

Antifebrin in Pyrexia. By WM. JULIUS MICKLE, M.D.,
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The following relates to antifebrin as an antipyretic remedy. The cases were those of insane adult males. And what I shall have to say chiefly concerns phthisical pyrexia. Subsequently, I will briefly touch on the use of antifebrin in various inflammatory febrile maladies affecting the insane.

For convenience, will first be stated, in summary, some of the conclusions to which experience leads me: and then will be given brief abstracts of a few illustrative cases; both of phthisical, and of ordinary inflammatory, and other pyrexial, cases. In most of the instances in which it is not specified otherwise, the morning temperature was taken about 11 *a.m.*; the evening temperature at 9 to 10 *p.m.*

In subacute phthisis; if, for a time, the temperature shows moderate evening rise above the normal, the morning temp. being at or about normal; and then comes ascent to a moderately higher level of temp., both morning and evening, antifebrin, in a 5 grain dose, given late in the morning, lowers temp., and so checks the evening rise as to bring the evening temp. down, or nearly down, to the normal level.

In chronic phthisis; with a moderate evening rise of temp., the several earliest doses of 5 to 8 grains of antifebrin at night, not only reduce the temp. soon, but also make that of the following mornings both subnormal and lower than it had previously been. Omit antifebrin, and some days later the morning, and especially evening, temps. become raised, and the antifebrin at night reduces temp., and even that of the next morning, to normal.

In acute pneumonic phthisis, at first antifebrin reduces temp. moderately. It also changes the tendency, and the form of temp. chart, from those of morning rise of temp. to those of evening rise. Later on, antifebrin (grs. 8) reduces the temp. markedly, as a rule.

Speaking of chronic and acute cases more collectively; antifebrin, in some instances, given in the morning reduces a high morning temp., and keeps it reduced during the evening, a decided effect lasting 8, or 10, or more, hours. Yet, in some instances, given in the middle of the morning, it reduced the morning temp., but did not prevent a rise of

temp. in the evening, again, to the extent of 1° , 2° , or 3° *Fah.* But, in some instances, given on a high morning or evening temp. it reduced the temp. 4° or 5° , sometimes much less; the effect passing off in 6 or 4 hours; yet, subsequently, it did not keep down the evening temp. if given late in the morning, but did so markedly if given later on; and best if given (say) 4 hours before the evening temp. was taken.

The effect of a late morning, or midday, dose of antifebrin (8 or 5 grains) on the temp. of the afternoon and evening was usually more marked and protracted in chronic than in acute phthisis.

In chronic phthisis, with a temperature somewhat higher in the evening than in the morning; when the temp. began to range high, and 8 grs. of antifebrin were given at midday, the temp. by 6 p.m. and $9\frac{1}{2}$ p.m. was reduced, on the average, 4.7° *Fah.*; the temp., taken at the later of these two last-named hours, having usually risen about half a degree during the last 2 or 3 hours of this space of time. With temps. ranging less high the reduction of temp. at 9 p.m. was, on the average, 2.4° *Fah.*, under similar circumstances of treatment. In another case the average reduction of temp., so long afterwards (9 hours), was less, but here only 5 grains of antifebrin were given, *per* dose. In another, wherein the evening temp. usually, the morning temp. sometimes, was the lower of the two, and the temps. began to range higher, the high morning temps. under 10 grains of antifebrin, given immediately, were reduced, on the average, 3.8° *Fah.* during the evenings, that is to say from $6\frac{1}{2}$ to $10\frac{1}{2}$ hours later. In another case, with tendency to evening rise of temperature, when the morning temps. became high (102°) 8 grains of antifebrin, taken before midday, did not prevent the existence of a slightly higher temp. late in the evening (10 hours later); but on similar occasions 12 grains of antifebrin so reduced the temp. that even 9 or 10 hours later it was down 4.2° *Fah.*

As a rule, in chronic cases evening temps. of 100° — 3° were soon reduced by antifebrin, and the patients had warm perspiration.

On some occasions, in some cases—acute, subacute, or chronic—antifebrin failed to prevent some rise of temp.; or failed to affect temp. clearly or conspicuously.

