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GENERAL STAFF MEETING
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UNIVERSITY OF MINNESOTA

CONTENTS

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ABSTRACT

THROMBOCYTOPENIC PURPURA

By Rudolph Koucky

1. Ref.:

(1) Pierson, B.
Purpura Hemorrhagica.
Staff Meeting Bull.,
Minn. Gen Hosp., 3, #10:
(December 10,) '31.

(2) McLean, S., Kreidel, K. and Coffey, J
Hemorrhagic Thrombocytopenia in Children
J.A.M.A. 98: 387-393, (Jan.30) '32.
(Columbia Univ.)

(3) Rankin, F. W. and Anderson, P. S.
Splenectomy for Hemorrhagic Purpura of Children.
Ann. Surg. 93: 749 - 754, (Mar.) '31.
(Mayo Clinic)

(4) Pemberton, J. De J.
Results of Splenectomy in Splenic Anemia, Hemolytic Jaundice and Hemorrhagic Purpura.
Ann. Surg. 94: 755 - 765, (Oct.) '31
(Mayo Clinic)

(5) Guller, E. I. and Lawrance, J. S.
Idiopathic Thrombopenic Purpura.
Ann. Int. Med. 4: 1535 - 1544, (June) '31. (Rochester Univ., N.Y.)

(6) Jones, H. W. and Tocantins, L.
The Treatment of Thrombopenic Hemorrhagica.
J.A.M.A. 100: 83-88, (Jan.14) '33.
(Jefferson Med. School)

(7) Kugelmass, J.N.
The Management of Hemorrhagic Problems in Infancy and Childhood.
J.A.M.A. 99: 895-902 (Sept. 10) '32.
(New York)

(8) Tyllie, W. G. and Ellis R.W.B.
The Clinical Interpretation of Some Hemorrhagic States.
Arch. Dis. Child. 6:313-325, (Dec.) '31. (Westminister Hosp., London)

(9) Lescher, F. G. and Hubble, D.
A Correlation of Certain Blood Diseases on the Hypothesis of Bone Marrow Deficiency or Hypoplasia.
Quart. J. Med. 1:425-457, (July) '32.

(10) Fischer, L. C.
Platelet Counts after Splenectomy and other Operations.
Proc. Soc. Exp. Biol. and Med. 29:316-318, 1931. (Minn. Gen. Hosp)

Summary of Clinico-Pathologic Features (Ref 1)

1. Group of hemorrhagic states (thrombocytopenic purpura) characterized by (a) diminution in number of platelets, (b) normal clotting time, (c) prolonged bleeding time, (d) failure of clot to retract, and (e) positive tourniquet test.

2. Most common in early youth (80% before 40), females (3:1) not hereditary.

3. Bleeding into skin, from orifices (100%) mucus membranes (70%) and brain (2%).

4. Theory of pathogenesis leading to splenectomy is either abnormal destruction of platelets by spleen (Kaznelson 1916) or splenic inhibition of production of platelets in bone marrow. (Frank)

5. General belief is basic cause of bleeding is decreased number of platelets. (Note: Now questioned)

6. No specific change exists in spleen; follicular hyperplasia and increased amount of inter-sinusoidal reticular tissue found. (Not specific)

7. While generally believed that bleeding depends on number of platelets (under 100,000) investigation shows no absolute correlation.

6. Results of splenectomy (summary):

	Type	Cases	Mort%	"Cures"%
Spence	Acute	12	83	
	Chronic	80	10	70
	Mixed	101	20	70
Rankin	Mixed	40	?	90
Whipple etc.	Mixed	30	?	50
Marsh	Acute	9	90	10

9. Acute cases should be treated by supportive means and splenectomy only as emergency.

10. By extensive preoperative transfusions, mortality of splenectomy can be reduced in acute stage.

11. Liver treatment has apparently been tried in few cases with success.

Presentation in 1931 (above) gives "textbook" impression of "Essential Thrombocytopenic Purpura" current in literature of that time. Disease appeared to be specific entity, diagnosed clinically by certain findings and tests and cured by removing a functionally diseased spleen (transfusions being preoperative supportive treatment). This impression is further advanced by Pemberton in a report of 326 splenectomies.

	Cases	Mort.	Well
Splenic anemia	167	10%	38%
Hemolytic jaundice	118	3%	70%
Purpura Hemorrhagica	41	5%	90%

Appears to have low mortality rate and high percentage of cures when correct diagnosis is made. It is said (Rankin) that a good history and study of blood will clinch diagnosis. Necessary data concerning blood are:

1. Increased bleeding time.
2. Decreased platelet count (60,000).
3. Non-retractile clot.
4. Normal or slightly increased coagulation time.
5. Positive cuff test (Syn: Rumpel-Leed's Test, diminished capillary resistance test).

