damage, and increased metabolic requirements in inadequately prepared and fortified (glycogen, vitamin B_1) tissues, there arises during fever an increased need for granulocytic and clasmatocytic elements in the areas of resultant tissue injury and damage. To this demand the bone marrow promptly attempts response, and to the degree that the supply of available additional cells remains in excess of the increased emigration to the tissues, a peripheral leucocytosis of varying degree occurs without a striking individual nuclear "left shift". If, however, the delivery of new cells is unable to keep pace with the emigration rate to the damaged tissues, a leucopenia with increasingly marked "left shift" develops, and persists until production once again exceeds tissue demands. The much more sensitive lymphocytes are fragmented and destroyed, and their regeneration inhibited at the same fever temperatures.

Conclusion. Artificially induced fever within therapeutic limits destroys lymphocytes and inhibits lymphopoiesis in the normal experimental animal, while at the same time resulting in an increase and extension of marrow myelopoiesis, tissue clasmatocytosis and peripheral granulocytic leucocytosis. The character and nature of this profound effect of fever upon the cellular equilibria may indicate an accessory rôle in the strengthening or weakening of the body defenses—depending upon the particular circumstance—and should be considered whenever artificial hyperpyrexia is contemplated as a means of treating human disease.

10906 P

Bundle-Branch Block and the Monophasic Electrocardiogram.

LINN J. BOYD AND DAVID SCHERF. (Introduced by I. S. Kleiner.)

From the Department of Pharmacology, The New York Medical College, Flower and Fifth Avenue Hospitals.

The accompanying investigations deal with the study of the alterations which are observed in the electrocardiogram when a bundle-branch block is added to a high take-off of the S-T segment and T-wave. Clinical observations have shown that in a recent coronary thrombosis with a high take-off, widening of the initial deflection occurs very rarely; this finding is not adequately explained by the difference in the blood supply of the specific tissues alone.

The combination of bundle-branch block and coronary thrombosis

represents an unusual clinical observation.[1] Averbuck and Rachmilevitz[2] have produced a bundle-branch block experimentally after ligation of the branches of the Ramus circumflexus sin. In these experiments the typical electrocardiogram of bundle-branch block did not appear.

A high take-off can be observed not only after ligation of the coronary arteries but also as the result of the influence of certain poisons (potassium chloride, pitressin, digitoxin). We selected *Viscum album* which can produce electrocardiographic alterations in cats and rabbits "suggestive of infarction"[3] when an anal-esophageal lead is employed.

The present experiments were performed on 14 cats and 16 dogs. The animals were anesthetized with nembutal and in a few cases with morphine-nembutal. The electrocardiograms were recorded with the 3 customary leads from the extremities. In the dog experiments after the appearance of the high take-off in the electrocardiogram the right bundle-branch was cut with a slender knife after the thorax and pericardium had been opened. The success of the operation was confirmed at the end of an experiment by autopsy; division of the bundle-branch actually was accomplished in 12 of 16 dog experiments. European *Viscum album* was employed; a 30-50% water extract was prepared by macerating the triturated dried leaves in cold water for 20 hours. One to 2 cc of the extract was injected into the jugular vein every 3-5 minutes. The amount necessary varied according to the size of the animal and the strength of the extract. Naturally these were not uniform.

A high take-off appeared with great regularity. It was very distinct in Leads II and III. Usually it was entirely absent or very indistinct in Lead I. Occasionally in Leads II and III a typical monophasic electrocardiogram appeared. There was no Q-wave and likewise no widening of the initial deflection appeared. The R-wave was lower. Usually sinus rhythm persisted without disturbance but at times an atrioventricular rhythm occurred transiently. Near the end of an experiment disturbances of contraction became distinctly demonstrable, but at autopsy no alterations of tonus of the musculature could be demonstrated. Neither the electrocardiogram nor the disturbance of contractility could be influenced by intravenous injection of aminophyllin or by 50% glucose or by methylene blue. In 4 experiments paroxysmal ventricular tachycardia appeared after aminophyllin.