In phthisis, therefore, in insane persons, with morbidly heightened temps., a moderate dose (5 to 8 grains; less in

the feeble) of antifebrin, given once, or at most twice, a day, has a marked effect in lowering temp.

When the temp. in acute or chronic phthisis reaches an unusually high degree, the effect of antifebrin in these doses in reducing temp. is less constant, and fails in some instances; although its effect in such cases is usually antipyretic, and it often lowers the temp. to a striking extent. But when the ordinary dose of antifebrin fails, the temp. remaining obstinately high, a larger dose (10 to 12 grains) often succeeds in a very decisive way, especially if now associated with tepid sponging of the body.

The effect of antifebrin in reducing temps. was usually marked in an hour or two, and continued from 2 to 10 or more hours; according to the conditions and circumstances of different cases, or of the same cases.

The pulse and respiration, as a rule, are lowered in frequency simultaneously with the fall in temp. under antifebrin. But the slowing of pulse and of respiration is apt to be less marked, proportionally, than the decrease of temp. In some examples the respiration was more lowered than was the pulse, proportionally;—in other examples the reverse was observed. In some instances the pulse-frequency was somewhat accelerated under antifebrin, notwithstanding that the temp. was diminished simultaneously. Less frequently, the same was true of respiration that was last stated as regards the pulse: namely, some acceleration notwithstanding the lowering of temp. When the temp. rose in spite of antifebrin the simultaneous rise of pulse and respiration was in some cases more than, in others less than, proportionate to the rise in temp. If the pulse was accelerated, simultaneously with a fall in temperature under antifebrin,—as in the exceptional examples a moment ago mentioned,—the pulse was sometimes found to fall again, as the temp. again rose and the effects of antifebrin were passing off. Here, the effect of antifebrin on the pulse was somewhat unfavourable, but of no decisive importance; the simultaneous lowering of temp. being a great, and far more than counterbalancing, benefit.

In one, unusually marked delusions of hostility and injury supervened on a large dose; but whether in any way connected therewith was not clear.

I utterly dissent from the observer (*Br. Med. Jl.*, March 3, 1888, p. 489) who states that the best initial dose in phthisical pyrexia is 10 grains. As a commencing dose, at least, this is

too large; and in many cases would not be altogether safe. Moreover, in many cases, its effects would be unnecessarily great—too great—upon the temperature, too disturbing to the organism. Five or four grains is sufficient to begin with. If it is attended only by good, but does not, in that dose, sufficiently control the temperature, it may be carefully increased, and the effects carefully watched. Only just so much must be administered, and with such frequency, as is capable of controlling the rise in temperature. Twelve grains I never exceed, and rarely prescribe so much. In feeble patients, with advanced disease, three grains is sometimes enough. To the very feeble, with far advanced pulmonary destruction, with marked exhaustion, or with cyanotic face and hands, I do not administer the drug at all. The drug is a good, but powerful, one; and skill and carefulness in handling it, therapeutically, must not be lacking. And I repeat that the doses I have mentioned were given once; at most, twice; in the 24 hours.

Since writing this paper, I find confirmation of these views in the experience of Stachiewicz, who in emaciated weak patients with advanced phthisis gave 1 to 2 grains; and to patients in fair general health, but either with recent progressive disintegration, or with old cavities and slowly progressing infiltration, of lungs, gave 4 to 8 grains.

As illustrations of the effect of antifebrin in reducing temp. in the inflammatory febrile states occurring in the insane I may mention such cases as those of:—

1. Vesical catarrh: hemiplegia: organic disease of brain: sclerosis of cord. Antifebrin, in five grain doses, had a fairly antipyretic effect.

2. Meningitis; hallucinatory confusion. When the temperatures ran high, antifebrin, grs. 8 to 12, reduced it for some time, and so that even 9 or 10 hours later the temperature was down 2° to 3°.— [Delirium came on whilst antifebrin was being taken].

3. General paralysis—last and bedrid stage—hypostatic congestion, and pneumonia; bedsores. Antifebrin grs. 4, and a fall of 6° in 2½ hours. Again, antifebrin grs. 3, and a fall of 2·2° in 2¾ hours; and of 4·4° in 9¼ hours. Another day, grs. 3, and a fall of 2·8° in 5 hours.