Past 18 months:

Literature since 1931 contains very little now of the "clear cut" picture of "Essential Thrombocytopenic Purpura" as outlined above. Instead, there is definite trend toward doubt and question regarding specificity of such a disease and importance of splenectomy as a factor in cure.

Problem Today:

Following report (McLean, et al., Columbia, Ref.2) illustrates clinical problems. Authors saw 21 children with purpura. Age ranged from 19 months to 12 years; bleeding had been present 48 hours to 3 1/2 years. Cutaneous in 100% and mucosal in 80%. Every case showed typical laboratory findings and other tests: i.e., thrombocytopenia (85% below 60,000), prolonged bleeding time, normal coagulation time and deficient clot retraction. No parallelism found between degree of bleeding and platelet count. Twelve cases (60%) were accompanied or immediately preceded by acute infection. (Essential or Symptomatic Purpura ?) Treatment as follows:

Untreated (7 cases: 4 acute and severe, 1 acute and moderately severe, 3 chronic and mild). 5 remain asymptomatic (5 mo. to 5 yr.), 1 well o weeks later and cannot be traced.

Transfusion (8 cases: 5 acute, 3 chronic): 4 well 4 to 18 months later, 1 well after tonsillectomy, 2 still in hospital, 1 still has purpura.

Splenectomy (6 cases: 3 acute, 1 subacute and 2 chronic, generally worse than previous groups): 3 died (mortality 1/2), favorable results 3.

Questions: The above experience and others similar bring up several questions:

1. Is "Essential Thrombocytopenic Purpura" a specific disease? Can it be separated from other purpuras?
2. Is reduction in platelets primary cause of bleeding?
3. Is platelet deficiency caused by over-destruction or under-production?
4. In either cases is spleen responsible for deficiency?

Can Essential Thrombocytopenic Purpura be separated from other purpurae?

A classification of purpura on an etiological basis is still imperfect. Apparently the best attempt is that of Kugelmass:

TABLE

Hemorrhagic Diseases Resulting Primarily from Blood-Clotting Dysfunction.

Acquired:

I. Potential hemorrhagic disturbances.

II. Hemorrhagic disease of the new-born.

III. Thrombocytopenic purpura

- a. Essential
  - 1. Bone marrow disease
    - Agranulocytosis
    - Aplastic anemia
    - Aleukia hemorrhagica
    - Erythroblastic anemia
    - Niemann-Pick
    - Leukemia, tumors
  - 2. Splenic disease
    - Banti's
    - Gaucher's
    - Hemolytic icterus
- b. Symptomatic
  - 3. Infectious diseases
    - Endocarditis
    - Sepsis
    - Syphilis
    - Tuberculosis
    - Typhoid
    - Hemorrhagic measles
    - Hemorrhagic scarlet fever
    - Hemorrhagic smallpox
  - 4. Drugs
    - Mercury, bismuth, and arsenic compounds and potassium iodide
    - Arsphenemine
    - Quinine
    - Phenolphthalein

IV. Hemorrhagic diseases of the liver
- 1. Congenital obstruction of bile ducts.
- 2. Liver infections, tuberculosis.
- 3. Cirrhosis
- 4. Poisoning (Chloroform, Phosphorus)

Familial:

I. Hereditary hemophilia
II. Hereditary thrombasthenic purpura.
III. Congenital thrombocytopenia
IV. Congenital fibropenia
V. Atypical hemorrhagic diseases.

Hemorrhagic Diseases Resulting Primarily from Vascular Dysfunction

Acquired:

I.	Nutritional	Scurvy Marasmus Infantilism (Herter's)
II.	Allergic	Purpura simples Erythema multiforme Schonlein-Henoch syndromes Purpura fulminans Acute infectious diseases
III.	Infectious	Subacute bacterial endocarditis Acute infectious diseases Sepsis Syphilis Tuberculosis Uremia
IV.	Toxic	Drugs Venom

Familial:

I. Hereditary telangiectasis

II. Atypical hemorrhagic diseases

It is to be noted that in the large group of "symptomatic" purpura, the same history and laboratory results are encountered as in the "essential" type. When one includes upper respiratory infection, tonsillitis, chronic lymphadenitis, in the group; and finally, when one adds the group designated as infectious vascular dysfunction there seems to be little left in the purely "essential" class.

This author includes under "Hereditary Thromboasthenic Purpura", the cases of purpura hemorrhagica with normal platelet counts which have been recorded by several authors (see Lescher). The platelets, though normal in number, are deficient in function (hypothetical).

