tein. Inasmuch as this protein and these hemocyanins are of huge molecular size it may be that the formation of slowly settling aggregates is a peculiarity of macromolecular systems. However, the sera I have used were unusually powerful (846_3 contained over 14 mg of antibody-protein per ml) and other sizes of antigenic molecules must be investigated under comparable conditions before such an assumption would be justified.

Summary. An unusual zone of greatly delayed sedimentation was observed in titrations of the hemocyanins of *Limulus polyphemus* and *Fulgur carica* with their precipitins. The extent of the zone was influenced by both the relative and the absolute concentration of the two specific reactants.

10063

Spontaneous Agranulocytosis in the Cat.*

JOHN S. LAWRENCE AND JEROME T. SYVERTON. (Introduced by W. S. McCann.)

From the Departments of Medicine and Bacteriology, University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

During the course of making some routine blood counts on cats one animal was found with only 350 white blood cells per mm^3 and no neutrophils in the peripheral blood. A portion of the liver of this animal was ground up with Alundum in Locke's solution. After settling, the supernatant fluid was used for injection into 5 additional cats. This resulted in the development of the same blood picture in 2 of these 5 cats. Following this a similar preparation was made from the liver of Cat 36 and 6 additional cats injected with this material, part of them receiving the material intraperitoneally and a part subcutaneously. This process was continued as shown in Chart 1 until 13 transmissions were accomplished.

Following injection a typical animal has a period of about 5 days when it appears normal. Then, it is frequently noted that food is left in the cage and the temperature is usually found to be elevated (39° to 41°C by rectum). The animal becomes slightly listless and, after a day or two (*i. e.*, the 6th to the 8th day) may not care to stand on its feet. There is no nasal or eye discharge except in a rare

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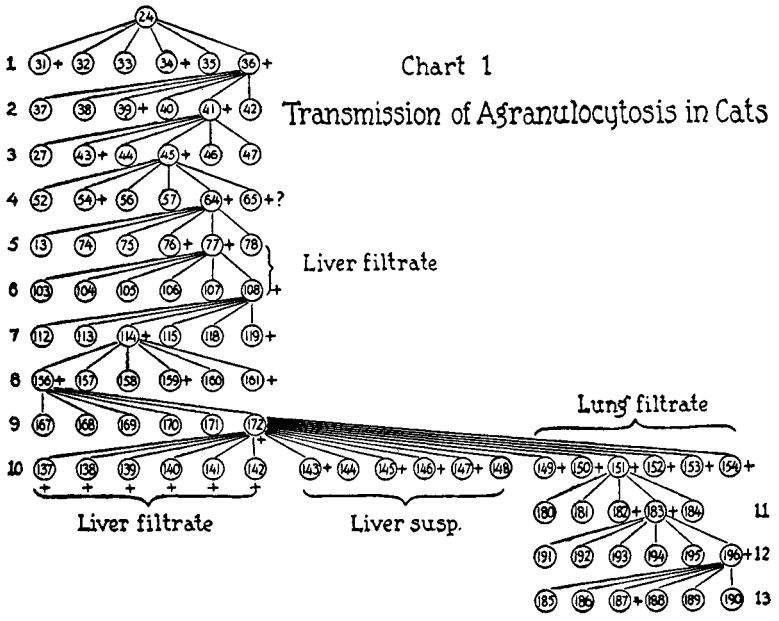
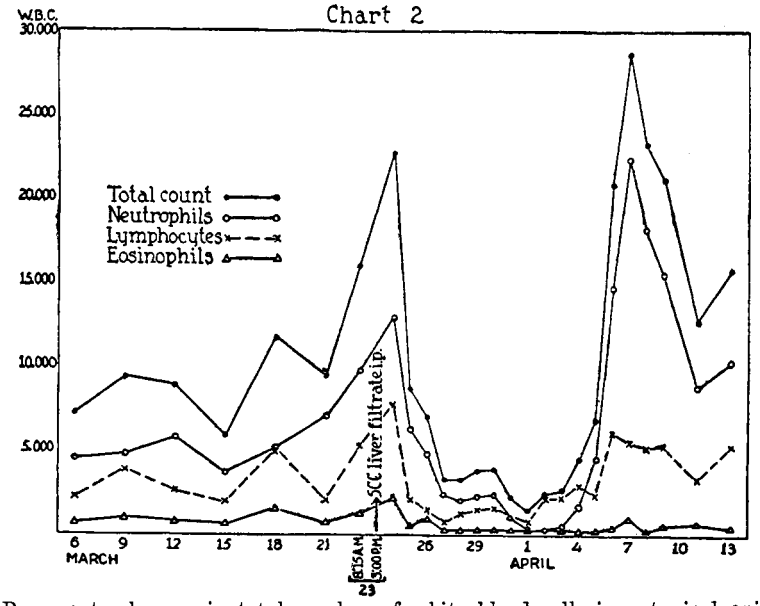


Numbers on sides of chart designate successive transfers of the disease. The + marks indicate those animals that developed typical signs of the disease.



