March 29, '33) Proc. Staff Meet. of Mayo Clinic gives a summary of their experience with this test. It records the knowledge gained from 107 cases of

jaundice in which the test was used. In acute intrahepatic jaundice, the test is almost uniformly positive, whereas in chronic intrahepatic jaundice positive results are obtained only in the occasional case. In obstructive jaundice, a considerable percentage of positive results were observed which was contrary to other workers in this field. The opinion presented is that in intrahepatic types of jaundice a fairly definite relationship exists between degree of hepatic destruction and urinary output of galactose. They also found, in general, that the more long standing and complete the obstruction the greater the likelihood of a positive galactose test. In moderately severe and well-developed cases of intrahepatic jaundice, the test is uniformly positive; however, in the earlier stages the test is usually negative. Test not to be used as an absolute differential criteria between obstructive and intrahepatic jaundice, however the test is of distinct value in certain cases of doubt.

C. J. Watson studied the average daily elimination of urobilinogen (9), and the average urobilinogen ratio between that found in feces and that in urine. At the present time, he is working out a series in which he shows definite changes in the ratio of urobilinogen in the urine and feces depending upon whether the condition is intrahepatic and extrahepatic. Roughly, he finds that in an intrahepatic type of jaundice the ratio of urobilinogen in urine increases relatively over that in feces, whereas in the obstructive type this is not so unless the obstruction is of long standing.

Surgical aspect (2):

"The combination of pain with jaundice usually denotes obstruction of the common bile duct by a calculus. That this should be a not uncommon occurrence in the subacute and chronic stages of hepatic atrophy forms the most frequent justification for exploration. Although exploration has not proved to be of any particular value in cases of unmixed hepatic atrophy, and although there is some evidence that it has been harmful, there is, nevertheless, always the possibility that the surgeon may discover a condition such as the presence of gallstones."

"Other investigators have reported experiences similar to ours in which the diagnosis of primary hepatic atrophy was ascertained with certainty only by laparotomy."

"Brown stated that in his experience drainage of the bile causes much improvement. In Romer's cases, marked improvement was exhibited after laparotomy; apparently, the patient recovered completely. Whipple would not operate if the diagnosis could be clearly established by other means, although he thought it not harmful to prove the diagnosis in this way. The latter is probably the more acceptable position."

"Probably the most significant differential point distinguishing unmixed atrophy of the liver from obstructing lesions of the biliary tract is that that in hepatic atrophy bile is persistently found in the material obtained by duodenal drainage of deeply jaundiced patients who usually have associated severe toxemia. Another significant fact is that severe pain was never an initial accompaniment of the icterus, and chills and fever were extremely rare, having been recorded in only one case in the series with the onset of jaundice."

Treatment: (3)

Until research discloses the causative factor of this condition, therapy must necessarily be preventive and symptomatic in nature.

Caution in use of chloroform, arsphenamine, etc. is necessary.

For deficiency in glycogen in liver, Umber advises that in the presence of icterus and other hepatic disturbances, insulin and levulose (the latter being the carbohydrate most easily absorbed by the liver) should be used. The patient usually receives from 10 - 30 units of insulin b.i.d. following which 20 - 30 grams levulose are given by mouth or by enema or intravenously. A diet rich

in carbohydrates but low in protein is advised.

A solution of sodium bicarbonate (12%) and glucose (5%) should be given by proctoclysis 500 - 1000 cc. every 4, 6 and 8 hours. All attempts to remove the toxic substances in the bile may be made early in the course of the disorder by means of duodenobiliary drainage. Otherwise treatment is symptomatic.

According to Minot and Cutler's work calcium has a protective action for the liver. Given by mouth and intravenously, its use seems logical and certainly does no harm (11).

