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University of Minnesota

Digitalis

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INDEX

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William A. O'Brien, M.D.

I. LAST WEEK

Date: February 4, 1937

Place: Recreation Room, Nurses' Hall

Time: 12:15 to 1:25

Program: Movie: Wild Life in Minnesota.

Abstract: Gallbladder Disease. Cause of Death from Cholecystitis.

Present: 147

Discussion: H. R. Ransom
Evarts A. Graham
E. A. Boyden

II. MOVIE

Title: Yesterday, Today and Tomorrow

Released by: Audio Productions

III. ABSTRACT

DIGITALIS

F. H. Crago

History

Digitalis, digitalis purpurea, or foxglove is the best known member of the group of plants which possess a characteristic action on the heart. Digitalis was also the first to obtain recognition for its action on the heart. It is said to be mentioned in the treatise of the Welsh physicians of 1250 A.D. and a description was given by Fuchsins in 1542. After this it is mentioned by writers as being useful in the treatment of epilepsy, anasarca, wounds and ulcers, internally or locally. Gerrarde (1597) and Parkinson (1640) mention it as an expectorant and emetic. It then practically fell into disuse until it was given resurrection by William Weathering, a Birmingham physician (1785), in his treatise, "An account of the foxglove and some of its medical uses: with practical remarks on dropsy and other diseases." He recorded the first reliable observations on its medicinal properties. Although he was most impressed with its diuretic properties, and it was to demonstrate this effect that he published his book, yet he also observed and commented upon cases of heart failure in which digitalis had had a good effect.

It was not until 1542 that the plant was named. Dr. Leonard Fuchs, a botanist, was writing his famous "De Historia Stirpium" and was trying to classify "Foxes Glofe," known to the Germans as "Fingerhuth." He translated it into Latin, modified it slightly and recorded the name in his book as "Digitalis Purpurea."

From this time until 1775 when more intelligent study of digitalis was undertaken, the herb had its ups and downs. In 1597, it was recommended as good to "cut and consume flegme and humors and to scour and clean the breast." In 1600, a decoction of it was thought good for gargling to correct inflammation and fever, while the leaves cured bowel problems. From 1630 to 1719, no less than 6 authorities said that digitalis had no tonic values and one author deemed the drug too acrid and poisonous for internal use. It is of interest that the drug appeared in the London Pharmacopoeia of 1650 and 1720, was an outcast in 1775 but was taken back in 1788. A number of experiments were carried out by investigators such as Salerne, Schumann (1785) and others but no analysis of the action was made, the observers contenting themselves with the symptoms induced. Vulpian (1855) was the first to use this method of experiment to elucidate the action of digitalis. Most of the digitalis used in this country is cultivated on drug farms, especially in the west, and it grows wild in the states of Washington, Oregon and New York. Minnesota is well known for its cultivation of digitalis leaves.

Pharmacology

The pharmacopeial preparations of

digitalis are made from the leaves, in which digitoxin is the chief glucoside possessing the characteristic cardiac action and is probably accompanied by one or more less clearly identified glucosides (digitalein and digalen) which act on the heart less strongly. Digitoxin is soluble in alcohol and is by far the most powerful of the digitalis glucosides. The most important action of digitalis, of course, is on the heart and in the healthy mammal this is shown by increased strength of contraction and greater exertability. After administration of the drug in the therapeutic stage, the rhythm of the heart is distinctly slower than before the drug, for the inhibitory apparatus is set in activity, and the slowing is accordingly due to a prolongation of the pause in diastole. The ventricles contract to a smaller size and empty themselves more completely. Digitalis tends to lessen the dilatation of the weak and dilated heart, that is, the relaxation of the ventricle during diastole is less than before administration. If the heart is normal or does not dilate during diastole, digitalis increases the relaxation. It is well accepted that digitalis has an inhibitory effect due to the stimulation of the vagus center, for digitalis hardly slows the heart after section of the vagi (Cushney). The changes in the ventricles then are those due to inhibitory activity and to direct cardiac action, the first tending to lessen the number of beats and to increase the relaxation of the fibers, the second tending to strengthen the systole and to limit the relaxation while not affecting the rhythm. The inhibitory stimulation causes more or less increase in the dilatation, while it lessens the contraction in the auricles. The muscular action is the same as in the ventricles, causing a tendency toward more complete systole and less complete relaxation. The conductivity in the bundle of His is reduced, both by direct action and also through the inhibitory action of the stimulated vagus. The tendency to spontaneous beats is increased both in the auricles and the ventricles. The rate of impulse formation at the sino-auricular node is reduced by inhibition, so that the rate of the heart is slowed.

