Pathology is the study of disease producing constellations and their effect on living organisms. It has reared itself since the time of Virchow to the status of a science, if any field in biology may be truly called a science, and as such has and can divorce itself from its previous servile position as the hand maid of medicine; yet, for us its greatest raison d'être is the part it plays in elucidating the processes of disease in man. It is well to remember from the very beginning however that the purpose of any science is to reconstruct physical experience into a system of law and order, to bring natural phenomena closer to our comprehension.

The domain of science is one of "causal explanations." Purpose, as such, lies outside of this realm; teleology must find its proper scope elsewhere. The moon was not hung aloft in the heavens to keep our gas bills down, neither does blood clot to prevent a man from bleeding to death. The formation of the clot may be the saving factor, but its formation is a result of a definite series of genetically related processes or steps, the absence of any one of which precludes the possibility of success, the presence of them all is tantamount to its completion. So again, bacteria, per se, are not the cause of disease, but rather are they but a single link in a long concatenation of causally connected events which include such other links as hereditary background, environment, age, sex, mental attitude, previous state of health and the variable factors such as type, morphology, mass, and virulence of the bacteria themselves.

What is disease? It may be considered as the reflection of a pathological process or lesion upon the organism as a whole. What is a pathological lesion? It may be defined as a morphological expression of disproportion of values between stimuli and living cells. All living processes may be considered as a resultant of the interplay between various stimuli and the response of living tissue to these stimuli. If the stimulation is of short duration and of mild intensity and the activated tissue returns quickly to a state of equilibrium, then the process may be considered as physiological.
If on the other hand the stimuli are of great intensity and prolonged in time, then the result may usually be considered as pathological. To state this in another way - irritants are environmental factors which are responsible for the emancipation of organismic potentialities. The degree of disporoportion between the stimulating effect of an irritant and the response on the part of the organism determines physiology or pathology. A cloth dipped in water heated to 55°C and applied to a part causes a physiological increase in activity of a part with a pleasing effect and a rapid return to its previous state when the mild irritant is removed. Increase the temperature of the water to 100°C and it stimulates just a bit too much, and on removal there is no rapid return to the status quo ante because actual damage has been done to the tissue and this "burn" is pathological.

As beginning pathologists let us take a part of our early guidance from that great pathologist, Virchow, who said many years ago:

(1) All knowledge of disease must be based upon objective, anatomical experience.

(2) Conclusions as to the nature of disease must be based on this experience and be made strictly according to natural laws of cause and effect.

There may be many exceptions to these rules at the present time but they still may serve as a sure foundation for accurate, restrained, scientific thinking in pathology. At times, per chance we shall leave our special field and indulge in theorizing and interpretation and where facts fail us take the perfectly legitimate heuristic, somewhat circuitous route to truth, but when so doing we knowingly leave the sphere of pure science and enter the domain of philosophy and metaphysics.

With these few introductory remarks let us begin our work with a consideration of some of the changes that take place in tissues.
Morphological Fluidity
The basic factor in growth; characteristic of higher forms; antedates birth, postdates death.

Differentiation - a function of environment
1. Mitotic - at rest
2. Amitotic - inactive cells

Growth Requirements
1. Transudation - increased nutritive supply
2. Assimilation - ability of the tissue to use it; depends on the permeability of the cell
3. Procreation - formation of new protoplasm

Protomers
Smallest living units which have all of the characteristics of living protoplasm. These increase in geometrical progression from generation, the nuclear plasma material, however, remaining in constant proportion.

Cloudy Swelling
When on the positive side it is the first step in the process of greater assimilation and increase in protoplasmic content.