---

[1] White, P. D., *Am. Heart J.*, 1934, **10**, 260.

[2] Averbuck, S. H., and Rachmilevitz, M., *Z. ges. exp. Med.*, 1931, **75**, 562.

[3] Henze, C., and Ludwig, W., *Arch. f. exp. Path. u. Pharm.*, 1937, **187**, 694.

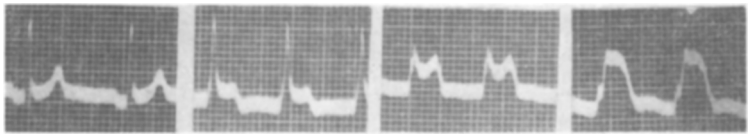

FIG. 1 (Lead II).

Fig. 1 shows the gradual development of a high take-off with transition to a monophasic electrocardiogram. Usually a sinus rhythm was present although at times it was not readily recognizable owing to the remarkably low P-waves; atrioventricular rhythm also appeared transiently. Stimulation of the vagus always produced a distinct depression.

If the right bundle-branch was severed after the appearance of the high take-off, no additional alterations appeared in the initial or terminal deflection or very minor changes became demonstrable as would naturally be anticipated from the progressive effect of *Viscum album*. There was no widening of the initial deflection and the terminal deflection did not become oppositely directed.

In Fig. 2 the first series shows the beginning of the appearance of a high take-off in Leads II and III. In the second series the terminal deflection joins the initial deflection to form a monophasic electrocardiogram. The initial deflection in Lead I has remained small and is directed downward. After the right bundle-branch was severed

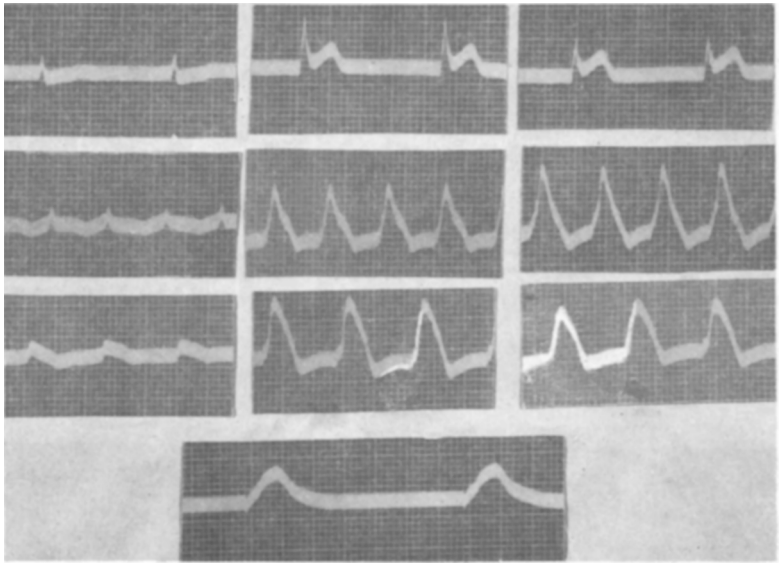

FIG. 2.

(third series) the characteristic changes of a bundle-branch block fail to appear. The lowest tracing shows a progressive widening of the ventricular complex with slowing of the spread of excitation (slow ascent of the R-wave and increasing bradycardia) in the final stage of the intoxication.

If the right bundle-branch was severed at a time when the high take-off was still not distinctly developed, a widening of the initial deflection appeared. With progressive action of *Viscum album* this widening became indistinct.