When a patient is given digitalis by any of the several routes, after a fairly definite time of absorption and circulation the drug reaches the myocardium and after travelling through the capillaries part of it leaves the circulation and lodges in the cells of the myocardium. The active principles of digitalis are glucosides and after ingestion, absorption and fixation by the heart muscle occurs, the fixed glucosides are then gradually split into two components, one an aglykon or genin, which exerts the digitalis action and the other a sugar which is inert (Christian). It is well known that there is a latent period between the administration of digitalis and any effect. When digitalis has once been given and absorbed into the circulation it enters the heart muscle and is there firmly bound so that it cannot be displaced. Clinically, then this means that the effect of a single dose of digitalis cannot be judged until after a certain interval of time has elapsed following administration and that if overdosage is given there are no known means of removing it from the heart muscle. Digitalis given then has the property of splitting into an active and inactive substance and with a single dose the amount of active digitalis substance diminishes gradually over a long period of time. It is this feature of its action that permits of a subsequent dose being given at the time the effect of the first dose is declining and thus to restore the effectiveness of the action. Not only does the heart "fix" digitalis but it has been shown that fixation also occurs in the skeletal muscles, liver, kidneys but very little, if any, in the lungs. Except in the kidney, digitalis fixed in the tissues other than the heart appears to exert no effect. Therefore if digitalis is given intravenously since it only passes throug the lung which fixes no digitalis, the heart will get the full amount of the drug, and fix and utilize an amount proportionate to the concentration of it as it passes through the heart, the rate of circulation being unchanged. That which escapes from the heart is never returned because it is taken up by the liver, kidneys and skeletal muscles.

Digitalis given by mouth is absorbed and passes into the portal circulation to go through the liver on its way to the heart. The liver is said to fix about as much digitalis as the heart and thus it should be necessary to use a much larger dose by mouth than by the intravenous route. Clinically, however, this is not the case because another factor enters in, namely the time during which the digitalis is in the circulation. This time is short where the drug is given intravenously but prolonged when given by the gastro-intestinal route. These two factors apparently offset each other and reduce the observed difference of effect (Christian). The rate of flow through the heart muscle of blood containing digitalis then has an influence on fixation, the slower or the more prolonged the flow the greater the fixation, concentration remaining unchanged. In cardiac insufficiency, the circulation is slowed and inefficient in the coronary as well as the systemic circulation. Thus the time of contact between digitalis and the myocardium is greater and more of the drug will be fixed. This may well explain the fact that digitalis given to a normally functioning heart causes much less change in function than the same amount given to a patient with coronary insufficiency.

There is a direct relation between muscle mass and fixation of digitalis, concentration and time of flow remaining unchanged. Therefore a hypertrophied heart fixes more digitalis than one of normal weight and therefore more effect is obtained from a given dose of digitalis when the heart is hypertrophied than when normal in size. Cloetta has carried out experiments on animals with aortic insufficiency and found that in those receiving digitalis the heart showed less hypertrophy than in those not receiving it. Digitalis reduced the increase in weight of the heart with aortic insufficiency from 80% to 38% above that of controls without valve lesions. He also found that the digitalis treated hearts with aortic insufficiency were almost equal in reserve energy to the hearts with normal values, while the untreated hearts were much more rapidly exhausted. Therefore, Christian believes that cardiac enlargement even without signs of failure is an indication for the use of digitalis.