Hypertrophy
Increase in protoplasmic content and structures already present

Hyperplasia
Numerical increase in cell elements and protoplasmic content. Both content and function are constant in type

Regeneration
An inherent characteristic of living matter. Young cells form an ANLAGEN whose direction of differentiation is then a function of environment. There is always a tendency to overproduce.
Connective Tissue - from fibroblasts
Cartilage - from perichondroblasts or fibroblasts
Bone - from periosteum, endosteum or chondroblasts (?)
Vessels - endothelial buds from preexisting vessels
Blood - reappearance of myeloid foci of embryonic type in bone marrow, liver and spleen
Muscles - hypertrophy rather than hyperplasia the rule
Neuroglia - from new forms astrocytes
Nerve - by extension from the proximal part of the fiber only
Ganglion Cell - no true regeneration when totally destroyed
Epithelial Cells
Liver - Parenchymal - no true regeneration if integrity of the architectural plan has been disturbed

Abnormal Regeneration
Abortive or pathological, the result of destruction of normal skeletal structure by trauma or disease

Scar Tissue - substitution of lower tissue in injury
Regression Movements

I. Atrophy - quantitative regressive movement in tissue
  1. Reduced in size
  2. Patchy reduction in protoplasm
  3. Apparent excess of nuclear structures
  4. Pigment collection
  5. Reduced oxidation
  6. Reduced function
  7. Hydopsical dissolution

Causes
  1. Interruption of nerve cell control
  2. Insufficiency of self regulation
  3. Nutritive interference

II. Cloudy Swelling
  Granular degeneration of cell protoplasm in form of precipitated suspensoids. First stage of degeneration when on the negative side. When severe the nuclei may undergo 1. "lyknosis", 2. "Karyorrhaxis" and 3. Chromatolysis

III. Fatty Changes
  1. Infiltration - extracellular collection of large fat cells as the result of nutritive disturbances in circulatory stasis
  2. Phanerosis - intracellular disintegration of cellular protoplasm as the result of toxic activity
  3. Lypae mia - excess fat in the blood stream, seen in pregnancy, starvation, acido sis, anaesthesia and alcoholism
  4. Adipocere - waxy transformation of dead bodies in which splitting and degenerating fat derivative replaces the muscles

IV. Hyaline Transformation
  Waxy, smooth, glistening, faintly blueish pink staining material seen most frequently in the intimal lining of the blood vessels, and in the muscles in typhoid fever, trichinosis, icterous neonatorum, snake bite, etc.

V. Amyloid Substitution
  Bacon-like hyaloid protein degeneration product seen in chronic wasting and purulent processes like Tbc, syphilis, osteomyelitis, etc. giving staining reactions similar to starch but which is thought to be a mixture of protein substance and chondroitin sulphuric acid.

VI. Mucoid Substitution
  Drowning and disintegration of epithelial mucoid cells in their own secretions; coagulates in strings and stains basically

VII. Colloid Degeneration
  Like the others a purely descriptive term referring to substances which look like that substance seen in the thyroid gland. A desquamation of secretory cells due to retention of jelly-like product which coagulates in discs and stains pink with acid dyes

VIII. Carbohydrate Changes
  Glycogen content of organs is always in inverse proportion to fat.
  1. Diabetes Mellitus - upset in COH metabolism
  2. Von Gierke's Disease - excessive storage of glycogen

IX. Protein Changes
  Uric acid the result of breakdown of nucleoproteins
  1. Excessive uric acid, 2; Monosodium urate (tophi) in the cartilages 3. Arthritis
Calcium

Normal - 10 mprms. % in blood, maintained by the activity of the parathyroid glands

Two types
1. Indefinable - firmly bound in such tissues as the bones
2. Diffusible
   a. Unionized - playing very little part in the active metabolism of the body
   b. Ionized - the amount in ionic form depends on the carbonic acid tension; when it is reduced the equation goes from left to right and the insoluble tricalcium phosphate is re-precipitated.

$$\text{Ca}_3\text{(PO}_4\text{)}_2 + 3\text{H}_2\text{CO}_3 \rightarrow 2\text{CaHPO}_4 + \text{Ca(H}_2\text{O}_4\text{)}_2$$

