CLINICAL INVESTIGATIONS OF THE NATURE OF ACTION OF RAUWOLFIA ALKALOID, AJMALINE, IN DISTURBANCES OF CARDIAC RHYTHM, PARTICULARLY EXTRASYSTOLES*

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After the introduction of *Rauwolfia serpentina* into the therapy of hypertension, there was a great increase of interest in the isolation and investigation of the alkaloids contained in this plant. As well as the Rauwolfia extracts[7], reserpine alone or in combination with other pure alkaloids from Rauwolfia, such as rescinnamine, raupine, ajmalicine, etc. is of importance in the treatment of hypertension.[8]

Pharmacologicial investigations of ajmaline, already known for some tens of years, indicated the possibility that it would have an effect on disturbances of cardiac rhythm, thus justifying a thorough clinical investigation, especially since the therapeutic application of this alkaloid in rhythm disturbances has not yet been discussed in the literature.

As early as 1939, Bijlsma and van Dongen found that ajmaline produces a prolongation of the refractory time and the transmission time in animal hearts. Recently Zipf has investigated this alkaloid in great detail. As compared with reserpine and rescinnamine, the central sedative effect is absent. In addition to the above result, experiments indicate a reduction of the heart frequency, and the intraventricular excitation propagation is also slowed down (with a dose rate of 0.52 mg./kg. in the warm-blooded heart). Larger doses produce total blockage or heart arrest. No cumulative effect was observed in a chronic test.

In addition, ajamline increases the resistance to electrical stimuli which give rise to auricular fibrillation. It prevents the development of heterotypic stimuli in barium chloride poisoning or adrenaline action. Aconitine arrhythmia in guinea-pigs can be reduced or delayed by previously dosing with 3 mg. per kg. of body-weight (Goeing and Kempe). According to Benthe, ajmaline exhibits relatively strong fibrillation-preventing properties in comparison with quinine, quinidine, fagarine, procaine, procainamide and serpentine. In contrast to the substances mentioned, ajmaline prolongs the refractory period significantly, and according to Zipf, in hypodynamic warm-blooded hearts a positive inotropic effect is actually observed. In regard to the possibility of intravenous administration without the risk of producing a dangerous condition of collapse, special importance attaches to the slight impression of the blood-pressure-reducing component, which generally comes into view clinically only in combination with other Rauwolfia alkaloids, e.g., reserpine. In dogs, we generally observed a slight drop of blood-pressure after i.v. injection (0.5 to 1.0 mg./kg.), while the blood circulation was unaffected. After intracarotic injection of ajmaline (0.5 to 1.0 mg./kg.) we observed, in 14 tests, first a mean rise of blood pressure from 145 to 158 mm. Hg. After 2-5 minutes in some cases there was a slight but not significant drop below the initial value (Kovach, Faldi, Kleinsorge, Popp, Koltay).

In relation to the clinical application of ajmaline it is also worthy of note that Zipf reports interruption or lessening of peripheral adrenergic or nor-adrenergic effects as well as a coronary-enlarging effect after administration of small doses. The degree of toxicity is very low.

As to what happens to the ajmaline in the organism, little is so far known. According to Benthe, ajmaline resembles quinidine and differs from procaine in that it cannot be washed out of the isolated heart-muscle ranular preparation ("froschpraeparat"). From this it can be concluded that there is not only an effect on the cell membranes but also a closer bond with the heart-muscle cells themselves. Investigations of the blood level and the separation of the ajmaline are at the present time still rendered difficult by the complexity of the quantitative demonstration method. We will discuss this later, separately.

For the qualitative determination, we used the method of demonstration described by Heinrich for ajmaline with antimony pentachloride in chloroform. However, the extraction of the ajmaline from the urine proved to be a very slow process and, since the chloroform in many cases formed with the ajmaline-containing urine a firm emulsion, involved a high consumption of chloroform. My co-worker Sutter eliminated these disadvantages by using an extraction apparatus for difficult solvents. We were thus able to demonstrate even 100 of ajmaline in the urine with certainty.

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We investigated the separation of ajmaline in the urine after intravenous, intramuscular and oral administration, using 30 test subjects with normal separation characteristics.

After intravenous administration of 50 mg., it was in all cases possible to observe ajmaline in the urine within the first hour, after 10 minutes in the earliest cases (catheter urine). A positive indication in the urine was obtained up to 4-5 hours after administration.

After intramuscular administration of 50 mg., ajmaline was also observed in the urine at the earliest after about 30 to 60 minutes, for a duration of several hours. Only in one case, and due to some unknown cause, ajmaline had not separated in the urine after 4 hours.