A study of the table and a realization that there is a rapidly increasing number of reports of borderline cases (see McLeans series: 60% with infection) makes the possibility of essential, thrombocytopenic purpura open to question? Nevertheless "there is a general agreement among clinicians (with few exceptions) that this disorder can be separated from other purpuras and that a deficiency in platelets is its most important sign".

Is thrombocytopenia responsible for bleeding?

All authors are agreed that there is no absolute correlation between number of platelets and degree of bleeding. Moreover, a low platelet count has no part in initiating bleeding. Thrombopenia may be present without bleeding. There is some defect in the capillary wall as well. Others postulate a deficiency of some internal secretion (as in hemophilia and females of hemophilic families). The relative importance and the possible interaction of these various elements in production of bleeding is not settled. At this time it can be said that there probably is a defect in the capillary wall in most cases and the bleeding is aggravated by platelet deficiency (and endocrine dysfunction as in hemophilia and vitamin insufficiency as in scurvy).

Is Platelet Deficiency due to Over-destruction or Under-Production?

A study of the literature by Lescher leads him to believe that there is very little evidence to indicate platelet destruction. The generally accepted belief is that there is deficient production of platelets by the bone marrow.

Is the Disease caused by Excessive Splenic Function?

(Kaznelson's theory of excessive destruction; Frank's theory of inhibition of bone marrow). Four types of reactions on the part of the platelets after splenectomy have been observed:

1. Rapid and persistent rise (result in clinical cures).
2. Temporary rise and subsequent fall to previous level.
3. No change.
4. Decrease in number.

In interpreting these reactions, it is to be remembered that a number of conditions modify the platelet count: diet, light, trauma, operation, transfusion, etc. Fischer found a much sharper rise of platelets after splenectomy (of operative group).

It seems obvious that if the spleen has any effect on platelets, it must be exercising a different effect in various types of cases. The role of the spleen in purpura therefore still remains in doubt. The interaction of platelets, capillary defects, blood plasma (endocrine hormones, vitamines, etc) bone marrow, spleen, reticuloendothelial system is too intricate for solution at present time.

Evidences from Results of Treatment on Nature of Disease.

Results of splenectomy has been reviewed. As noted previously 50 to 90% (70% average) are improved. These results are not the entire story. (Excellent review by Jones and Tocantins) "Hexing" (faith healing, etc.) carries a high percentage of cures. The customary promise of improvement is in the next change of the moon (i.e. in 3 to 4 weeks). Spontaneous remission occurs in 14 out of 15 cases (D.C. Smith). Many never have recurrences. Some are cured by simple removal of infectious processes (8%).

In the acute severe types such conservative methods cannot be practiced.

Blood transfusion (in small amounts) administered frequently is almost a specific in this type of case. 46% of entire group (Jones) given this treatment with excellent results. 300 c.c. used but 100 cc. often effective but it must be repeated frequently enough to control the bleeding time (as often as 3 transfusions in 24 hours). An example is given:

8 A.M. - Bleeding time 62 min.
8:30 A.M. - 600 cc. transfusion.
9.00 A.M. - Bleeding time 62 min.
1:00 P.M. - 540 cc. blood
2:00 P.M. - Bleeding time 57 min.
7:00 P.M. - Bleeding time 62 min.
7:00 P.M. - 520 cc. blood
8:00 P.M. - Bleeding time 21 min.
12:00 P.M. - Bleeding time 5 min.

The authors are convinced that change would not occur if the transfusions are not repeated, i.e., not a delayed reaction to transfusion.

Failures and exacerbations after transfusion are attributed to insufficient number of transfusions, i.e., failure to change bleeding time is indication for more blood; and properly given blood. The three stages of treatment (during acute stage, in convalescence and late in treatment of the acute progressive purpura) are intravenous transfusion and use of diet, iron, ultraviolet ray, viosterol, etc.

Other conservative treatment (Jones includes these in same paragraph with "hexing"): liver therapy, ergot, turpentine, etc. Diet is given separate paragraph. It is emphasized by Kugelmass (high protein diet) who claims remissions and cures by this method. Jones believes its greatest value lies in the fact that the swallowed blood gives anorexia and the bleeding gums give pain. A high protein, high vitamin diet suitable to the patient is given.