*Abstracts of some cases of phthisical pyrexia in adult males.—
Effects of antifebrin.*

1. Phthisis with congestive and inflammatory symptoms at one apex: diarrhoeal attack during which was tendency to

evening rise of temp., then a.m. and p.m. temps. about 99° ; then gradually rising temps., with *p.m.* exacerbations, and the morning temp. reaching 100.3° ; Antifebrin, grains 5 were given immediately, and the evening temp. was lowered to 99.4° . Next day, a.m. temp. 101.4° , antifeb. grs. 5, and p.m. temp. 98.4° ;—next day a.m. temp. 101° , antifeb. grs. 5, and p.m. temp. 99° ;—next day a.m. temp. 102° , the same dose taken, and p.m. temp. 98.4° . Subsequently, the temps. being below 100° , antifebrin was omitted; thereafter was usually a slight evening rise of temp. Thus, in a case with tendency marked to evening rise of temp., a single daily dose of 5 grains of antifebrin very decidedly reduced the, otherwise, rising temp., and so that the p.m. temp., 10 hours later, was within the range of 98.4° to 99.4° , the average fall of 2.4° contrasting strongly with what would have been a rise had it not been for the antifebrin's influence.

2. Chronic phthisis, tendency to evening rise of temp. For a space of time, morning temps. about normal, evening temps. just above 100° ; subsequently evening temps. about 99° ; then morning temps. between 100° and 101° ; and the evening temp. reaching 101.5° , 8 weeks before death; of antifebrin, grs. 5, were given, and reduced the temps. then; those of the following mornings, also, being again down to normal, or even below it. Here the first two or three night-doses were followed by a slightly subnormal temp., even so late as next morning.

Lungs: old, leathery adhesions; vomica at apex, and cirrhosis and slight bronchiectasis: caseous nodules and granulations scattered throughout lungs. Left lung the more diseased one. Kidneys slightly granular. Liver slightly lardaceous.

3. Phthisis and mitral regurgitation. Pneumonia and hæmoptysis supervenient on quiescent chronic tuberculization of right lung's apex, and lighting up rapid tubercular changes until death, $5\frac{1}{2}$ months later, at the end of December.

In August, Quinine in divided doses, grs. xv daily, yet temps. at times 102° — 4° .

In Sept., moderate effect of antifebrin, given occasionally, in reducing temp.

In end of Oct. and beginning of Nov., 4 grs. of quinine did not prevent the morning rise of temp., but added to its evening fall. From Nov. 22 to the latter part of Dec., patient on antifebrin, usually twice a day.

The tendency was, and had been, to a morning rise of temp.; but antifebrin (8 grain-doses) not only brought the temp.

down, but also changed the thermic rhythm, converting the cyclic tendency to a morning rise of temp. into a tendency to an evening elevation; and if given before the time of usual high morning temp. prevented the latter.

On Nov. 25th, 26th, and 28th, the high temp. of the morning was reduced by antifebrin in the 8-grain morning dose, and remained well down by 9.30 *p.m.*—Nov. 29th, 30th, and Dec. 1st to 5th, the antifebrin draught, usually given about two hours before the morning temp. was taken, reduced the latter to about 100°, except on one day, when it was 101·3°, and on another 102°. During the later days of this space of time the temp. rose somewhat again by evening (9 to 10 *p.m.*), and to 101°—2½°; but on two occasions only to 100°.

Now, after this, on Dec. 6th, no antifebrin was taken in the morning, and the temp. at 11.30 *a.m.* was 102·6°.—Haust. antifebrin grs. 8.—At 4 *p.m.* temp. knocked down to 98°; but by 9¼ *p.m.* temp. again 102·6°; Rep. haust. antifebrin; which lowered temp., but by next morning the temp. was again high (102·2°). Rep. haust. antifebrin, and this reduced temp., which by evening was still only 101·4°. On 8th Dec. antifebrin failed. On the 9th, given in *a.m.*, one hour before, it reduced temp. to 101°; but by 9.30 *p.m.* the temp. had again risen a little, and was 101·6°. On Dec. 12th a rising morning temp. of 101·5° was brought down, by antifebrin, 1° in one hour, but by night had again sprung up, and to the height of 103·4°; and on the 13th the draught, taken on a morning temp. of 101·4°, did not avert the evening rise to a higher level. On the 14th, antifebrin at 3 *p.m.* failed to prevent the temp. from rising by 9.30 *p.m.* On the 19th and 20th, antifebrin had produced but comparatively slight effect in three-quarters of an hour, and in half an hour. After this the usual rise of evening temp.—marked for several days—was stopped thus:—temp. 11 *a.m.* 100·5°; antifebrin at 5 *p.m.*; temp. at 10 *p.m.*, 98° only. Next day, given at 11.30 *a.m.*, it failed to prevent some little rise (four-fifths of a degree) by 9.30 *p.m.*—Thus, in this case, we trace a usual effect of antifebrin in a markedly falling temp.; and in a change of morning rise to evening rise. Also, given an hour or two before the time of usual high temp., antifebrin reduced the temp. of that time to about 100°; but to prevent an evening rise it (latterly at least) had to be given in the afternoon, a morning dose not being sufficiently protracted in effect for that purpose.