Impressions:

1. Acute yellow atrophy is a rare disease. More prevalent in last few years.
2. Anatomical picture at autopsy may not correspond with the clinical picture.
3. Usually find different stages in the liver at autopsy. (Red and yellow changes)
4. Final change is that of nodular hyperplasia.
5. Only 1 case in cross index at Minn. Gen. Hosp. since 1928.
6. Roughly, about 50% of cases are between 20 and 30 years.
7. Sex incidence about 8 females to 5 males.
8. No new factors in etiology have been advanced in last few years. Cinchophen is newest etiological factor.
9. Diagnosis best made on history, icterus index, serum, bilirubin curve and possibly galactose tolerance test.
10. Acute colic may occur (as in Judd's case) to confuse the picture.
11. Course may be acute, subacute or chronic.
12. Usually fatal although occasional cases survive.
13. Treatment mostly symptomatic. Administration of levulose and glucose advised.

II. CASE REPORT:

SUBACUTE YELLOW ATROPHY OF LIVER.

Path. Koucky.

Case is of white female, 69 years of age, seen in Out-patient Department of Minnesota General Hospital 3-20-33, again brought to same department 3-22-33 at which time patient expired. Not admitted to hospital.

Bleeding

1928 - Vaginal bleeding began. Growth removed from cervix which stopped bleeding. Menopause at 51.

Jaundice

11-1-32 - Observed jaundice, some weakness and slight weight loss. Jaundice became progressive, stools white and urine dark. No pain associated with jaundice.

3-5-33 - Jaundice, acholic stools and dark urine continue. Began to bleed again from vagina, using 2 to 3 pads daily. Bleeding unassociated with pain.

3-10-33 - Edema of ankles and feet observed.

Examination

3-20-33 - O.P.D. History not significant. Has 10 children, all living and well. No miscarriages. Physical examination: Markedly jaundiced. Some diminution of hearing noted. Heart - blood pressure 144/88, systolic murmur heard over mitral area, some nelargement present. Abdomen - large; shifting dulness in flanks thought to be present. Extremities - slight pitting edema of ankles and feet. Hospitalization for further study advised. Arrangements made for admission.

Exitus

3-22-33 - O.P.D. Brought for admission by ambulance. Moribund. Pulse imperceptible. Caffeine sodium benzoate given by hypodermic. Adrenalin administered into heart muscle. Patient could not be revived. Pronounced dead at 11:20 A.M.

Autopsy

Edema, jaundice, moles

Body is well-developed and nourished, white female, 69 years of age, measuring about 166 cm. in length and weighing approximately 180 lbs. Rigor absent. Hypostasis just beginning. 1+ edema present of feet. No cyanosis. 3+ jaundice. Pupils equal, each measuring 6 mm. in diameter. Several flat, dark moles over trunk but none over extremities. Soft papilloma of skin. Abdomen flabby, numerous striae gravidarum present. Puncture wounds and ecchymoses in right antecubital space. Subcutaneous fat abundant and deeply stained by bile.

Ascites

Peritoneal Cavity contains about 600 to 800 cc. bile stained fluid. Serous surfaces not inflamed. No evidence of acute exudate. Appendix subcecal and hangs free.

Pleural Cavities contain slight excess fluid. No adhesions. Pericardial Sac smooth and glistening.

Normal

Heart weighs 350 grams. Musculature of good consistance. No evidence of fibrosis or degeneration. Heart not dilated or hypertrophied. Valves soft and well formed. Mural endocardium smooth. Root of Aorta of good size and shows no syphilis. Coronaries slightly involved by atheromatous patches but open and wide throughout.

Right Lung 350 grams, Left 275. Moderate degree of atelectasis in both lower lobes, estimated about 50% in left lower and 5% in right lower lobe. No pneumonia or apical fibrosis.

Spleen 170 grams, quite firm. Capsule smooth. Markings perhaps slightly exaggerated.

2nd-3rd stage

Liver weighs 1150 grams. No perihepatic adhesions. Surface rough, resembling very much coarse, stained leather. It is granular and shows diffuse mottling of yellow and red throughout liver surface, most marked in edges of right and left lobes. Liver very tough, fibrous, cuts with definitely increased resistance. Cut surface irregularly covered with yellow areas which range up to about 3 mm. in diameter. Many arranged in clusters and more prominent about periphery of liver and central portion being more or less free. Intervening liver substance of very dark red color in which liver markings are fairly well retained.