Function
1. Blood Clotting
   - Fibrinogen - Gébelin - Sa -- Thrombin
   - Thrombin - Fibrinogen -- Fibrin
2. Increases contraction of heart muscle
3. Direct relationship to nervous irritability
4. Formation of bones
5. Balance in hydrogen ion maintenance

Causes of Increase in Calcium
1. Hysterectomy - withdrawal of Ca. from bones as seen in osteomalacia. Calcification follows in the acid juices of such tissues as the stomach and kidney in the presence of alkaline tissue juices
2. Parathyroid underactivity - in case of tumor displacement of a great deal of the tissue
3. Paget's Disease of Bones - classification rather obscure at the moment but there is increase in Ca.

Decrease in Calcium
1. Parathyroid over activity
2. Alkalaeemia
   a. Gastrointestinal - loss of HCl by vomiting
   b. Hyperpneoa - blowing of of CO$_2$
   c. Alkalie ingestion - excess NaOH
3. Rickets - in complete absorption from G. I. tract
4. Nephritis - incomplete riddance?

Calcification
1. Always in degenerated, necrotic, hyaline tissue such as arterial walls in hypertension, atherosclerotic plaques, avascular tumors, scar tissue, abscesses, Tbc. nodes, & exudates, cysts, incrusted parasites etc.
2. Why Calcification?
   a. Physical deposition theory
   b. Fatty acids form insoluble soaps
   c. Super saturation maintained by high CO tension
4. Necrosis and hyaline metamorphosis

Why in bone at all?
Growing bone contains an enzyme capable of splitting hexose phosphate into hexose & inorganic phosphate.

Concretions
A. Nephrolithiasis
B. Cholelithiasis
C. Pancreatic lithiasis
vascular tumors, scar tissue, abscesses, 
the nodes & muscles, cysts, parametria (trichinella)

Why calcification:

1. Physical deposition
2. Fatly acids to form rosettes
3. Super saturation maintains high Ca²⁺ tension
4. Neural & hyaline metamorphosis

Why calcification is done at all
Growing bone contains an enzyme capable of splitting pyrophosphate into phosphate & an organic phosphate ffft. Ca₃(PO₄)₂ 85% bone.

Conclusions:

(1) Kidney stones - nephrolithiasis

Koryn, J. A. M. A. 104: 715, 1933
Lindenfield, J. Med. 31: 541-54
Experimental production (see cause)

11. Oxalate
12. Excess Ca or ox acid
13. Parathyroid or renal intertis
14. Urine and crystals in animals & in E.coli feces
15. Vitamin A deficiency
16. Infected & severe bleeding, striking, slaph K.B.Peter
17. Incrustation in absence of infection
(2) Gall Bladder

(1) Cholesterol - stone
(2) Pigment - stone
(3) Infection -
(4) Miscellaneous

Theories

Wennerberg, Arch. Path., 17-1, 34

(1) A.W. 1924 - high blood cholesterol, + stones
(2) Concluded 1933 - Wennerberg - blood cholesterol stones
(3) Naunyn - 1896 - decomposition of pigments of GB
(4) Cohan & Graham 1939 - support Naunyn. Account for crystals in extraneous gallstones

Skeels: The increasing improvement of the bile and cholesterol content rendered smaller quantities of cholesterol directly and its not owing to the presence of fat it is guttulat separation which occurs, and since an entirely foreign substances are lacking, there is nothing to prevent aggregation of the droplets. (A. Skeels Colloid Chemistry 7/1/1928-2, 503)
The consultation of official sources, etc., by the government, resulted in the gradual deregulation of the financial sector, which led to a significant increase in the volume of stock exchanges and other financial institutions.

Section 12 of the Financial Services Act, as amended in 2012, governs this area, concerning the official market.

The amount from outside sources of the government, as mentioned in subsection 12.3 of the Financial Services Act, is not specified in the current document.

Moreover, the consultation of official sources, as mentioned in subsection 12.3 of the Financial Services Act, is not specified in the current document.

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