After oral administration of 100 mg. ajmaline, the substance was identified in the urine after one hour, except in 3 cases. The duration of separation was however non-characteristic, varying between 3 and 8 hours.

It appeared to us that various types of extrasystoles would constitute a particularly significant indication for the application of ajmaline (Arytmal, 50 mg. dragees, 50 mg. ampoules. Manufacturers: Gebr. Giulini GmbH, Ludwighshafen, Rhein). Because the occurrence of extrasystoles is only sporadic or periodic, the physician is often inclined to underestimate their significance, especially with youngish patients; on the other hand, because of subjective troubles to which they give rise, these disturbances are often overestimated by the patients. Even though extrasystoles are often of a functional nature, treatment is certainly necessary if they occur too frequently, since the long-term diminution of the stroke volume may lead to hypoxaemic heart damage. Working with dogs, Wiggers found that a bigeminal rhythm with a frequency of 80/min. reduces the coronary blood circulation by 27%. The pressure falls in the right ventricle observed in heart. Catheter investigations are also impressive as indicators of a reduced ventricle filling in the presence of even a single extrasystole (Fig. 1).

On the diagnonsis of extrasystoles, Schmidt-Voigt recently expressed his views in detail in Med. Klin. Mention may also be made of the thorough exposition presented by Spang. In practice, it is impossible to make a close analysis of the causes of extrasystoles without resorting to electrocardiographic and/or phonocardiographic analysis, since any part of the stimulus-transmitting system from the sinus nodes to the branching of the Hiss bundle can give rise to the development of extrasystolic stimuli. There are many possible causes:—

1. Central nervous stimuli due to hyperexcitability of the central nervous system as a result of psychic stimuli ("expectation extrasystoles") or organic injuries;

2. Organic heart injuries, e.g. myocarditis, infarcts, disturbances of the blood circulation, over-extension of the auricle or ventricle in heart troubles etc.;

3. Toxic injuries to the heart muscle e.g., due to nicotine, caffeine or glycosides, or in cases of morbus Basedow, coma diabeticum and uraemicum etc.;

4. Mechanical stimulation of the heart muscle (e.g. heart catheter investigations).

Every attempt should be made to apply causal therapy, depending on the origin of the extrasystoles, e.g., compensation of the heart, improvement of the coronary blood circulation, elimination of

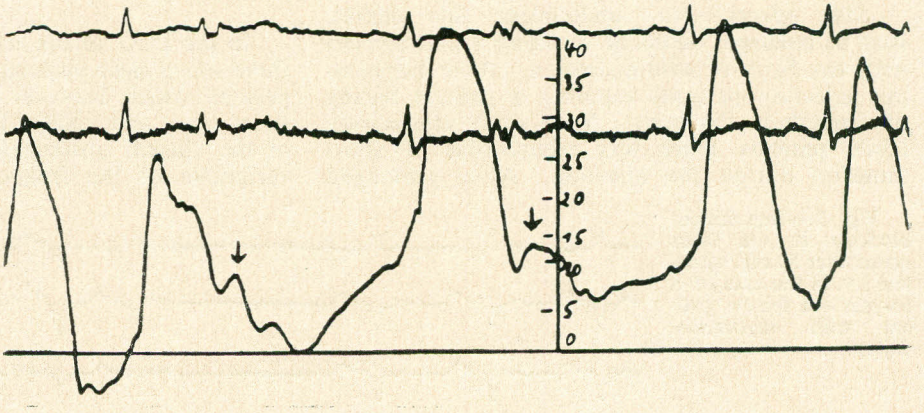


Fig. 1.—In a heart catheter investigation, the pressure values in the right ventricle are definitely lower during an extrasystolic beat than during regular beats (reduced ventricle filling).

toxic injuries and avoidance or toning down of psychic excitation. At the same time, symptomatic therapy also plays a big part, its action extending to all forms of extrasystoles. The best results obtained hitherto are probably those with quinidine and procainamide. However, these substances, espcially quinidine, are known to produce allergic and toxic side effects of many different types, mostly at high dose rates, but often also at effective dose rates. Because of the risk of collapse involved neither of these substances can be used as routine, for intravenous applications, which renders the interrupation of an acute and persistent disturbance of cardiac rhythm more difficult. Other medicaments for the treatment of extrasystoles, such as atropine, sympathicomimetics, and salts of barium, potassium and magnesium play a smaller part only. Influencing by peripheral ganglion blockers (TEAB), previously reported by us, also has only a scientific significance.

Clinical Use of Ajmaline

In order to obtain a picture of the effectiveness of ajmaline, we first used only the pure alkaloid. The investigations were carried out in collaboration with my co-worker Volkner.