4. Chronic phthisis. Beginning sixteen days before death, antifebrin, in 4 or 5 grains doses, given after high evening temperatures, reduced the latter, and was followed by ordinary, *i.e.*, normal, morning temperatures. But one morning the temperature rose to 102·2°. Antifebrin was given at three *p.m.*, and, instead of continuing to rise, the temperature at 9.30 *p.m.* was only 101·2°.

Necropsy. Advanced caseation; considerable cavitation; old adhesions; 20 ozs. fluid in a pleural cavity. Basic congestion, and pneumonic patches.

5. First attack of phthisis about 10 years before death, entirely cured. A second attack of phthisis coming on about 3 years before death. From time to time, a cardiac apex murmur. In March, nearly eleven months before death, double basic pneumonia, delirium, irritability, destructiveness. At this time, also, dulness and somewhat bronchial breathing at apices, anteriorly. *Necropsy*; left lung, partly consolidated by caseous material, partly riddled by cavities; partly congested, œdematous. Old, calcareous and putty-like remnants of old cured tubercle. Right lung; in pleural cavity some lymph-flakes and 10 ozs. serous fluid; at the apex, cirrhosis, old dried-up tubercular changes, and a cavity. Heart; dilated left chambers, wide mitral orifice; aortic-valve changes. Pale, fatty-looking kidneys. Liver; slight cirrhosis, and perihepatic adhesions.

After having been on grs. 14 of quinine in the 24 hours, and this being omitted, he was ordered antifebrin 8 grs. in May; and had it much in May, June, and July; on a few days in Aug. and Sept.; on a good many days in Oct. The tendency was to evening rise of temperature. The antifebrin was, during the earlier part of the treatment, given at 2 *p.m.*, and repeated at night if necessary. The evening temps., which, earlier in June, had been 99° to 100° (except once 101·3°) became higher (99°-101°) after hæmoptysis on June 15th; and in July were irregular, occasionally 102½° to 103°. To briefly sum up;—Antifebrin, in doses of 8 grains, reduced the temperature decisively by two hours afterwards, the patient being also put, by its operation, into a warm perspiration.

6. Phthisis of over a year's duration. Died April 1st, 1887. In March, from 1st to 7th, grs. 10 quinine daily, and temps. (all but two), both *a.m.* and *p.m.*, ranged from 100° to 102°. Only a few doses of antifebrin, but these of marked effect, commencing March 7th. Before and after the days on

which antifebrin was taken, there was, usually, a slight morning rise of temp., but sometimes a slight evening rise. Then, for three days, the temps. beginning to run higher, antifebrin (grs. 10) was given after the morning temp. was taken.

1. Antifebrin $10\frac{1}{2}$ hours previously reduced *p.m.* temp. $2\cdot4^{\circ}$ below *a.m.* temp.

2. Antifebrin $6\frac{1}{2}$ hours previously reduced *p.m.* temp. $4\cdot2^{\circ}$ below *a.m.* temp.

3. Antifebrin $9\frac{1}{2}$ hours previously reduced *p.m.* temp. $4\cdot8^{\circ}$ below *a.m.* temp.

Patient, intensely irritable and entertaining delusions of evil intent against his life, now refused medicine.