Indications for Splenectomy:

1. Acute progressive cases which do not respond to other methods (80% mortality)

2. Chronic case with a normal (or nearly so) blood count but with increased bleeding time and low platelet count. (Kugelmass would try high protein diet)

3. Chronic cases with anemia not improved by transfusions, removal of infectious foci and the other treatment (diet).

Ligation of splenic artery:

34 cases to date with only 2 deaths. Results similar to splenectomy. Necrosis or infarction do not occur. Spleen becomes 28 to 70% decreased in size. Indications for such operation same as for splenectomy.

Interpretation of results of treatment not entirely clear. It seems that from the recent reports there is becoming less reason for classification into special group called "essential" purpura. Also, appears that splenectomy is not specific cure in every type of case. Spontaneous cures frequent. Several conservative methods are successful: transfusions, diet and removal of infections. When these fail, splenectomy indicated but does not always cure. Appears that thrombocytopenic purpuras are heterogeneous group without any particular type being plainly "essential". Type of chronic, recurring purpura in which most extensive search has failed to reveal a cause appears to be entitled to this name? When other forms of therapy have failed, this type often responds to splenectomy? These two conditions, absence of cause and response to splenectomy after failure of other methods appear to be only real reasons for making a sub-division entitled "essential thrombocytopenic purpura".

Impressions:

1. General clinico-pathologic features of essential thrombocytopenic purpura again reviewed and comparison with literature of past 18 months made.

2. Presentations up to 1931 gave clear-cut picture of this disease while subsequent to this time considerable doubt is expressed as to specificity and importance of splenectomy as sole method of treatment.

3. Symptomatic purpura and infectious vascular dysfunction comprise

large percentage of "new" cases. As more and more etiological factors are discovered, "essential" group becomes smaller.

4. An increasing number of borderline cases are presented in literature.

5. A new subgroup "hereditary thrombo-asthenic purpura" proposed by some to indicate a congenital deficiency in function of platelets. A similar subgroup "hereditary asthenia of capillaries" could be proposed.

6. There is no absolute correlation between platelet count and degree of bleeding. Thrombopenia is not necessary.

7. A vascular defect is present alone in some cases and probably in all to some extent.

8. Endocrine dysfunction, disturbance of diet and vitamins apparently play a part.

9. No data is presented to indicate that there is over-destruction of platelets.

10. General belief is that under-production is cause of thrombopenia.

11. At least four types of reactions on part of platelets occur after splenectomy.

12. This seems to indicate that the spleen probably has no specific action on platelets.

13. Some cases show rapid and persistent rise of platelets. This is interpreted to indicate a specific type of purpura curable by splenectomy(?).

14. The interaction of platelets, capillary dysfunction, blood plasma, bonemarrow, spleen, and reticulo-endothelial system is too intricate for analysis at present time.

15. The results of therapy indicate that thrombocytopenia purpuras are heterogeneous group.

16. Many undergo spontaneous remissions without recurrence.

17. The acute progressive type responds to transfusions if given frequently enough to control bleeding time.

18. Diet and removal of infections are forms of treatment emphasized.

19. The acute progressive types generally die if they do not respond to conservative measures and splenectomy gives little hope in these cases (80% mortality).

20. Splenectomy is indicated only in chronic cases without apparent etiological factor which have failed to respond to other forms of treatment.

21. Ligation of the splenic artery is a new procedure which may prove of value.

II. CASE REPORT

ESSENTIAL THROMBOCYTOPENIC PURPURA CONGENITAL ANOMALIES

Path. Koucky.

Case is white female, 12 years old, admitted to Minnesota General Hospital 1-6-33, expired 2-6-33 (31 days).

Blue Baby?

9-4-20 - Born, weighed 5 lb. 14 oz., instrumental delivery at 7th month of gestation after 4 hours of labor. Said to have been blue baby at birth. Physician who attended child said she had a congenital heart and gave a poor prognosis. (Some question as to reliability of information. Other physicians who attended child subsequently were unable to obtain history of cyanosis at time of birth.) Cyanosis disappeared at age of 2 months and from that time child appeared normal. Another states child was not blue after 4 to 5 hours after birth.

Note: Controversy of interest in interpretation. Cardiac lesion (congenital or rheumatic?)

Infections

3 wks. or 3 yrs. (?) - Histories differ as to age of illness. At this time had scarlet fever complicated by mastoiditis, otitis, pneumonia, meningitis and Bright's Disease. Hospitalized for three months.

Bleeding

Age 3 years - Occasional nosebleeds.

Age 7 years - Attack of measles. Never well up to this time. Pale, tired easily and was markedly underweight. Frequent colds, tonsilitis, 4 attacks of pneumonia, otitis media persisted since attack of scarlet fever. Following measles, began to bleed from nose and rectum. Hemorrhages recurred about 2 or 3 times a year.