Cohn and Stewart demonstrated an increase in height of the left ventricular excursion in man under the influence of digitalis and a decrease in height when the drug wore off. They, however, noticed no decrease in size of the ventricle.

Considerable attention has been given to the metabolic effects of digitalis glucosides on the heart but the results are very conflicting. Peters and Visscher have shown by carefully controlled diastolic ventricular volumes that both the total energy liberation and the external efficiency of the heart are definitely increased and they believe that this reflects an increase in true myocardial efficiency. "In every instance, among the clinically useful glucosides employed, there was an unmistakable increase in efficiency along with a variable increase in energy liberation."

Tachycardia and Insufficiency

When arterial pressures fall, due to primary vasodilatation or to diminished cardiac output, the heart accelerates and strives to restore arterial pressure to normal. The pathways involved in this reflex acceleration are: one over the afferent branches of the vagus from the root of the aorta, and the other through the sinus nerve. The latter is distributed solely to the carotid sinus (Wiggers). Tachycardia and insufficiency has been regarded in the past as a cause of the insufficiency but no particular explanation of the acceleration itself has been offered. The circulation is maintained by proper balance of reflex adjustments, and primary changes in ventricular rate tends to bring compensatory changes in systolic discharge and in blood pressure. Conversely changes in blood pressure produce a reciprocal effect in heart rate. It has been shown by Warfield that in peripheral circulatory insufficiency this reflex mechanism is responsible for the rapid heart rate. He believes that therapy should be directed to improvement of the

adverse factors in the peripheral circulation and not toward slowing the heart for the tachycardia which is but the physiological result. Digitalis therapy therefore in the absence of cardiac insufficiency would be of little avail. Wiggers has shown that the faster the heart beats, the more the period of diastolic filling is cut short and the more the systolic discharge is decreased. However, his calculations show that this decrease is more than compensated by the cardiac rate up to 200 per minute, so that the minute output steadily becomes greater. This compensatory acceleration must not be disturbed for to do so would cause a drop in blood pressure sufficient to endanger life. In circulatory insufficiency with normal rhythm of cardiac origin, there is a physiological response in rate. Digitalis here then is of definite value because of its direct action on the myocardium.

Effects of Digitalis on Sinus Slowing

Lewis believes that the favorable action of the drug on the heart is due solely to its ability to reduce the ventricular rate and this result is only obtained in auricular fibrillation. In decompensation with normal rhythm, Robinson, Eggleston, Cohn, White and Marvin find that therapeutic doses produce little effect at the pacemaker but that slowing is an indirect effect which follows the improvement in the circulation produced by the action of digitalis upon the muscle of the ventricle. Circulation improved, physiological mechanisms produce a reciprocal adaptation of rate and the tachycardia subsides. In cardiac insufficiency with normal sinus rhythm, acceleration is not the cause of failure but is a physiological result of the failure. Primary slowing is not a direct effect of digitalis and is not the therapeutic objective. Improvement in muscular efficiency of the heart is the direct result thereby decreasing the rate (Luten).

Digitalis and Normal Rhythm

The beneficial results of digitalis therapy when failure occurs with normal rhythm are usually much less striking. By a series of carefully controlled cases, Luten showed that digitalis by mouth affected certain cases of normal rhythm favorably. Improvement in symptoms, diuresis, loss of edema and decrease in size of the liver were noted. In his series, cases with myocardial insufficiency showed the most constant benefit. Improvement did not depend upon ventricular rate and any slowing of the heart rate when it did occur was to a certain degree independent of the general improvement and sometimes seemed to follow it. Patients with myocardial insufficiency improved under proper digitalis administration in about the same proportion of cases as did patients with auricular fibrillation. Cases with aortic lesions did less well. Marvin found that administration of digitalis in suitable large doses to patients with advanced congestive heart failure, regular rhythm, and edema caused improvement in the group of "arteriosclerotic heart disease" or "myocardial insufficiency." The drug was found almost devoid of effect in rheumatic heart disease with normal rhythm. It was found occasionally beneficial in patients with syphilitic heart disease. These general effects of digitalis have been observed by still other investigators. From the study of 100 selected cases of severe congestive heart failure with normal rhythm, Parkinson concludes that heart failure with normal rhythm indicates a more advanced degree of myocardial insufficiency than does a corresponding degree of failure with auricular fibrillation, where a part is due to the disorder of rhythm and ventricular tachycardia. He believes that digitalis benefits some of these patients to a great extent but the results are seldom comparable with those obtained in auricular fibrillation. The "stage" of heart failure is a very important consideration when expecting favorable results from digitalis. The response to treatment becomes less satisfactory with each succeeding episode of failure.