Intravenous injections of 50 mg. Arythmal (dissolved first in 5 cm. and then in 2 cm. of liquid) were given first, with continuous monitoring by ECG, with an image tube to provide continuous visibility for the injecting physician. It was possible to reduce the injection time from an initial value of 5 minutes to 1 minute without producing unpleasant side effects in patients. Further dilution of ampoule contents with common salt or grape-sugar solution was not undertaken. We injected the preparation intramuscularly in the gluteal musculature without producing painful sensations in patients. There were no local stimulus phenomena.

Side effects.—No undesirable side effects, such as collapse, illness or vomiting were observed with any form of administration. After intravenous injection patients reported a general feeling of warmth in the body. With some vegetatively labile patients there was tachycardia of short duration during the injection. After prolonged oral administration, 20% of the patients complained of loss of appetite and stomach troubles. These troubles could be attributable to the pronounced unpleasant taste of ajmaline, which in the meantime has been eliminated in the case of the commercial preparation Arythmal by making sugar-coated pills. In a few cases slight fatigue was reported when high dose rates were used, (300 mg. pro die).

In the ECG a blockage was observed in the sinus node in one case after intravenous administration of 50 mg. ajmaline. One 65-year old female patient suffered from extrasystoles in consequence of a degenerative myocardial injury. After intravenous injection of 50 mg. ajmaline there was intermittent blockage of the sinus node with systolic deficiency ("Systolenausfall") lasting 10 minutes. However, the patient did not complain of any troubles (Fig. 2).

Control investigations.—All the tests were made first after intravenous administration, so that an exact analysis could be made of the nature of the action on the heart, its onset and its duration. In order to exclude purely psychic effects of the injection itself on extrasystoles, we injected 10 subjects with common salt solution as placebo, in a series of comparison tests; to give the same subjective feelings (feeling of warmth) as after ajmaline injections, calcium gluconium at 10% strength was included. In no case were the extrasystoles associated with ajmaline observed.

Results of tests.—In 50 cases with auricular or ventricular extrasystoles we injected arythmal intravenously. In 49 cases, systasis of the extrasystoles occurred during or shortly after the injections, with a duration of 15-25 minutes. With 5 patients the extrasystoles had not reappeared as late as an hour after the injection. Only in one case of auricular extrasystoles did the i.v. administration of 50 mg. ajmaline fail to interrupt the extrasystoles.

In the ECG of the successfully treated patients there was a clear prolongation of the PQ and QRS periods which however became normal after a short time, and always before the disappearance of the clinical observable effect. No substantial variations of the frequency, in the sense of a

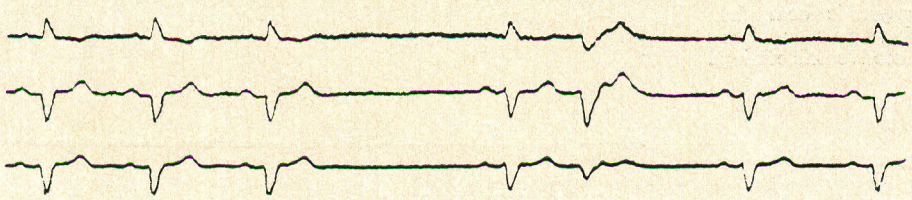


Fig. 2.—Intermittent blocking in the sinus nodes after 50 mg. ajmaline i. v. in the case of a 65-year old female patient with myocardial injury.

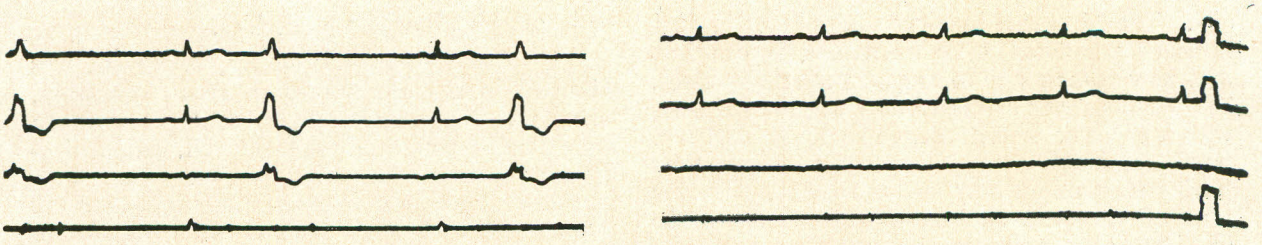


Fig. 3. (a) and (b).—Elimination of a bigeminal rhythm consequent on an arteriosclerotic disturbance of the blood circulation, after 50 mg. ajmaline i. v.

