

are rare, but the preparations of digitalin will almost invariably cause some slight pain and slight local induration for a day or two.

The active principles of this drug are absorbed from both the stomach and the intestine, the rate of absorption depending, of course, on the preparation used, its concentration, solubility, and the condition of the stomach. Digitalis is ordinarily absorbed slowly unless there is some local irritating influence to make the absorption more rapid, hence the systemic effects of digitalis do not appear ordinarily for from six to twelve hours after the ingestion of the first dose.

*Systemic Action.*—The primary and chief constitutional effect of digitalis is on the *circulatory system*. The blood is not altered by digitalis except that it may become of lower specific gravity by a better circulation taking up more lymph. In non-poisonous doses the heart is slowed, its contraction is more energetic, and the blood-pressure is raised. The diastole is prolonged principally by the action of this drug on the pneumogastric center in the medulla, the stimulation of which tends to slow the heart. The contraction of the heart is more energetic on account of the irritation which this drug causes to the cardiac muscle, and this irritation and the resulting increased contraction is greatest on the part of the heart when there is the most muscular tissue, hence the effect is more pronounced on the ventricles than on the auricles, and more on the left ventricle than on the right. Under the action of digitalis the cardiac muscle improves in tone and hypertrophies because of the prolonged diastole giving much needed rest and hence causing muscle-recuperation, and the stimulation which the cardiac muscle receives acting like any other regulated gymnastic exercise to muscle tissue.

Three stages of the action of digitalis on the heart are recognized, the first stage being the one just stated, which is the desired therapeutic action. During this stage we believe that the cavities of the heart which physiologically do not completely empty themselves are absolutely emptied by the sturdy contraction. The papillary muscles tend to contract more completely as well as the other parts of the muscle walls of the ventricles and thus tend to diminish a valvular insufficiency. The prolonged diastole from the stimulation of the pneumogastric nerve tends to a more complete dilatation and therefore the blood more completely fills the cavities of the heart. This dilatation seems to be due to the inhibitory action on the pneumogastric center in the medulla, and also partially to the stimulation of the terminal endings of these nerves in the heart. The increased contraction of the heart, which also contains more blood than before the administration of the drug, expels more with each beat and under greater tension, and this results in raising the arterial blood-pressure.

To repeat, *with therapeutic doses* of digitalis the heart is slowed, the rhythm is normal, and the various parts of the heart contract more sturdily, the action on the auricles and ventricles being the same except that it is more marked where there is more muscle tissue.

*With larger doses* of this drug, or when the action is greater than therapeutics require, one of two conditions predominates: Either the stimulation of the pneumogastric or the stimulation of the cardiac muscle is too great, and generally the former predominates and the heart becomes very much slowed, and we have what is called the *second stage* of digitalis action. This inhibition acts more decidedly on the auricles than on the ventricles, the latter being more stimulated by the irritation of their greater amount of muscle tissue, and an

irregular cardiac rhythm is caused, the auricles and ventricles not beating harmoniously although both ventricles always contract synchronously. We then have a very slow pulse and an irregular rhythm.

This stage is the stage of danger and the beginning of the *third stage* is not far distant, which is not the stage in which the pneumogastrics are paralyzed as has been stated, but in which the irritation of this drug on the cardiac muscle becomes so great as to cause the heart to beat very rapidly in spite of the inhibition. There may even be permanent contraction of the ventricles or a permanent systole of the whole heart and stoppage of the circulation. After such stoppage of the circulation the heart may dilate and remain dilated.

Digitalis is a *vasoconstrictor*, causing narrowing of the peripheral blood-vessels by stimulation primarily of the vasomotor center in the medulla oblongata, but it also stimulates the muscular coat of the arterioles. We have then an increased blood-pressure from three causes; from stimulation of the vasomotor center, from stimulation of the muscle-coat in the vessel walls, and from the increased amount of blood thrown into the aorta by the heart; hence the blood-flow in the capillaries is accelerated. The flow of blood through the arterioles and capillaries would, of course, be modified by the degree of the action of the digitalis on the heart. When the heart was toxically disturbed by digitalis the flow of blood in the arterioles would be decreased. Digitalis also increases the blood-flow in the pulmonary circulation as well as in the systemic.

Overaction of digitalis can cause irregular contraction of the blood-vessels so as to cause one or more extremities to feel cold and perhaps numb. Such overaction can also cause a feeling of constriction in the head, especially noticeable in the occipital region.

It is probable that when a heart is in normal condition the blood-pressure will not be much raised by the action of digitalis. If the heart, however, is defective, the blood-pressure is raised by its therapeutic use. In therapeutic dosage, however, it does not much contract the arterioles, although it has been claimed (Loeb) that the coronary arteries under the action of digitalis are lessened in caliber. This is probably not clinically the fact when digitalis is badly needed for a dilated heart, but may be the reason that, when there is supposed to be sclerosis of the coronary vessels with symptoms of angina pectoris, digitalis will generally add to the pain and increase the danger, and should not be used. Digitalis should never be used in internal hemorrhage, unless the hemorrhage is a capillary oozing or venous bleeding. Digitalis may therefore be of value in hemorrhage from the nostrils, in venous bleeding into the bronchial tubes, in venous bleeding from the kidneys, and in hemorrhoids.

An ordinary therapeutic dose of digitalis when the heart is in good condition affects the *nervous system* but little, but when the heart is in such condition as to require digitalis, by improving the circulation in the brain, it is a cerebral stimulant, and the mental condition of the patient is more active, and a drowsy or uncomfortable feeling of fulness in the head disappears. The medulla centers are all stimulated by digitalis.

Too large doses or cumulative doses of digitalis can overstimulate other centers in the medulla besides the cardiac inhibitory and vasoconstrictor, and may cause nausea and vomiting. Overaction of digitalis can also cause dilated pupils, blurred vision, irregular respiration, and finally convulsions.