Digitalis Eosinophilia

The earliest case of eosinophilia as the result of the ingestion of

digitalis was reported by Reckt who observed that an eosinophilia of from 12 to 18% in two patients could be produced by the administration of digitalis. Smith and Benner report a case in which recurrences of eosinophilia reaching 30% coincided with successive periods of digitalization. Romano and Geiger report a case in a 70 year old white man in which an eosinophilia of 22% was noted during digitalis administration. Eighteen days after withdrawal of the drug, this percentage had decreased to 2% and again rose to the previous level on re-administering digitalis. Rare cases of eosinophilia due to digitalis exist.

Auricular Fibrillation as a Toxic Manifestation of Digitalis

MacKenzie was the first to describe a case of auricular fibrillation coming on in a 17 year old female with rheumatic history after the administration of digitalis. His patient again reverted to normal rhythm after withdrawal of the drug. Reid reported two cases in which partial heart block and then auricular fibrillation developed after large doses of digitalis. Toxic effects of digitalis described by Reid are coupled rhythm, partial heart block with an acceleration of the sinus rate, the onset of auricular fibrillation, and paroxysmal tachycardia originating in the ventricle. Resnik reports a group of seven patients in whom the appearance of transient auricular fibrillation seemed directly related to the administration of digitalis. The rhythm became normal a few days after the withdrawal of the drug. He concluded that auricular fibrillation following digitalis was due in some cases to strong stimulation of the vagus nerves, but that in most instances it was due to direct action upon the heart muscle and that myocardial failure is an important predisposing factor in the production of transient auricular fibrillation by direct action and possibly by the vagal action of digitalis. Tung reports a series of 15 cases in which full digitalization caused the appearance of auricular fibrillation together with other signs of digitalis intoxication. He concluded that under certain circumstances transient auricular fibrillation is a toxic manifestation of digitalis and its occurrence is an indication for withdrawal of the drug.

Case Report

L.G., male, age 45.

Twenty-eight years ago had rheumatic fever. No following attacks. Nine months before admission began having slight precordial pain, dyspnoea and orthopnea. Five weeks before admission precordial pain became more marked and he noticed edema and some ascites. Local medical physician prescribed 20 drops digitalis t.i.d. 6 weeks before admission and this dose was taken for 2 weeks. He was then given 1½ grains of the powdered leaf t.i.d. for the next 4 weeks. This totals approximately 98 cat units in 6 weeks. On admission, electrocardiogram showed auricular fibrillation and bigemini. The apex rate during fibrilliation was 118 with a pulse deficit of 25. Digitalis was discontinued and in 2 days normal sinus rhythm returned. The apex rate at this time remained at about 90. Decompensation progressed, however, and the patient expired on the 17th hospital day.