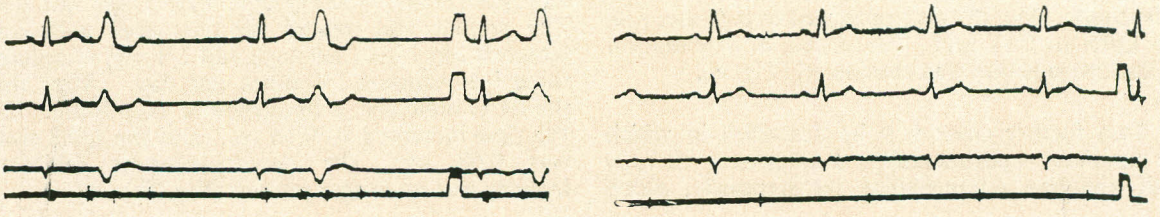


Fig. 4 (a) and (b).—18-year old patient with a bigeminal rhythm following on myocarditis. After i. v. injection of 50 mg. ajmaline, heart beats are regular.

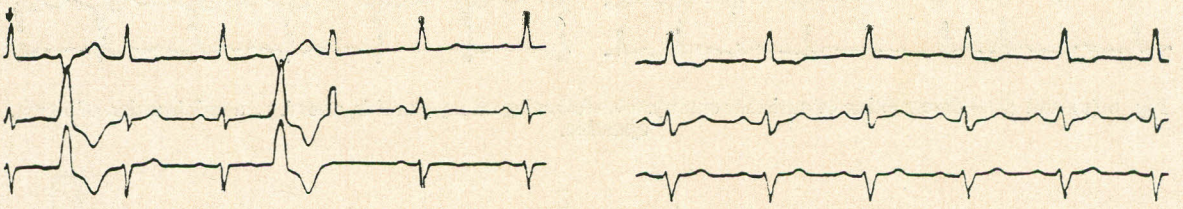


Fig. 5 (a) and (b).—Interruption of ventricular extrasystoles due to degenerative myocardial injury by i. v. injection of 50 mg. ajmaline.

deceleration of the heart-beat rate, such as were found in the pharmacological investigations, were observed in the clinical tests. This may be because in the isolated heart-muscle preparation ajmaline acts only on the nervous centres of the heart, whereas in patients there is also the central-nervous effect.

To demonstrate the effectiveness of ajmaline on the symptoms of extrasystoles of various origins, some case histories will now be described :-

1. A 54-year old patient, Paul B., had complained for 10 years of angina pectoris troubles, which had occurred during the last few months in an intensified form and in combination with heart irregularities ("Herzstolpern"). The ECG indicated ventricular extrasystoles in the rhythm 1:1 (bigeminism). No glycoside preparations were administered. The mean frequency was 64 beats/minute PQ 0.14 sec. QRS 0.06 sec. The ST sections were isoelectric, the T spikes fairly high. Though no pathological changes were observed in the ECG apart from the extrasystoles, in view of the general findings, we assumed the cause of the trouble to be a deficiency in the blood circulation, of arterio-sclerotic origin. Injection of 50 mg. ajmaline produced an interruption of the extrasystolic stimuli. The PQ time increased to 0.17 and the QRS to 0.08 sec. (Fig. 3).

2. The 18-year old patient, Peter M., was brought to our clinic on account of heart sensations consequent on myocarditis. The ECG indicated bigeminism. Atropine was first injected, without success, to exclude vagus stimulus. After i.v. administration of 50 mg. ajmaline the excited heart state became normal. Before the injection the PQ period was 0.13 and the QRS 0.08 sec. After the injection PQ increased to 0.17 and QRS to 0.10 (Fig. 4).

3. The 65-year old female patient, Klra K., came to our clinic on account of irregularity of heart beats and shortage of breath. She stated that there had been swelling of the legs for short periods. The ECG showed a frequency of 85 beats/minute, PQ time 0.17 sec. and QRS 0.08 sec.; ventricular extrasystoles were also indicated. After injection of 50 mg. ajmaline the frequency was unchanged. The extrasystoles were eliminated. PQ increased to 0.20 and QRS to 0.12 sec. (Fig. 5).

4. The 25 year old patient, Calus Peter F., had previously suffered from rheumatic myocarditis and now complained of angina pectoris troubles. The ECG showed extrasystoles; each normal beat, with a PQ time of 0.12 sec. and QRS of 0.01 sec. was associated with 3 auricular extrasystoles having their origin near the sinus node. The PQ time of the extrasystoles was 0.10 sec. and the QRS 0.08 sec. After the 3rd auricular extrasystole there was a compensatory pause of 0.08 sec. The mean frequency was of 150 beats/minute. After i.v. injection of 50 mg. ajmaline the frequency was 110/minute. The PQ time increased to 0.18 sec. and the QRS to 0.11 sec. The centre of stimulation of the extrasystoles was eliminated (Fig. 6).