Stones

Gall-bladder thick wall, distended with stones and inspissated bile. Bile ducts are patent and slightly thickened. No stones in ducts.

Gastro-intestinal Tract: Esophagus no change. Stomach is large, filled with gas. No ulcerations. Duodenum no tumors. Small bowel not thickened or dilated and shows no inflammation, ulceration, tumor or malformation.

Pancreas soft and pink. Head of pancreas no tumors or fibrosis. No fat necrosis, cysts or tumor.

Adrenals good size and show no hemorrhage, degeneration or cysts.

Right kidney 160 grams, Left 175. Capsules strip with little difficulty, leaving finely granular surface. Kidney substance, on cross section, appears diminished in amount. Pelves not inflamed.

Bladder not thickened or trabeculated. No cystitis or tumor.

Polyp

Genital Organs: Uterus is large, with adnexae weighs 525 grams. Appears to be size of 2 months' pregnancy. Tubes not thickened or inflamed. Ovaries hard and fibrous. On cross section, central part of ovary appears somewhat yellowish. On opening uterus, walls are extremely heavy, soft and boggy. Interior of uterine cavity is covered with bloody material. Mucosa is rough and cystic, has several large, clear cysts about cervical region. In right upper pole of uterus, a nodule of cystic glands is present which penetrates into the musculature of uterus for a distance of about 1.5 to 2 cm., and which approaches outer surface of uterus to distance of about 1 cm. Opposite this cystic area, there is a long, polypoid, grayish-red mass which fills the uterine cavity. This appears to be a polyp to which has been attached blood clots and fibrin.

No appreciable enlargement of Lymph Nodes.

Organs of Neck - not dissected.

Head: Brain removed in usual manner. Cerebro-spinal fluid and meninges show no change. Brain on exterior and in substance (and ventricles) shows no gross changes.

Microscopic: Frozen sections of liver show fairly typical picture of subacute yellow atrophy. One of sections of uterus from cystic area shows simple cystic hyperplasia of glands.

Diagnoses:

1. Subacute yellow atrophy of liver.
2. Cystic hyperplasia of endometrium.
3. Polypi of endometrium.
4. Hypertrophy of uterus.
5. Pulmonary atelectasis.
6. Arteriolarsclerosis of kidneys.
7. Cholecystitis, chronic.
8. Cholelithiasis
9. Edema of ankles
10. Icterus III.

III. DIURNAL VARIATIONS IN EFFICIENCY

A number of standards of performance or function on the part of the body have been accepted as indexes of its normality. Perhaps the most noteworthy illustration is found in the normal body temperature. This is something that can be readily measured with comparative accuracy, and departures from the expected figures are among the fundamental physical signs of disease. Body temperature, however, even in admittedly perfect health, is subject to characteristic slight diurnal variations that cannot be directly correlated with changes in the environment. The temperature of man reaches a maximum at about 4 or 5 p.m. (37.5 C., or 99.5 F.) and a minimum at about 3 a.m. (36.8 C., or 98.2 F.), at a time when the bodily functions are least active. It has been observed that if the habits of man are altered so that he sleeps during the day and works during the night, the character of his diurnal temperature variation is altered and the periods of maximum and minimum temperatures become inverted.