Age 9 years - Whooping cough. Still bleeding. (O.P.D.)

Increased bleeding time, Congenital heart
4-20-29 - (O.P.D.) - Complaints: Heart trouble, poor hearing, under-development. Laboratory: Blood - Hb. 80%, rbc's 4,000,000, wbc's 10,400, Pmn's 62%, L 36%, E 2%. Coagulation time - 4 1/2 minutes. Bleeding time 11 minutes. X-ray: 6 Ft. plate of heart - Measurements - transverse thoracic 19.0 ml 6.5, mr. 2.8, total 9.2, long 9.8. Moderate enlargement, chiefly of right ventricle with distinct bulging of conus pulmonalis. Appearance suggests somewhat congenital type of cardiac enlargement. Suggest fluoroscopic examination for more definite diagnosis.

4-39-28 - (O.P.D.) - Fluoroscopic and film examination of heart with barium filled esophagus - Distinct broadening in superior mediasinum suggesting possibly enlarged thymus. No evidence of displacement of esophagus posteriorly indicating no enlargement of left auricle. Appearance, therefore, would suggest congenital heart with enlargement entirely on right side and no involvement of left heart. Opinion: Probable congenital heart. Impressions and recommendation: Perforated ear drums, defective hearing, congenital heart, rheumatic heart (?). Advise - rest and tonsil and adenoidectomy.

12-15-32 - Severe upper respiratory infection.

Bleeding Continues
1-3-33 - (Age 12) - Severe attack of bleeding from nose and rectum. Lost about one pint of blood.

Hospital
1-6-33 - Admitted. Resume of previous history: Sequence, dates and exact nature of child's illnesses very indefinite because of unreliable history obtained from mother on different occasions. Apparently child suffered numerous repeated infections. Said by some historians to have been a blue baby at birth, while others failed to give this history. Began to bleed either at age 3 or 7. Frank gross hemorrhages from nose and rectum present since age of 7 (5 yrs).

Family History:
Father said to be a hemophiliac. Father and mother living. Two sisters living and well, one died at age of 3 1/2 weeks of influenza. Mother had one miscarriage. No brothers in family.

Physical Examination: Length - 117 cm. Weight - 34 kilograms. Extremely pale and of poor nutrition. General bodily build considerably below normal. No enlarged lymph nodes. Lungs - appear normal. Heart - apex in 4th interspace, to and fro murmur heard during systole and diastole, rate 115. Abdomen - negative except for possible palpation of spleen, (one of 3 examiners thought that he felt spleen)

Laboratory: 5 urine examinations - numerous wbc's in uncatheterized specimen. Blood - Hb. 45%, rbc's 3,100,000, wbc's 5,600, L 28%, Pmn's 72%. Original bleeding time - 14 min., clotting - 3 min. 40 sec., clot non-retractile at end of 36 hours. From this time on, bleeding and clotting time determinations and platelet counts recorded after procedures such as transfusion and operation.

Family Study
Bleeding and clotting times on remainder of family as follows: Mother - bleeding time 30 sec. clotting time 6 min. 30 sec., platelet 236,600; one sister - bleeding 4 min., platelet 315,000, clotting 7 min.; second sister - bleeding 30 min., clotting 2 min., platelet 290,000. In these 3 relatives, clot non-retractile. Father still bled after 30 minutes, clotting 6 min., platelet 352,000, clot of retractile type (not hemophiliac). Progress: general, preoperative course; continued bleeding from nose and rectum. Eleven blood transfusions given, both direct and citrate method. Bleeding and clotting time and platelet count as follows:

Date	Bleeding time	Clotting time	Platelet	
1-11-33	22 min	6½ min	164,050	Clot
1-12-33	14 min	5 min	174,250	non-
1-13-33	13 min	5 min	191,250	retrac-
1-16-33	30 min	12 min	384,730	tile
1-18-33	6 min	-	236,050	"
1-24-33	5 min	4 min	-------	

Splenectomy

1-25-33 - Operation: Splenectomy done. Operation uncomplicated. Spleen removed, weight 143 grams. Gross appearance and microscopic section normal spleen. No eosinophilia in sinuses as reported typical by some for essential thronbocytopenic purpura. Following operation and extensive transfusions platelet count rose to 490,000.

Chest Complication

1-26-33 - T 104. Cough and slight pain in chest. X-ray shows dense, very irregular, mottled shadow extending out from mediastinum with very feathery appearance on both sides. Involves central two-thirds of lung fields. Appearance suggests some type of aspiration process, involving central portion of lung near larger bronchi. May represent hemorrhage into lung. Diagnosis: Probable aspiration; hemorrhage into lung parenchyma, bilateral.