Preparations of Digitalis

One grain tablets of the B.P. are equal to 10 M of the tincture each. Upsher Smith of Minnesota produced a standardized table of 1 grain equal to 1 cat unit. One tablet equals 15 M. of the tincture. "Digoxin" is a pure crystalline glucoside which has been isolated at the Wellcome Chemical Works. It is suitable for intravenous use. An intravenous dose of 1.0 mgs. (gr. 1/60) causes ventricular slowing beginning in 5 to 10 minutes and is maximal in 1 to 2 hours. The rate of fall is slightly greater than that observed after the intravenous injection of 0.25 mgs. (gr. 1/240) ouabain of 90% standardized activity. One tablet of Digoxin 0.25 mgs. is equivalent to 15 M. of tincture. Strophanthus preparations are uncertain in their composition and the toxicity is greater. For rapid action, it

may be given intravenously gr. 1/150 and effects are apparent in a few minutes. Ouabain is a preparation of g. Strophanthin made from Strophanthus gratus; gr. 1/240 (0.25 mgs.) is the usual single intravenous dose. It is more effective than ordinary Strophanthin. When given by mouth, it is uncertain in its effects because of the variable rate of absorption from the intestine. However, ouabain may be given by mouth in solution (solubain) or in tablet form.

Methods of Administration

One cat unit of the present day reliable preparations usually equals 100 mgs. or 1½ grains of the powdered leaf which is necessary to kill a kilogram cat when injected in solution into a vein. According to Eggleston, about 0.15 cat units per pound may be needed to effect complete saturation with digitalis. For convenience, the calculated dose is given as 2.5 grains per 10 lbs. of body weight. If 1½ grains is equal to 15 M. of the tincture, then 25 M. per 10 lbs. will be needed. Actually in practice this dose is often too high and 1½ grains per 10 lbs. body weight is safer. Eggleston's method for rapid digitalization is as follows: one half of the calculated total dose is given as the first dose; one-third, 4 to 6 hours later; and small doses at 4 hour intervals until the calculated amount is reached providing symptoms of overdosage do not occur. In this way, the full amount can be given within 24 hours. The method must be used with care to select cases in which these effects are desired. It must be remembered, however, that the rate of excretion is about 1½ grains or 1 cat unit per 24 hours. This must be taken into consideration when the calculated digitalization dose is being given. Cases of acute or chronic infections, with the probability of the presence of endocardial infections, should be given the Eggleston method, if at all, only after careful study, because of the possibility of embolism and the possibility of associated myocardial changes predisposing to block. Patients show a remarkable variation in their rates of absorption and individual idiosyncrasies are constantly arising.

Symptoms of Overdosage

Symptoms of overdosage and poisoning are as follows: Nausea, vomiting, abdominal pain and often diarrhea. The patient may complain of general depression, giddiness, headache, precordial discomfort and great muscular weakness. At first, the pulse rate may be irregular and slow (Cushney) but later may become rapid and fatal coma follows. As mentioned above, auricular fibrillation is often a toxic manifestation. Willius reports a case of digitalis poisoning with marked cerebral symptoms characterized by dizziness and attacks of unconsciousness. Disturbance in color vision, all objects appearing yellow or green color to the patient, is a frequent symptoms of the cerebral intoxication of digitalis.

Electrocardiographic Changes due to Digitalis

The most characteristic changes in the electrocardiogram due to overdosage of digitalis are those found in the T-wave and S-T interval. These changes may appear within 2 hours after oral administration of the drug and may persist for days (8 to 14) after withdrawing the drug. There is usually a depression of the S-T phase with flattening and inversion of the T-wave and are usually seen in leads II and III but sometimes also in lead I. Very large and toxic doses may produce slurring and widening of the QRS complexes and diminution in the height of the R-wave. The P-R interval may also be prolonged showing early evidence of heart block. McGuire reports the case of a patient ingesting 300 grains of digitalis followed in 12 hours by respiratory failure. Electrocardiographic changes here were complete A-V dissociation; auricular rate 170; ventricular rate 60 to 70; marked depression of S-T segments in leads I and II, and inversion of T-waves.

