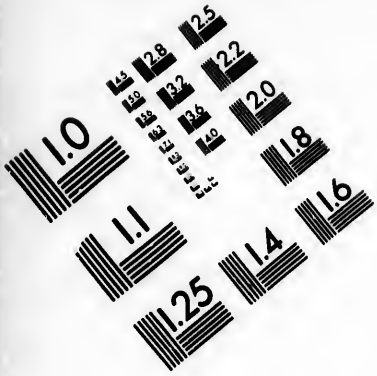



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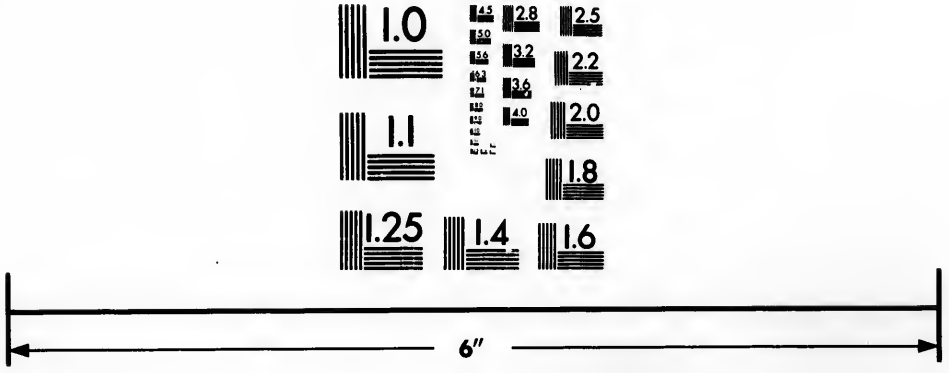


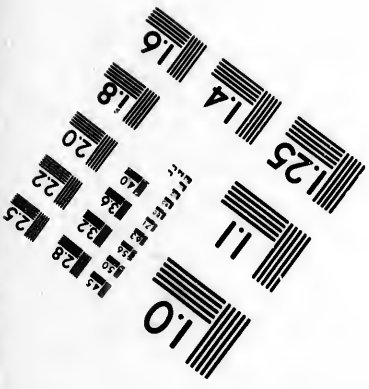


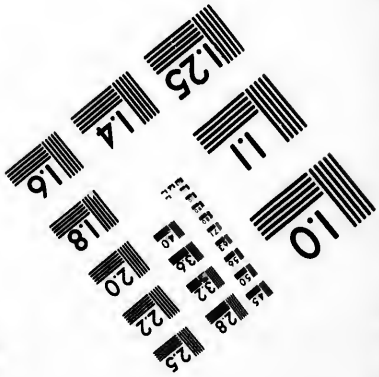


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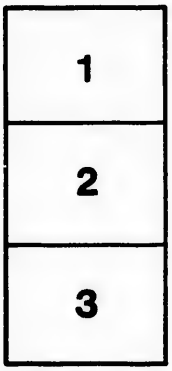


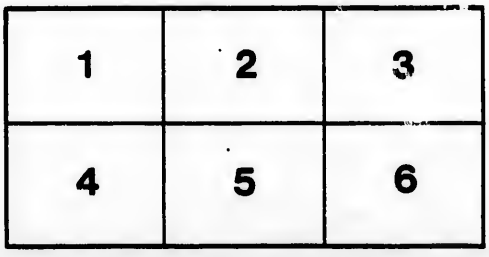

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# REPORT ON PHARMACOLOGY AND THERAPEUTICS.

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## ANTIPYRETICS.

It is proposed in the following article to give an account of two drugs recently introduced into practice belonging to this class, and to point out in a general way their worth as compared with agents of the same class that are, and have been for some time, in more or less every-day use. As these two agents are purely antipyretics, and have no influence directly, as far as is known, over the duration of any of the pyrexial diseases, it will be appropriate to indicate what are the necessary qualities of a good antipyretic. First, a desirable antipyretic should be able to act with promptitude; second, it should be certain in its action; third, its effects should last several hours; fourth, the subsequent ascent of the temperature should take place gradually; fifth, it should be devoid of untoward effects, especially those of a dangerous nature.

After considering the actions of these agents, we will be able to see in how far they fall short of those qualities.

## ANTIPYRIN.

This is an alkaloid, which, like kairin, is obtained synthetically from the chinoline series. It acts as pure antipyretic, reducing an elevated temperature from whatever cause produced.