1-28-33 - Fever continued. Findings in lungs as before. X-ray shows practically no change.

1-30-33 - X-ray shows process extended in right lung considerably. Down to diaphragm and well out to periphery. Process on left appears about same. Diagnosis - Uncertain.

Abscess

2-1-33 - Process about same as on previous examination. Some rarefaction in lower portion of both sides, suggesting some breaking down into abscess formation. During this interval, temperature remained approximately between 102 and 104. Repeated bleeding from nose and rectum occurred. Blood transfusions given.

Exitus

2-6-33 - Almost continuous bleeding from rectum. Temperature remains elevated. X-ray findings in chest approximately same. More difficulty in breathing. Pulse weaker. Child expired at 8:04 P.M.

Operation Wounds

AUTOPSY: - Body is well-developed, poorly nourished, white female, 12 years of age, measuring 122 cm. in length weighing approximately 30 lbs. No edema, cyanosis or jaundice. 14 cm. subcostal incision on left side fairly well healed. Numerous puncture wounds in groin and antecubital spaces with numerous ecchymoses in these areas. Petechial hemorrhages not observed. Transfusion scar in right antecubital space.

Normal

PERITONEAL CAVITY moist and glistening. No peritonitis. Normal APPENDIX.

PLEURAL CAVITIES smooth and glistening. No excess fluid. PERICARDIAL SAC no excess fluid. No adhesions.

Valvular deformity

HEART 160 grams. Left ventricle definitely hypertrophied. Vessels at base have normal relationship to each other and are normal in size. Interventricular septum closed. Foramen ovale closed. No defect of septa. Valves of right side of heart are soft and have normal size and shape. Mitral valve soft, and not thickened or deformed. Artic valve thickened. Two cusps fused to form a single cusp. Edge of these two fused valves, as well as other valves, very definitely thickened, rolled up and deformed. No vegetations made out (old or new). Entire valve somewhat fibrotic. ROOT OF AORTA good size. Coronaries no anomalies.

Pneumonia lobar

LEFT LUNG, 550 grams, RIGHT 650 grams. Extensive pneumonic process on both sides. Involves major portion of both upper lobes and posterior part of lower lobes. Anterior part and bases of lungs non-pneumonic. Pneumonic area uniform (of lobar type) gray and soft in appearance. On cross section, considerable pus exudes from alveoli and no granular plugs can be seen. Appearance suggests late gray hepatization of lobar pneumonia. Zone about 2 cm. surrounding this infiltration which is hemorrhagic and periphery fades away into normal lung parenchyma with a zone of petechial hemorrhages. No abscess or area of breaking down at any point.

SPLEEN - removed.

LIVER - 1025 grams, large, rounded edges. Substance very soft and yellowish. Periportal spaces appear normal.

GALL-BLADDER thin wall contains no stones. Ducts patent and well formed.

Bloody

GASTRO-INTESTINAL TRACT filled with blood. From esophagus through colon, mucosa is speckled with small areas of hemorrhage. These are up to 5 or 6 mm. in diameter and appear to be about evenly distributed throughout gastro-intestinal tract. Bowel itself only slightly thickened (with some edema).

PANCREAS soft and pink.

ADRENALS usual size, no adenomas, hemorrhage or degeneration.

RIGHT KIDNEY 125 grams, LEFT 140 grams. Capsules strip easily. Substance somewhat red. Surface smooth. Usual amount of pelvic fat present. Does not appear to cut with increased resistance.

Bladder not trabeculated or thickened. No cystitis.

Anomalies

GENITAL ORGANS: Uterus quite small for child of 12. Tubes and ligaments well-developed. No ovarian substance that can be recognized as such. On both sides, ovarian ligaments show abrupt terminations (no appreciable enlargement) and no evidence of ovary. Sections of this area taken for microscopic examination. On both sides in line with ovarian vessels, small yellowish granules noted, 2 on left side and 1 on right. Measure about 2 mm. in diameter, bright yellow and well localized. Taken for microscopic examination. (Absence of ovaries aroused interest in female hemophilia possibility?)

Arch of AORTA appears a little large. Immediately below origin of left subclavian artery, there is congenital valve made up of intima of the aorta. This valve is about 1 cm. in breadth and extends below intima for distance of about 2.5 cm. as a pocket. Blade of scissor can be slipped into pocket and valve cut open. This type of congenital valve of arch of aorta has been described by Maude Abbott. Remainder of aorta shows no change.