Two further cases will be described in which we applied, experimentally, a long-term therapy with ajmaline administered intravenously, alone or in combination with glycosides.

5. The 65-year old patient, Albin R., was admitted in a severely decompensated condition. There was acute heart failure, consequent on an old extended infarct of the front wall, with auricular and ventricular extrasystoles. The heart frequency fluctuated between 120/minute and 150 /minute. PQ 0.14, QRS 0.10 sec. After injection of combined strophanthine (1/4 mg.) and ajmaline (50 mg.), both auricular and ventricular extrasystoles were eliminated (Fig. 7a). The frequency was 100/minute, the PQ time 0.13, QRS 0.08 sec. The patient was treated for one week with one tablet of ajmaline (200 mg.) and 1/4 mg. strophanthine intravenously, 4 times per day. After this the ECG indicated a frequency of 60/minute. The PQ time increased to 0.16 sec. and the QRS time was 0.08 sec. The decompensation exhibited initially was no longer present (Fig. 7b).

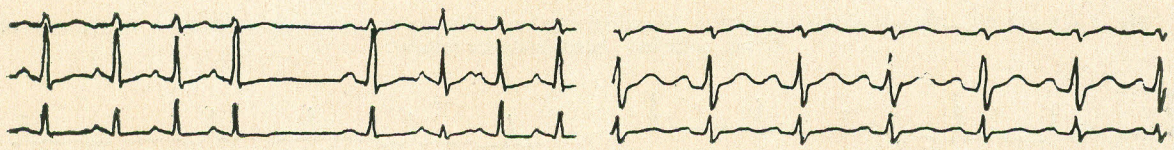


Fig. 6 (a) and (b).—Interruption of auricular extrasystoles following on myocarditis, after i. v.. administration of 50 mg. ajmaline.

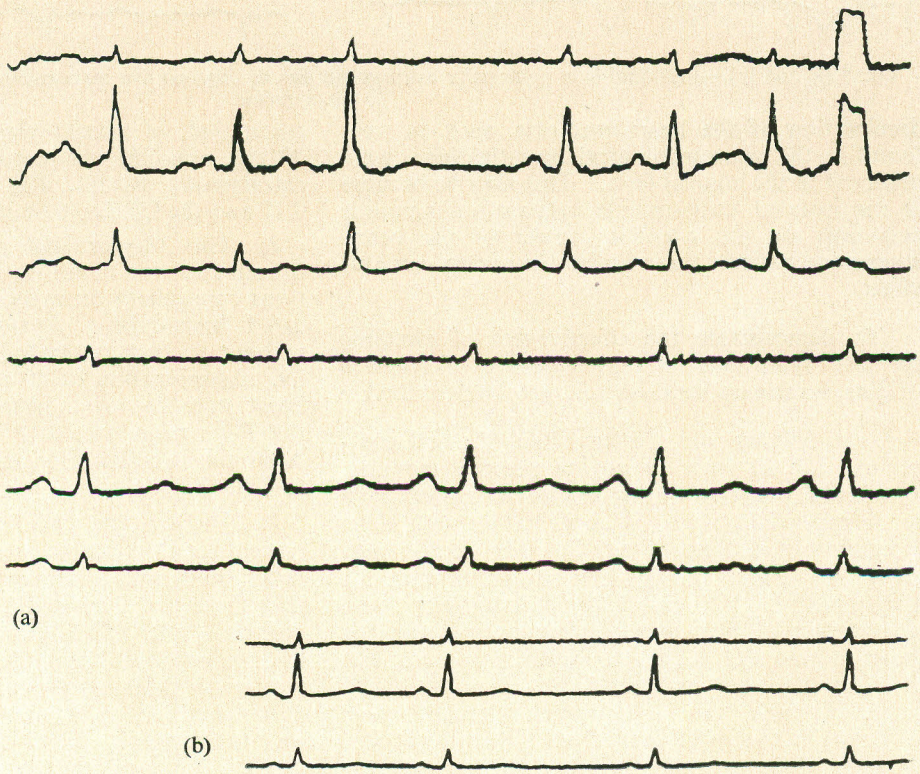


Fig. 7.—Auricular and ventricular extrasystoles in acute heart failure about 6 months after extended infarct of the front wall. After 50 mg. ajmaline and 1/4 mg. strophanthine, given intravenously regular rhythm (a). After 6 days treatment with ajmaline (200 mg. daily oral) and strophanthine (1/4 mg daily i. v.), regular rhythmic pattern (b).

6. In another case, ajmaline injections were given intravenously for 15 days, with a daily dose of 50 mg. The injections were accepted without reaction. At first there was an extrasystolic stimulus from the right limb of the Hiss bundle, with a 2:1 rhythm. After 15 injections, every 5th beat was followed by an extrasystole.