Judging from the cases reported up to the present, it appears to have a more powerful influence on the pyrexia of typhoid and

tuberculosis than that of any other disease. Prof. Pribram of Prague reports nine cases of typhoid fever treated with it. In three of these cases, one of which was very severe, the disease ran a practically non-febrile course from the administration of a dose of antipyrin every time the temperature reached 100°F. In the first, which ran a course of 14 days, the above result was obtained by the administration of an ounce of the drug for the whole period. In the second, which lasted 24 days, 4 ozs. were administered ; while the third case, which had a duration of 13 days, only required a little more than half an ounce for the whole period to keep the temperature below 100°. In the remaining six cases, Prof. Pribram ordered only a sufficient quantity of the antipyrin to keep the temperature reduced to 100°, and this result was obtained by doses not exceeding 20 grains in the 24 hours. With the exception of one who died from double pneumonia, all the patients recovered.

The results of the antipyrin treatment of Prof. Pribram's cases may be thus summarized: By the use of large doses in three cases, the course was non-febrile ; the use of small doses in six cases prevented a rise above 100°.

Antipyrin is eliminated with the urine. This elimination commences about three hours after a single dose is given, and continues for a period of twelve hours. Its presence is detected in the urine by the chloride of iron, which, when added, changes the color of the urine to a brownish-red. The depth of the reaction with the iron test corresponds closely with the sinking of the temperature. The more influence exerted on the temperature, the more pronounced is the color on the addition of the test.

Demuth has recently reported a large number of febrile cases treated with antipyrin, including three cases of scarlet fever, four of diphtheritic angina, six of pulmonary tuberculosis, three of facial erysipelas, three of acute rheumatism, two of intermittent fever, one of typhoid, and four of pneumonia. To adults he administered half a drachm, repeated this in three hours, and then gave 15 grains every two or three hours until the wished-for reduction of temperature was brought about. In all, usually

not more than one and a half drachms was necessary, and the time occupied in attaining this was about twelve hours. The temperature fell promptly, often to the normal, and in a few of the cases to below the normal. Following the reduction of the temperature, there was a fall in the pulse-rate.

The antipyretic effects of the antipyrin was most constant in typhoid, next in the tuberculous cases. It was less marked in the diphtheritic cases, but in every case there was a distinct antifebrile action. Demuth did not have any untoward effects in his cases. In no case was there any cinchonism. The drug was taken readily, and did not cause any irritation of the stomach. Collapse symptoms were never present. In a few cases where the temperature was brought below the normal, the pulse was small, but it soon regained in power, even before the temperature had risen to the normal. In not one case could he observe that it had any directly favorable influence over the course of the disease for which it was given. As soon as its effects had passed off, the temperature regained its previous might. Its action did not usually last any longer than twelve hours.

Argutinski and others report various forms of rashes due to antipyrin. This observer has more than once noticed such from even as small a dose as seven grains.

Profuse sweating has been observed after the use of antipyrin, but this is of rare occurrence compared with the frequency with which it attends the use of salicylic acid, kairin, hydrochinon, &c.

Pavay, after a considerable trial of antipyrin, comes to the following conclusions:—

1. Antipyrin always reduces a high temperature in doses of from 2.0 to 4.0 (℥ss to ℥i), the minimum depression amounting to 2.5°F., the greatest to 7.2°F.

2. The reduction of the temperature sets in from one to two hours after the dose is given, and continues from 12 to 16 hours.

3. It does not exercise any marked influence on the pulse or respirations. The tension in the arterial system being increased after the fall of the temperature.

4. Sweating is generally observed, but never to such a degree as is observed when salicylic acid is given in antipyretic doses.

5. Nausea, vomiting, pain in the stomach, vertigo and noises in the ears only very seldom observed. Collapse never.

6. It possesses marked advantages over resorcin, hydrochinon and kairin, on account of its freedom from dangerous effects.

7. It acts with great certainty as an antipyretic in pulmonary tuberculosis, pneumonia and typhoid fever.

8. In acute rheumatism, it has an influence on the fever; none on the pain.

9. When injected under the skin or into the rectum, its antipyretic action is just as marked and as certain as when taken internally.

10. Its easy solubility and pleasant taste makes it a desirable antipyretic for children.

11. Its action does not diminish, even when given for a lengthened period.

12. It should be given with caution when there is cardiac weakness.

13. In pulmonary tuberculosis, it acts quicker and more certain than any other antipyretic. This is its great advantage.

### THALLIN.

Thallin is also a synthetic alkaloid obtained from the chinoline series. It forms salts, the lactates, sulphates and the hydrochlorates, especially, being adopted on account of their stability and easy solubility for internal administration.

Jaksch, first assistant in Nothnagel's klinik, reports 86 cases of different febrile disorders treated by these different thallin salts. The majority were cases of typhoid, acute rheumatism, erysipelas, puerperal sepsis, pneumonia and tuberculosis. In all the antipyretic action was marked, especially in the tuberculous cases. The temperature minimum occurred usually from two to four hours after the administration of the salt, while the duration of the fall was not longer than five hours. The ascent was generally attended with a rigor. In no case was any direct influence over the course of the disease evident.