Auricular Fibrillation

Digitalis and its allies owe their well founded reputation to their strik-

ing effects in well managed cases of auricular fibrillation. In the latter, a circus movement replaces the rhythmic activity of the pacemaker so that impulses are transmitted irregularly through the bundle of His. Digitalis has a depressant effect on the bundle of His, both direct and vagal so that the number of impulses transmitted to the ventricles is diminished and the ventricular rate is slowed. Slowing of the ventricular rate permits a longer diastole, so that the ventricles are better filled and the duration of the phase of nutrition and of rest is increased and the force of systole is thereby strengthened. Lewis believes that persistent fibrillation means disease of the ventricular muscle but in a recent study by Luten of 431 consecutive cases of arrhythmia he found no suspicion of ventricular disease in 42 cases. Auricular fibrillation then is to be referred to the auricle. In Luten's series, mitral valve lesions were present in about one-third of the cases and congestive heart failure was present in about two-thirds. Luten then believes that it is not the fibrillation which has caused the failure but the failure which has caused the fibrillation. Luten found that in toxic cases of auricular fibrillation without heart failure digitalis produced no slowing. In 47 out of 97 cases of auricular fibrillation without heart failure, digitalis was administered but in no instance was there a slowing effect on the pulse. Digitalis is the drug par excellence in the treatment of auricular fibrillation. Use of quinidine is usually restricted to those in whom the heart is normal apart from fibrillation. It is dangerous in the presence of heart failure or an active infection.

Auricular Flutter

Auricular flutter is uncommon and has an incidence relative to fibrillation of only 1:13. Flutter is most often associated with chronic rheumatic heart disease or with cardiac enlargement in elderly males. It complicates less often, high blood pressure, hyperthyroidism, acute febrile conditions, coronary thrombosis, or syphilis (Parkinson). Digitalis acts both in the vagus and auricular muscle and its action here is similar to that of quinidine. In Parkinson's series of 52 cases of auricular flutter, digitalis removed the flutter far more often than did quinidine. Digitalis alone restores normal rhythm in over one-third of the cases and in another one-third it induces fibrillation. Quinidine converts flutter directly to normal rhythm in about one case in five. The circus movement in the auricle is usually quickened after digitalis and if it is continued the flutter wave may take a shorter path and turn into fibrillation. If digitalis is then stopped, normal rhythm may recur.

Hyperthyroidism and Auricular Fibrillation

The effect of digitalis in auricular fibrillation of hyperthyroid origin is variable. In a series of 108 cases reported by Barker, 23% had auricular fibrillation. Auricular fibrillation in Grave's disease is much more often transient or paroxysmal than that due to other causes. He found that digitalis was somewhat less effective in auricular fibrillation due to Grave's disease than in fibrillation due to other causes. On the average, the amounts of the drug tolerated were larger and the beneficial effects were less striking. The approximate tolerance was estimated in 49 of his cases and it was found that these patients had a tolerance which was 134% of the normal average. The average basal metabolic rate of these patients was +48%. The response of some to the intravenous administration of ouabain or digifolin was determined and found to be on the whole less striking than that of patients with auricular fibrillation not due to Grave's disease. From this series, it is seen that in general patients with the higher metabolic rates have higher initial ventricular rates, tolerate larger amounts of digitalis and show less ventricular slowing in response to digitalis. Most of the Barker's series who showed satisfactory slowing of the heart following digitalis therapy were patients with relatively little elevation of the metabolic rate. These observations in respect to digitalis were

similar to those of Foster, Sturgis and Grant (cited by Barker). Quinidine is most useful in thyrotoxic cases in whom normal rhythm has not returned after appropriate treatment of the hyperthyroid state.

Case Report

female, age 61.

The following is an example of the poor effects obtained by digitalis on auricular fibrillation secondary to hyperthyroidism.

Six weeks prior to admission complained of tachycardia, weakness, tired feeling, fatiguability and moderate edema of ankles. For 3 weeks before admission took 8 drops of digitalis t.i.d. and had been nauseated and vomited with each dose. Physical examination: Patient was nervous, had slight tremor of hands; heart slightly enlarged to left apex, rate 70, and totally irregular, pulse deficit of 40; slight edema of ankles; Basal metabolism rate +28%. She was given 4 cat units by mouth during 2 days which caused vomiting on each attempt. This was discontinued for 5 days. She then received these cat units per day for 5 days with a persistence of nausea and occasional vomiting and without effect on the fibrillation. Was then given 1 cat unit each day for 7 days followed by 20 cat units during the next 6 days without effect on the fibrillation. Nausea and vomiting persisted. Quinidine then begun and in 3 days pulse was 80 and fibrillation had disappeared. The patient was seen 2 months after discharge and on a daily dose of quinidine gr. 3/ the rhythm remained regular and the patient "never felt better in her life."