Ajmaline was given intramuscularly to 30 patients, at first experimentally and then for therapeutic purposes. After the intramuscular injection 2 hour ECG examinations were made at intervals of 15 minutes. Suppression of the extrasystoles occurred about 10 to 15 minutes after the injection. In no case was any substantial broadening of the QRS complex or prolongation of the PQ time observed as after the intravenous injection, nor were there any frequency changes. 30 to 45 minutes after the injection the extrasystoles reappeared in most cases. Injections of 1—3 ampoules daily, given on 20 consecutive days, were also taken without reaction.

Two cases will now be described to demonstrate the effect of intramuscular injection of ajmaline :—

7. The 73-year old patient, Eugen F., complained of angina pectoris troubles. Clinical and ECG examination indicated a degenerative heart-muscle injury with general arteriosclerosis, with an extrasystolic stimulus the ventricular muscle : The ECG indicated a frequency of 66/min. a PQ time of 0.15 sec. and a QRS time of 0.07 sec. The T spikes were low. Extrasystoes were present. Fifteen minute after intramuscular injection of 50 mg. ajmaline no frequency change had occurred. The PQ and QRS times were only silghtly increased to 0.17 and 0.08 sec. respectively. On the other hand, the centre of extrasystolic stimulation was eliminated. Thirty minute after the injection, widely isolated extrasystoles were observed again (Fig. 8).

8. The 20-year old female patient, Leonore W., complained of irregular heart beats. Ventricular extrasystoles of unidentified origin, with a 2:1 rhythm, were observed. Before the injection, the frequency was 75/minute the PQ time 0.16 sec. and the QRS time 0.09 sec. After injection of 50 mg. ajmaline i.m. the frequency and the PQ and QRS times were unchanged, but on the other hand the extrasystolic stimulus was observed to be suppressed. No extrasystoles reappeared within an hour after the injection (Fig. 9).

Ajmaline was administered orally over a long

(a)

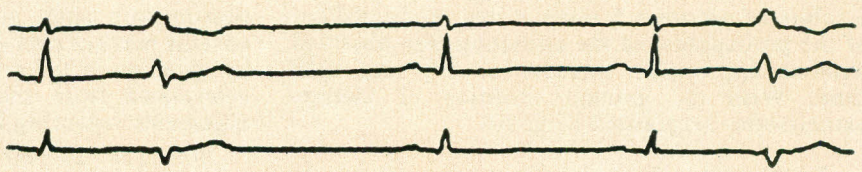


Fig. 8 (a) and (b).—73-year old patient with ventricular extrasystoles, with degenerative myocardial injury. 15 minutes after i. m. injection of 50 mg. ajmaline, elimination of extrasystolic rhythmic centre.

(b)

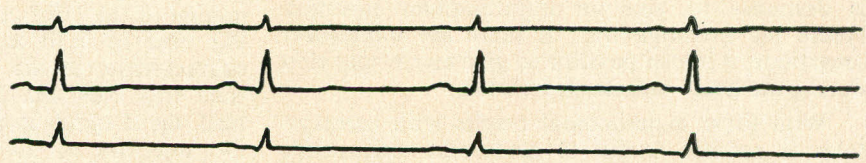


Fig. 9 (a).—Interruption of ventricular extrasystoles in a case of degenerative myocardial injury. 15minutes after i.m. injection of 50 mg. ajmaline, elimination of extrasystolic rhythmic centre.

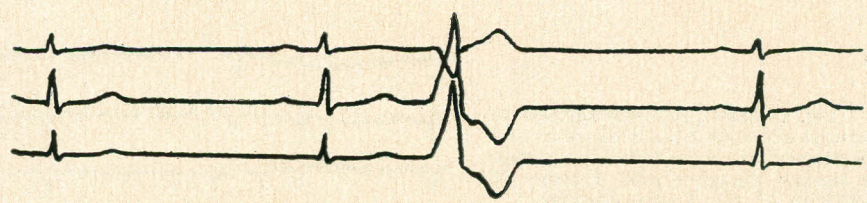
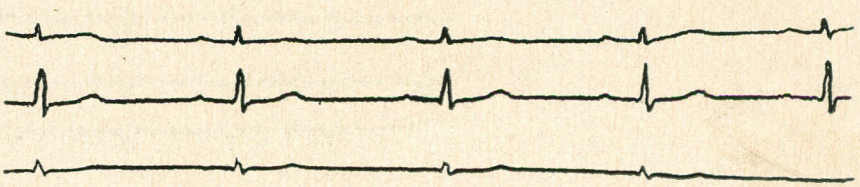