ENLARGED LYMPH NODES:

Large mass of mediastinal lymph nodes about hilus of lung and bifurcation of the trachea. Largest of these measures about 4 cm. in length and about 2.5 cm. in diameter. Lymph nodes extend up into base of neck as high as thyroid gland. In mesentery, there is a plaque of lymph nodes. Along base of mesentery, these lymph nodes are close together, largest measures about 1.5 cm. in diameter. At bowel margin of mesentery, there are numerous, small lymph nodes measuring 3 or 4 mm. in diameter. Appears to be definite hyperplasia of these nodes and they are considerably larger than ordinarily observed at this age.

ORGANS OF NECK: Thyroid and parathyroids removed. Thyroid small and shows no adenomas. Parathyroids normal size.

HEAD: Scalp shows no change. Very definite thickening of meninges present over entire brain which is most marked over cortex and at base over brain stem. Brain substance itself shows no hemorrhage either into arachnoid spaces, brain substance or ventricles.

MICROSCOPIC: Rapid sections done to confirm diagnosis.

Lung - typical lobar pneumonia in late gray hepatization stage.

Liver - no infiltration with small round cells. No leukemia.

Kidneys - some thickening and increase of cells in some of glomeruli.

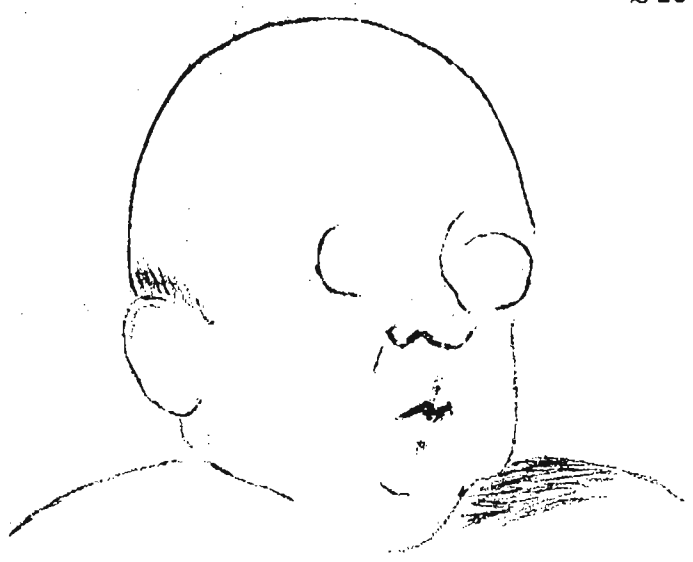
Lymph nodes - marked hyperplasia. No leukemia.

Spleen - described in pathological report.

Sections of area in broad ligament adjacent to ovarian ligament show no ovarian structure whatsoever. One section shows small, columnar cell lined tubules.

Sections of heart valves - show presence of blood vessels indicating probable congenital origin of defect.

Discussion (Bell's conference,) Case presented 2-7-33. Final diagnosis appeared to be probably thrombocytopenic purpura. Clinicians considerably against diagnosis in that there was no response to splenectomy? platelets



Birthday:

February, already noted for number of birthdays of famous men, now has another to add to its list -- Dr. William Austin O'Brien, age 40, Tuesday, February 28.

Silent Interlude (apologies to O'Neil and the Public Health Lectures): dangerous age, obesity, don't overeat, have a hobby, let down a little, more exercise, see a physician regularly, don't worry. More power to you: a gentleman and a scholar. Congratulations.

...ver showed typical findings of thrombo-...ytopenic purpura, and moreover that long ...nfection, noted in history and findings ...f mediastinal lymph nodes (over period ...f four years) and generalized lymphadeno-...athy found at autopsy, indicated purpura ...ay be secondary to chronic infection.

...r. Bell's opinion of heart - congenital ...eart defect. Dr. Clawson was of same ...pinion. Considered possibility that ...efect might be due to secondary infection ...nd microscopic examination necessary to ...ule this out. Made and ruled out.

...ignificance of absence of ovarian tissue ...ot discussed.

...IAGNOSES:

1. Essential thrombocytopenic purpura(?)
2. Secondary symptomatic purpura(?).
3. Chronic lymphoid hyperplasia.
4. Bilateral lobar pneumonia.
5. Splenectomy.
6. Spontaneous hemorrhages of bowel.
7. Cloudy swelling and fatty change of liver.
8. Congenital defect of aortic valve(?).
9. Congenital anomalous valve of arch of aorta.
10. Thickening of meninges.
11. Mild chronic glomerulonephritis.
12. Hypoplasia of internal genital organs.
13. Ovarian tissue absence.
14. Supernumerary adrenal cortex adenomas.