Myxedema Heart

Digitalis has no place in the treatment of decompensation due to myxedema heart. Thyroid extract given in appropriate doses usually causes a prompt recovery but symptoms return on withdrawal of the drug.

Constrictive Pericarditis

Chronic constrictive pericarditis consists of a chronic fibrous or callous thickening of the wall of the pericardial sac which is so contracted that the normal diastolic filling of the heart is prevented (Mattison). "It is an 'inflow stasis.' Diastolic filling is prevented and therefore systolic discharge is less. Digitalis obviously then is of no benefit in this condition and its only hope of cure lies in thoracic surgery."

Digitalis in Pneumonia

The question of giving digitalis to lobar pneumonia patients has been a long, hot and debated one. Many men give small amounts of the drug as a routine measure in the treatment of pneumonia. Cohn and Jamieson, in a clinical study, concluded that "the routine giving of digitalis to patients with lobar pneumonia is dangerous." Cohn and Lewis, in a study of 1456 patients observed at the Rockefeller Institute that giving digitalis does not seem to influence the course of events in lobar pneumonia. Its action appears to be beneficial in favorable cases in which auricular fibrillation and auricular flutter occur. The outcome in lobar pneumonia depends on the severity of the disease which in turn depends especially on the presence of bacteremia, the number of pulmonary lobes involved, and the existence of complications.

In a study of 835 cases of lobar pneumonia by Niles and Wykoff, it was concluded that the routine use of digitalis in pneumonia patients was unjustifiable. Wykoff, Dubois and Woodruff show that in a group of 742 cases of pneumonia in the Bellevue Hospital (New York) the mortality was 7.7% higher in the cases receiving digitalis than in the alternately selected control group which did not receive digitalis. Arnett and Harris, in a study of 77 cases of lobar pneumonia, conclude that on the whole digitalis does more harm than good in pneumonia.

Conclusions

1. A brief resume of the early history of digitalis is given with beliefs of some of the early workers.

2. The pharmacology of digitalis is discussed. The drug has a direct effect on the ventricular musculature of the heart, and the energy liberation and efficiency are increased.

3. Tachycardia is not a cause of decompensation but is secondary to it. The primary object of therapy is not a decrease in rate but an improvement in the muscular efficiency.

4. Digitalis is beneficial in cases of failure with normal rhythm but this improvement does not depend upon rate.

5. In certain individuals, digitalis may produce an eosinophilia up to 30%.

6. A not infrequent manifestation of digitalis poisoning is auricular fibrillation which may disappear after the drug is withdrawn. Other symptoms of overdosage are given.

7. Digitalis is the drug of choice in auricular fibrillation, the origin of which is not overdosage. The drug is of little value in decompensation from hyperthyroidism and of no value in myxedema, constrictive pericarditis, and pneumonia.

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IV. GOSSIP

The fourth and final week of the first series of post-graduate medical courses comes to a close Saturday. The pharmacists follow and soon after that the hospital executives study the problems of the small hospital. In April the medical series will resume with one week of radiographic interpretation, three days on the use of radium and x-ray in treatment, and three days on physiotherapy. The Center for Continuation Study is a realization of the dream of every physician in practice. It is an opportunity to relive his student days with his old friends in a building of his own on the campus. It takes away from returning to his Alma Mater all the inconvenience and lack of friendliness of the past. Photographic records were made this week of our "medical students" in their rooms, at table, in the lounge, and at class, all in the same building. Each succeeding group seems to grow more enthusiastic and their attitude and that of the teaching staff assures the future success of this new program of instruction.

Adios.