Habits of sleep also exhibit a diurnal character. The most essential factor in causing sleep seems to be muscular relaxation; this causes a loss of proprioceptive reflexes that in activity are always functioning. Kleitman, one of the foremost students of the subject, insists that anything that will produce muscular relaxation will lead to sleep. In the summertime there is a disinclination to engage in muscular activity because it produces warmth. One is therefore more inclined to relax the musculature and can fall asleep with east at almost any time of the day. Kleitman remarks, by way of illustration, that a warm stuffy atmosphere of a lecture room, especially if the chairs are comfortable, frequently produces sleep in some auditors, sometimes to their embarrassment. The percentage of sleepers increases if the lecturer's voice is monotonous and if the room is darkened for lantern slide projection. In explanation of the customary incidence of diurnal sleep, Kleitman believes that the cycle of day and night serves to develop in animals and man what Pavlov calls a "natural" conditioned reflex. Darkness makes for poor vision and discourages movements. This leads to inactivity and relaxation, and sleep follows. Repeating this performance a great many times results, according to Kleitman, in the establishment of a conditioned reflex of a temporal character--relaxation at a certain time. Likewise, waking may be developed into a time-conditioned reflex. It is further averred that children are born into a social organization where diurnal sleep is the universally accepted mode of sleeping. The first habit that the mother tries to develop in a baby is that of an unbroken night's sleep. As he gets older, other functions develop a periodicity that coincides with the enforced sleep periodicity. For instance, a temperature curve develops, with a minimum at night, and produces a disinclination to night activity. Even the modest tear apparatus, Kleitman points out, stops its function at bedtime, producing dry eyes and favoring their closure. Kleitman feels certain that, under conditions of artificial illumination and twenty-four hour activity of a

group, children brought up by that group could be trained into a twelve or a thirty-six hour cycle of existence, instead of the present twenty-four.

The foregoing considerations prompt one to ask whether there are other human activities that show a diurnal variation concomitant with that of the twenty-four hour cycle of sleep. In an investigation recently reported from the University of Chicago, a number of adult persons were subjected to several simple tests at different times of the day, and variations in performance were noted as regards the length of time required to carry out a certain task, or the number of errors made in a definite period of time, or both. The tests were made five times daily, for at least twenty days. The results obtained indicate a well marked variation in performance during the day, efficiency of performance increasing up to noon or afternoon and then declining for the rest of the waking period. The body temperature varies in the same sense. There are indications that the temperature is dependent on the tonus of the skeletal muscles, in that it falls on lying down and rises on getting up. Kleitman adds that, if the variations in temperature can be used as a criterion of changes in tonicity of the body musculature, it would appear that the gradual decrease in efficiency toward the end of the day might be due to greater muscular relaxation, which leads to a decrease in the number of proprioceptive impulses reaching the cerebral cortex and makes it increasingly difficult to maintain the state of wakefulness, irrespective of whether or not any fatiguing work was done during the day. It is hardest to keep awake during the early hours of the morning when the body temperature is lowest. Under ordinary conditions, Kleitman concludes, going to bed in the evening results in a still greater muscular relaxation, and sleep is precipitated. After all, these phenomena of human physiologic behavior are familiar from practical experience. What one fails to remember is that work and weariness play a part in determining human efficiency in a way that the individual worker--notably the intellectual worker--all too often forgets.

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IV. MEETING:

Date: April 13, 1933

Place: Interne's Lounge, 6th Floor, West Building.

Time: 12:10 to 1:14

Program: Tumors of Pleura

Present: 96

Discussion: L. G. Rigler
R. W. Koucky

Theme: L.G.R.: We have just the one film on this patient which illustrates one of the difficulties in the roentgen diagnosis. Has extensive hydropneumothorax on the right side. Heart displaced. Nothing in the right lung that can be made out.

Second case: Original examination of the chest showed definite density over the left apex coming down from above, erosion of the posterior portion of the ribs. Followed this up by detailed films of this area. Marked erosion of the posterior portion of the first rib, erosion of second rib, and little of third. Some erosion coming from spine, diffuse density in this area. Question of diagnosis arose. Hardly primary tumor of lung, pleura or scapula, as the scapula separated from it. Took pictures of the spine. Intravenous urogram showed beautiful kidney pelves on both sides. Ureter excluded on that basis. Tumor at apex with secondary erosion of rib is endothelioma.

R. W. K.: Surprising in reviewing the literature is the extreme confusion in classification of this type of tumor. A great many names such as combinations of carcinoma and sarcoma are used. Apparently everyone has attempted to include the neurogenic tumors in the same class as the endotheliomas. The work of Kienbock and later Masson defines clearly the neurogenic group. When all the forms of sarcoma, fibrosarcoma, and the more malignant type of tumors, etc. are excluded the pathological classifications become much more clear.

Record Librarian -- Gertrude Gunn