Lungs: caseation; infiltration; cavitation; congestion; thick old close adhesions; reddened bronchial mucosa. Right lung, less excavation and congestion, but more œdema, of the two. Large, slightly lardaceous spleen. Liver, slightly lardaceous, old perihepatic adhesions.

7. Chronic phthisis; bronchitis; emphysema. Two and three months before death antifebrin in doses of 8 grains. Marked effect, on June 25, 1887, of antifebrin given on a *p.m.* temp. of 101° , and next *a.m.*, temp. only 97° , and lower than it had been for weeks previously, at least. On first six days of July, antifebrin, taken on high *p.m.* temps., reduced them, and next *a.m.* temps. normal. On 7th, *a.m.* temp. 102° . *Haust.* antifebrin. *P.m.* temp. only 100° . After several more daily doses, temps. kept for a time below 100° . July 15 to 21, *a.m.* temps. about 99° ; *p.m.* temps. $101^{\circ}-2^{\circ}$, and evening *haust.* antifebrin. July 24, *a.m.* temp. $100\cdot5^{\circ}$, morning antifebrin; *p.m.* temp. only $99\cdot6^{\circ}$.—25th, *a.m.* temp. $101\cdot6^{\circ}$, morning antifebrin; *p.m.* temp. only $98\cdot4^{\circ}$.—On 26-7-8-9, midday high temps. ($102\cdot6^{\circ}$ to $104\cdot6^{\circ}$), midday antifebrin; and at 6 to 9.30 *p.m.*, temps., *on average*, down by $4\cdot7^{\circ}$ Fah.; rising again, in two instances, $\cdot4^{\circ}$ and $\cdot6^{\circ}$ during the last $2\frac{1}{2}$ and $3\frac{1}{2}$ of those hours, respectively. Later on, temp. down; *a.m.* temp. about normal, *p.m.* temp. $100^{\circ}-1^{\circ}$; ordered antifebrin if temp. was above 100° .

8. Phthisis. Beginning two months before death, antifebrin, grs. 5, repeated at night if necessary. Later, 8 grs. and 10 or 12 grs. In May, antipyretic effect usually well-marked. The two doses, per day, on June 4th, 5th, and 6th, not markedly antipyretic. In June, temps. usually high at night; patient sponged and antifebrin increased on June 24th, on which day the morning dose of 8 grs. did not prevent evening elevation to 103° , and grs. 12 were then

taken; next morning, *a.m.* temp. 98·3° (antifeb. then); at night, temp. 101·5°, and grs. 12 antifeb.; next morning, *a.m.* temp. 99·4°; and so on, until, for the first time lately, came a high *a.m.* temp., 102·6°, and antifeb. grs. 12 (first *a.m.* dose for several days), and *p.m.* temp. 98·4° (fall of 4·2° at *p.m.*, in spite tendency to *p.m.* rise, lately). Next day, no antifeb. until usual evening rise had occurred. Similar series of events on July 2nd and 3rd. To July 10th, high evening rise—morning temp. about normal.

Necropsy. Advanced excavation, caseation, congestion and œdema of lungs; old close thick adhesions.

CLINICAL NOTES AND CASES.

*Cases of Disease of the Brain in Imbeciles.** By FLETCHER BEACH, M.B., M.R.C.P., Medical Superintendent, Darentb Asylum.

Actual disease of the brain is not so common in imbecility as want of development. It is more usual to find the convolutions simply arranged than to find tumours, hydrocephalus, sclerosis, etc. The convolutions in some cases are quite half an inch in width, and in such cases the arrangement must necessarily be simple. Occasionally there is a fairly complex arrangement, especially where the imbecility has come on in childhood. Sometimes the brains are very large, at other times very small; sometimes the convolutions are wide, at others narrow, but whether the arrangement of the convolutions be simple or complex, the uniform conditions found are imperfectly developed brain cells.

On this occasion, actual disease of the brain will be more especially considered, and I proceed to give examples. The two conditions producing undue size are hydrocephalus and hypertrophy.

Hydrocephalus may be present at birth, or come on afterwards. Of course all cases of hydrocephalus do not become imbecile. Some die, some recover without intellectual impairment; others neither die nor recover, but become imbecile. Probably hereditary neurosis is the deciding cause. The shape of the head in hydrocephalus is different from that found in rickets. In hydrocephalus the

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