Fig. 3 shows a right bundle branch block. Examination after the conclusion of the experiment showed that the right bundle branch had been completely severed by 2 parallel cuts. After the bundle had been cut, the intoxication with *Viscum album* was induced. A total of 8 cc of the solution was injected intravenously within a period of 8 minutes. Fig. 3 shows the progressive action of the drug. The S-T segment is displaced increasingly upward and larger sections of

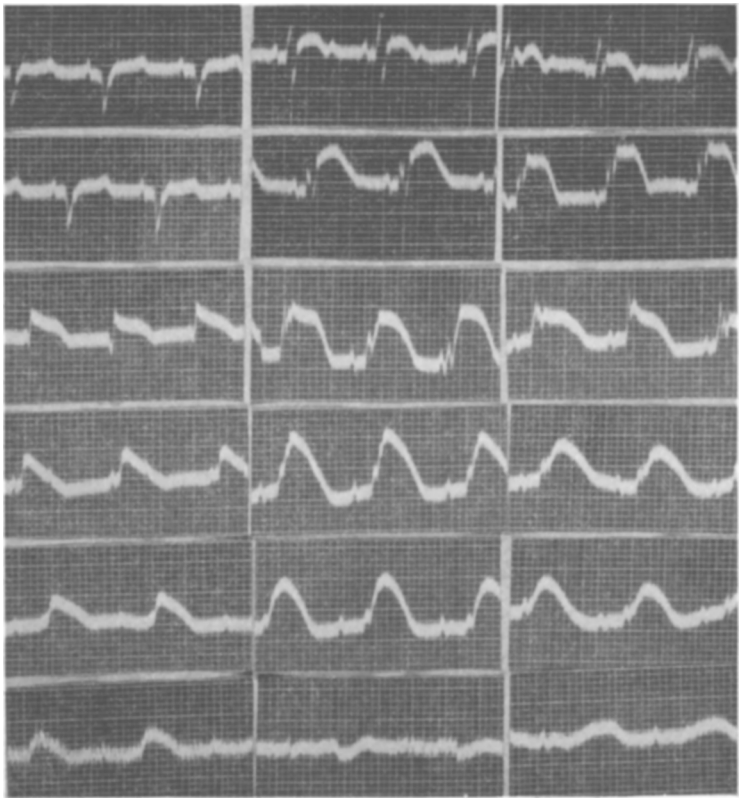

FIG. 3.

the initial complex become included in the S-T segment. In the second series the deep S-waves, produced by the block of the right bundle, are still visible although they are upwardly displaced in the direction of the S-T segment; in the third series they are no longer visible and a monophasic electrocardiogram appears. In the fifth and sixth series conduction from the auricle to the ventricle becomes longer and the slower ascent of the initial deflection which becomes increasingly obvious indicate a slower activation on the ventricle. The initial and terminal deflections can no longer be separated from each other.

Stimulation of the right or left accelerans produces an acceleration of rate but the changes in the terminal deflection, typical of sympathetic stimulation, do not occur.

The high take-off after the administration of *Viscum album* is the result of a profound damage of the muscle tissue itself. No proof was obtained which suggested that a disturbance of blood supply to the heart muscle was involved. We must assume that the activation of the heart is already altered so profoundly by *Viscum album* that the appearance of a bundle-branch block is unable to produce any further changes. Through the appearance of a high take-off and through the incorporation of the terminal deflection into the initial complex, it becomes impossible to demonstrate other alterations of the initial and terminal deflections.

Summary. In cats and dogs *Viscum album* produces a characteristic high take-off. If this is distinctly developed, one can no longer recognize a disturbance of intraventricular conduction (bundle-branch block) and stimulation of the accelerans does not alter the shape of the terminal deflection.

10907

Interdependence of Vitamin B_1 and Manganese. II. Manganese, Copper, Iron Metabolism in B_1 Deficient Rats.

MARTA SANDBERG, DAVID PERLA AND OLIVE M. HOLLY.

From the Laboratory Division, Montefiore Hospital, New York City.

Perla, and Perla and Sandberg[1, 2] in their work on the reproductive behavior of rats have demonstrated a metabolic interdependence of manganese and vitamin B_1. The present study was planned to pro-

1 Perla, D., *Science*, 1939, **89**, 132.

2 Perla, D., and Sandberg, M., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 522.