Mingazzini has found no difference in the action of the sulphate and lactate of thallin. Either salt, in doses of 0.12 (2 grains),

reduces the temperature about 1°F., the duration of the fall varying from four to six hours. After doses of .25 (about 4 grains), there is a fall of 2½°F. Doses of .50 (8 grains) reduces the temperature quicker and lower than when the same quantity is given in two divided doses at intervals of three hours.

Thallin can be administered hypodermically without causing either abscesses or subcutaneous infiltrations. The fall of temperature, when given this way, is not only quicker, but greater. During the fall of the temperature, sweating, which is often profuse, is generally present.

Mingazzini did not observe vomiting, cyanosis, or symptoms of collapse in any of his cases, profuse sweating and rigors being the only unpleasant untoward effects observable. The more marked and durable the antipyretic effect, the more severe and prolonged were the rigors. In a few cases the rigors lasted two hours. Another undesirable effect that this observer noticed was that the temperature very frequently attained a higher level after the elimination of the drug than it previously had.

Thallin is eliminated with the urine, which it colors dark green. On the addition of chloride of iron, the color changes to a red.

### ANTIPYRIN AND THALLIN COMPARED.

*First, with respect to the certainty of action.*—Both agents have a very certain action, for, when given in appropriate doses in cases attended with considerable pyrexia, they reduce the fever. They both act more powerfully as antipyretics in the pyrexia of pulmonary tuberculosis and typhoid fever than that of any other disease. When antipyrin is administered, the temperature commences to fall in from one to two hours after, and continues falling for a period of from four to six hours, when the maximum fall is reached. Thallin is somewhat longer in causing a fall of temperature, taking usually three hours before any marked effects are noticeable; but once the effects are manifest, the maximum depression is quickly reached, usually within two hours after.

As regards the duration of the antipyretic effects, the fall in the cases of antipyrin lasts usually twelve and even sometimes sixteen hours, but with thallin seldom longer than six hours.

The subsequent ascent after antipyrin is somewhat slower than it is with thallin.

*With respect to untoward effects*, neither agent can be said to be perfectly free from them, but they are less marked after antipyrin than after thallin. Both cause more or less sweating, but with neither is this a contra-indication of any moment. Rigors frequently attend the subsequent ascent of the temperature after thallin, while they are extremely seldom seen after antipyrin. Both cause exanthems, which quickly disappear after the effects pass off.

In estimating the positive qualities of an antipyretic agent for evil, by far the most important point to take into consideration is the influence that it exercises on the heart. An antipyretic which has a cardiac depressant action is a two edged tool. This is the reason that kairin has been practically discarded from practice. In full antipyretic doses it is apt to cause symptoms of collapse. It is the possession of these qualities that makes large doses (20 grains and upwards) of quinine such a dangerous remedy. Salicylic acid is not free from this action either. With regard to antipyrin, no indisputable case has been brought forward where any symptoms of collapse have been apparently directly due to it. As much, however, cannot be said of thallin.

From the knowledge we at present possess of these agents, we may conclude that they are equally effective, but that antipyrin is the safest. Whether it is absolutely safe when given in proper doses remains to be seen.

### THE ANTIPYRETIC ACTION OF ANTIPYRIN, QUININE AND THE SALICYLATES COMPARED.

There can be no question whatever about the far greater efficiency of antipyrin. Its action is certain. The antipyretic action of quinine and the salicylates, on the other hand, is far from being so, if we exclude the action of the former in malarial fever and of the latter in acute rheumatism. He who relies on the anti-febrile properties of either of these drugs in pulmonary tuberculosis or typhoid fever will meet with frequent and great

disappointments. Further, they both constantly give rise, in full antipyretic doses, to the unpleasant group of symptoms known as "cinchonism," and not uncommonly we find their cardiac depressant action present in a greater or less degree.

There has been a good deal of speculation over the supposed mode of action of antipyrin and thallin in reducing temperature. It is highly probable that both of these agents have a direct action in lessening the production of heat. The reduction they effect is certainly not wholly due to a vaso-motor paresis, for the fall generally commences before the patient begins to sweat, and it is as pronounced in those cases unattended with sweating as in those which are. Further, they effect reduction of the temperature when agaracin (a powerful anhidrotic) is simultaneously administered with them. Whether they have a direct anti-parasitical action or not has not been shown or rendered even probable. Neither, as yet, have been shown to have any power directly of influencing the duration of any of the febrile diseases.