Fig. 9 (b).—Interruption of vantricular extrasystoles by 50 mg. ajmaline i. m. No appreciable variation of PQ and QRS time.



period to 20 patients. The effect was not so sudden as after injection treatment. In 5 cases the patients complained of loss of appetite and of stomach troubles, no doubt because of the bad taste of the uncoated preparation; this gave rise to disturbance of the regular intake of the preparation. It was possible to remove this drawback in the meantime by sugar-coating. In the 20 other systematically treated cases, the extrasystoles could not be completely eliminated in 7 cases, in spite of a maximum dose rate of 1 tablet (250 mg. ajmaline) 5 times a day. Weakening of the extrasystoles was achieved in only 5 of these patients. In two cases, a more favourable effect was attainable with Wenckebach pills or digitoxin (heart decompensation) than with ajmaline alone. Of the 13 patients who responded to the oral ajmaline therapy after a few days, 9 suffered immediate relapse after cessation of the treatment lasting several weeks. Four patients had no extrasystoles during a post-observation period lasting 4 months.

9. The 65-year old female patient, Anna K., was admitted for treatment on account of a degenerative injury of the myocardium. There was an extrasystolic rhythm proceeding from various parts of the Hiss bundle. After 10-day treatment with 1 tablet of ajmaline 5 times a day, normalization of the propagation of the excitation was observed, without appreciable increase of PQ and QRS time. With the gradual cessation of therapy, extrasystoles reappeared (Fig. 10).

Extrasystoles occurring in heart cathete investigations can also be influenced by ajmaline. It is desirable to give an intramuscular injection before the investigation. If there are unpleasant sensations, it is also possible to give an i.v. injection during the heart catheter treatment.

With these experimental results with extrasystoles it seemed useful to undertake therapeutic tests with other disturbances of the rhythmic pattern also. In 2 patients with *paroxysmal tachycar dia* the fits of heart racing no longer occurred on giving ajmaline orally. Lessening of the sinus tachycardia was also observed in several cases. On the other hand, in cases of flutter and fibrillation of the auricle with absolute arrhythmia, no success was achieved either with an i.v. injection of 50 mg. nor with oral administration of ajmaline at dose rates up to 250 mg., daily. It is possible that the control of these disturbances also is a question of the dose rate. However, we could not at first decide to exceed the stated doses. Further relevant indications call for still more thorough and careful checking, e.g., the use of ajmaline in paroxysmal auricular fibrillation. Parade advocated the use of ajmaline for prophylaxis of ventricular fibrillation, particularly from the point of view that extrasystoles occurring after an infarct can constitute the "starter" for ventricular fibrillation.

Our experiences in the treatment of the WPW (Wolff-Parkinson-White) syndrome give encouragement for further therapy tests. Too early transmission of the excitation from the auricle to the ventricle can definitely be normalized by ajmaline, as the following cases show. Whether the WPA syndrome, as manifestation of an aberrant transmission path, an injured heart muscle or a general nervous over-excitability, can be controlled by ajmaline in the same way cannot of course be determined from the hitherto rather theoretical arguments regarding its genesis.

10. The 29-year old patient, Siegfried Z., suffered from a combined aortic valve defect. The ECG indicated a pronounced left-hand type with noding of the QRS compiex in the 2nd lead. The PQ time of 0.10 sec. exhibited the shortening characteristic of the WPW syndrome. The QRS time was 0.09 sec. ST was lowered in the first lead, the Z spikes in the first lead were flat. After i.v. injection of 50 mg. ajmaline there was no appreciable variation of frequency. The PQ

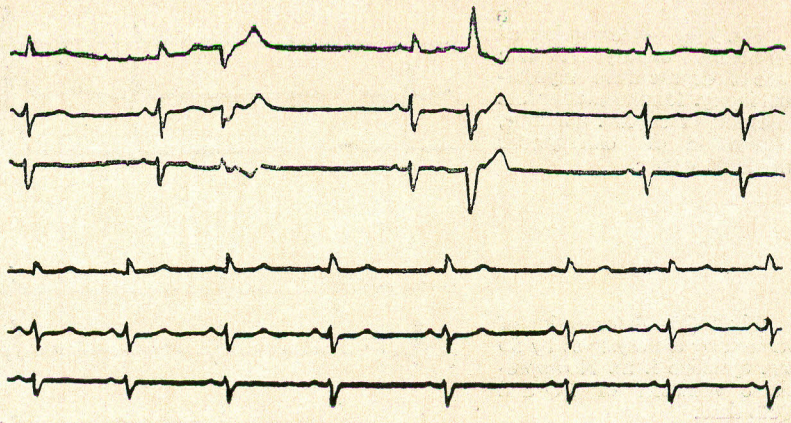


Fig. 10(a) and (b).—Elimination of various extrasystolic centres, in a case of degenerative myocardial injury, after a ten-day treatment with 1 tablet of ajmaline (50 mg.) 5 times (per day).