CULTURES:

Smears of lung - gram + diplococcoid resembling pneumococcus.
Those in smears had fuzzy outline and appeared degenerative. Cultures of various pneumonic lobes sterile.
Dr. Reimann's impression: 14 hour autopsy. Subsequent autolytic processes have destroyed vitality of pneumococcus.

Cultures from left lobe - show 3 or 4 staphylococci.

III. ANNOUNCEMENTS

1. MEETING

Date: February 23, 1933

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

Time: 12:15 to 1:20

Program: Pulmonary Embolism

Present: 94

Discussion: C. J. Watson
Gilbert Cottam
D. H. Bessessen
Richard M. Johnson

C. J. W.: I do not have a great deal to add on the subject, but I think from an experimental standpoint the relationship of platelets to formation of thrombi has been well demonstrated. Work of Evans has been mentioned in which it is shown platelet increase after operations reaches height at tenth day. It seems probable that the same is true in post-traumatic group, i.e., following any severe injury. It is probably a defense mechanism. It seems logical to attempt artificial reduction of platelets in certain cases. Try anti-platelet serum? used in animals. Take platelets from one animal, inject into another. Second animal's antibodies when injected into first animal cause marked diminution of platelets. In some it produced purpura hemorrhagica, an undesirable condition to bring about. It may be possible to follow platelets daily and when they reach certain height to give substance which would bring them down.

G. C.: Shape of clots interested me great deal. The fact that they were found in the case demonstrated today gives me the impression that in the initial phase of embolus formation it is quite likely that we can assume that the clot travels up from where it starts in an uncurled shape. At least it would seem a reasonable way to explain it. Symptoms come on rather slowly. Cases that come on rapidly and do not last long are different. After onset of symptoms there is a period of distress symptoms, but patient remains alive for variable length of time and then something happens.

The point that has been brought up about the blood platelets seems to offer a good deal of encouragement. I read Wilensky's study about a year ago. It corresponds closely with Evans. The fact that elevated platelet count occurs after ten to fourteen days time when so many pulmonary embolism cases occur is quite suggestive.

If we could be sure that there was only one embolus we could get something done. The history in so many cases shows evidence of showers. Pulmonary embolism is not so often due to single embolus but in many cases there is tendency to reformation of emboli. This was disappointing in two cases in which good results were obtained immediately after operation.

D. H. B.: From the standpoint of surgical treatment emboli are of two varieties, one which arises from clinical thrombosis and the other from latent thrombi. Clinically one is palpable. Such thrombi give rise to rather small emboli, and patient suffering from that particular condition may survive under conservative medical care. The latent thrombus is not palpated and gives rise to large plug which is more promptly fatal. In the later type of case surgical treatment may be successful. They had three examples of this variety in a clinic in Stockholm. Trendelenburg operation (successful in 1 case) has been modified by Meyers. With Meyer's modification there were 7 successful removals. Crafoord making special study of problem had three successful removals.

From the clinical standpoint it is rather important to recognize these distinctions if one is to attempt surgical removal of emboli. The usual procedure is to watch patients who give evidence of latent thrombus. Place emphasis on three symptoms: Gastric distress, slight elevation of temperature, and rise of pulse above normal for that temperature. When these three symptoms are present suspect latent thrombus. Watch case carefully. Have instruments ready. Often man who intends to perform job is on hand day and night.

When attack comes, watch patient until positive he is dying before you attempt to do anything. At that time there is no sensation so far as patient is concerned. Claim first attack is followed by recession of symptoms, then comes fatal attack which usually lasts about ten to fifteen minutes. When second attack takes place, patient is obviously dying, then perform operation. Of course, operation is done by man skilled in such procedures. Done rapidly, allowing about 8 minutes. No anesthesia.

Open between second and third intercostal space, removing portion of the second and third ribs, making T-shaped incision just to the left of sternum. Artery can be readily recognized because it is edematous, purplish, hard, and non-pulsating. By means of a tube artery is brought to the

surface. Special forceps removes clots. By previous observation of the case they are quite sure they are dealing with large clot. They plunge the forceps into the right and left arteries. Effort made to reestablish circulation by relieving pressure on tube. Blood loss not a great deal. After forceps are out with the help of special clamp suture is made. After the clots are removed, heart quickly goes into action. Effort made to use anesthesia then because sensation returns very quickly.

R. J.: I wish to emphasize what Dr. O'Brien said. Failure most often due to inert peroxide. By using modification this is avoided.

NEXT WEEK: Alfred Washington Adson, distinguished neuro-surgeon, Mayo Clinic.

Gertrude Gunn,
Record Librarian.