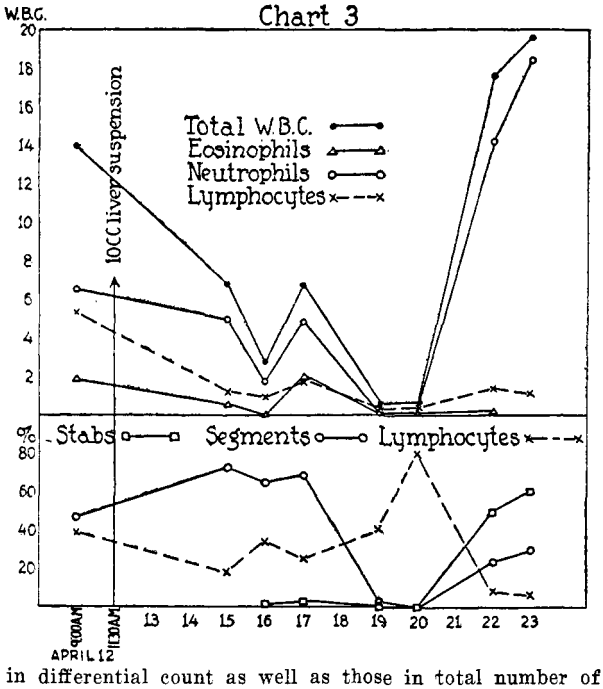
Represents changes in total number of white blood cells in a typical animal following injection of material containing the active agent.

animal. Diarrhea may occur but is, by no means, constant. Coinciding with the pyrexia, anorexia and listlessness there is marked

neutropenia and frequently the total white blood cell count goes to a very low level.

Chart 2 represents typical findings as regards the white blood cells in one of the animals that recovered. However, the response is not identical in all animals. In some instances, there is a steady decline until the low point is reached on the 6th to 8th day. In others, there is no change in the level of the white blood cell count until the 6th to 8th day when there is an abrupt fall. In these latter animals, there may be a very high percentage of neutrophils on the day preceding the development of the leucopenia.

The striking thing about the differential formula is that very large numbers of "stab" cells may appear just prior to the leucopenia or, if recovery occurs, at the time when the white blood cell count is increasing. This is well illustrated by Chart 3. The red



Changes in differential count as well as those in total number of the white blood cells are shown. Numbers on upper left side refer to white blood cells in thousands per mm³.

blood cell count shows no constant variations. The platelets remain normal or increased. After one or 2 days, at the height of the disease, the animal either dies or begins to eat and has a gradual or sudden increase in white blood cells.

The number of animals that would recover is not known as animals were sacrificed frequently at the height of the disease in order to get material for study or for transfer purposes. However, 7 animals did recover. In these animals, neutrophil counts below 2000 per mm^3 were maintained from 2 to 5 days, the majority having marked neutropenia for 4 to 5 days.

Thus far, only a few experiments have been carried out that bear on the infectious nature of the disease.

Bacteriological studies were essentially negative. The blood and liver, which provided source material for the inoculation of a wide variety of special media that were incubated under aerobic, anaerobic, and microaerophilic conditions, proved to be bacteria-free in 3 cats and yielded a few extraneous contaminants in 2 additional cats.

Further experiments, which were designed to bear on the filterability, or possible virus nature, of the causative agent, yielded evidence which suggests that a transmissible filterable agent is responsible for the disease. Three groups of cats, Groups A, B, and C, with 6 animals in each, were maintained as entirely separate units under rigid isolation for 18 days. Rectal temperatures were obtained at one to 2-day intervals during this time. Also, white blood cell and differential counts were made at one to 3-day intervals. Following the period of isolation, all of the cats were inoculated with material derived from a single moribund animal, Cat 172, which represented the tenth consecutive passage in the transmission series. The inoculum that was used for 2 groups of the cats, Group A and Group B, consisted in the supernate, unfiltered and as a bacteria-free Berkefeld V filtrate, respectively, of a centrifuged 10% liver tissue suspension that had been prepared by trituration of the liver with Alundum, using Locke's solution as the diluent. The third group of animals, Group C, received a Berkefeld V filtrate derived from the tissues and secretions of the upper respiratory tract. This was prepared as follows: The secretions and mucosa of the upper respiratory tract, including the turbinates and bronchi, were subjected to shaking with glass beads for one hour. The fluid portion then was pipetted off, mixed in equal parts with a 10% suspension of lung tissue, and the resultant mixture centrifuged for one hour at 2500 r.p.m. The supernate, following centrifugation, was filtered through a Berkefeld V filter and the resultant filtrate, which was proven to be free of bacteria, was used as the inoculum for the animals in Group C.

Daily temperature and white blood cell determinations were made

following injection. Sixteen of the 18 animals developed typical findings of the disease.

No detailed observations on the pathology of these animals have been made but studies are going on in this connection at present.

Arrangements are being made for the study of other virus diseases in the cat in order to determine whether the agent responsible for this blood picture is a hitherto unknown one or is one that has been known to produce disease in the cat but the effect of which on the blood was unknown.

In conclusion, evidence has been presented which seems to justify the statement that there is a transmissible disease in the cat characterized by neutropenia and leucopenia. The causative agent would seem to be a filterable agent or a virus.

10064 P

Relation of Chemically Induced Activity in Nerve to Changes in Demarcation Potential.*

T. SJÖSTRAND,† F. BRINK AND D. W. BRONK.

From the Eldridge Reeves Johnson Foundation and the Institute of Neurology, University of Pennsylvania, Philadelphia.

Repetitive activity often develops in mammalian nerves as a result of a localized injury (Adrian).[1] The phenomenon has been explained by assuming that circulating currents set up between the depolarized region of injury and the normal nerve result in periodic stimulation, at a frequency which depends on the rate of recovery of the normal nerve surface and the strength of the circulating currents. Recently, Fessard[2] has shown that repetitive activity can result when crystals of certain salts are applied to a nerve trunk, and that the region thus treated may be either positive or negative to the untreated parts. In recent work we have made an extended investigation of chemical activation of nerve, using isotonic solutions containing various effective salts applied to single active fibers dissected from the sciatic nerve of the frog. In these experiments

* Supported by a grant from the Supreme Council, Scottish Rite Masons.

† Fellow of the Rockefeller Foundation.

1 Adrian, E. D., *Proc. Roy. Soc. B*, 1930, **106**, 596.

2 Fessard, A., *L'Activité Rythmique des Nerfs Isolés*, Hermann and Co., Paris, 1936.