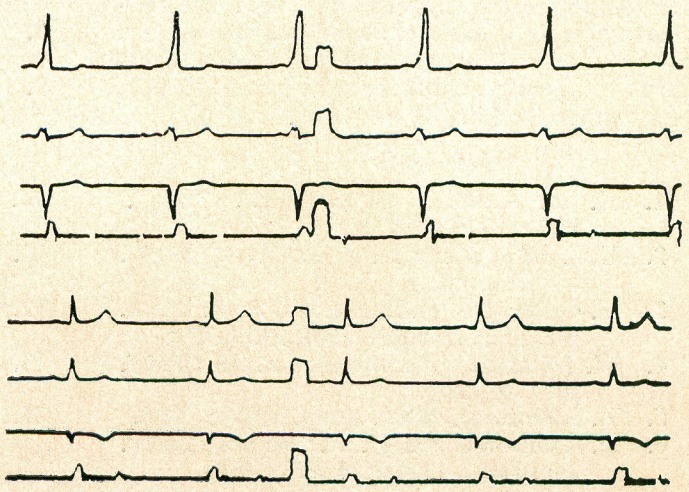


Fig. 11(a) and (b)—wpw syndrome in combined aortic- valve defect. After 50 mg. ajmaline i.v., correctly regulated transmission times. The PQ time increases from 0.10 sec to 0.14 sec., the slow rise of the R spike characteristic of the WPW syndrome is no longer observed after administration of ajmaline.

time increased to 0.14 sec. The slow rise to the R spike could no longer be observed, the splitting-up of the QRS complex in the second lead was eliminated. Moreover the ST sections and T spikes in the first lead became regular (Fig. 11).

Thirty patients with angina pectoris pains registered subjective improvement when given oral ajmaline therapy. There was however scarcely any difference in the ECG. It therefore seemed desirable to obtain, for disturbances of this type, a combination preparation with other coronary-enlarging substances (Gilucor [Gebr. Giulini GmbH, Ludwigshafen, Rhein]: ajmaline 20 mg. reserpinum hydrochloride. 0.05 mg., extract belladonna 5mg., 2.2- bisoxy - methyl - propandiol - (1.3) - tetranitrate [nitropenta] 8 mg.). Good results with this preparation were also recently reported by Martini and Busse. The use of this combination is also appropriate in cases of extrasystoles due to disturbances of blood circulation.

Combined use with substances working in the same way, in the oral therapy of disturbances of the heart rhythm, seems worth considering. Use of medicine compounded of equal parts of ajmaline and procainamide gave less satisfactory results than use of the pure alkaloid alone. Simultaneous use of tested strychnine is under investigation by us at the present time.

Parenteral therapy in the form of intravenous use of the preparation can be appropriate when it is desired to interrupt an arrhythmia of the heart or to initiate treatment quickly. Its extended use was not permissible for testing the preparation. Intramuscular administration will attain even greater significance for long-term therapy if and when a depot preparation with delayed resorption can be produced.

The simultaneous separate use of ajmaline with glycosides (also strophanthine and digitoxine) is, according to our experience, possible and even to be recommended in special cases (see case No.5). It does however call for a careful watch on the circulation conditions.

The mode of action of ajmaline observed by us clinically with extrasystoles of various origins coincides to a large extent with the results of the pharmacological investigations. In the control of disturbances of heart rhythm, an important part is played not only by the direct action on the rhythmic pattern but also by the improvement of the coronary blood circulation, the adrenolytic effect and the sedative effect which is noticeable only with rather high dose rates in man. Ajmaline by virtue of its positive inotropic action, especially on the weakened heart muscle, which we are at present investigating clinically, has advantageous differences from other preparations used in disturbances of rhythm, quinidine in particular. In the Rauwolfia alkaloid ajmaline we see an important new therapeutic substance whose use and further investigation may prove fruitful in the treatment of heart arrhythmia, in particular extrasystoles, which has not been very satisfactory up to the present.

Summary

A report is presented of the first clinical tests using the Rauwolfia alkaloid ajmaline as symptomatic therapeutic substance in disturbances of heart rhythm. In contrast to quinidine and procainamide, this substance can be used without danger of collapse. After administration of 50 mg., ajmaline there is nearly always an interruption of the extrasystolic rhythm. The effect is however

of relatively short duration, as is also the case after intramuscular application. With oral administration also, extrasystoles of various origins can be eliminated in more than half the cases. The use of ajmaline in other rhythmic disturbances is partly described, partly discussed.

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