

which has assumed the proportion of a scandal, to American medicine.

In the carefully prepared article which appears as a supplement to the above mentioned report, entitled "Coal-Tar Products, Especially Acetanilid," you have done well in calling attention to the dangers following the incautious use of acetanilid. You have done me the honor of referring to me as opposing the theory that the antipyretic influence is to be explained by the primary action of acetanilid on the corpus striatum, and as teaching the generally adopted view that its action is chiefly on the blood and circulation. In view of the importance of the subject, I feel that I am not trespassing too much on your space in asking permission to make my position a little more clear on the physiologic and toxic action of acetanilid.

The first point that attracts attention, from the clinical standpoint, is the marked discrepancy that is seen to exist among writers in regard to the size of the dose. The British Pharmacopoeia states that the ordinary average dose for an adult is from one to three grains; Sydney Ringer makes it four or five grains; the United States Dispensatory, from five to fifteen grains. In Germany several grams have been given at a dose; doses of four grams have been followed by serious collapse and recovery. On the other hand, patients have been made cyanotic and have collapsed with two or three grains, and death has more than once been reported from five grains. Numerous deaths from headache powders also have been reported; the principal constituent of these powders, as we know, is acetanilid. Recovery has taken place after the ingestion of nearly an ounce (31.1 gr.).

While idiosyncrasy or unusual susceptibility may, to some degree, enter into the explanation, yet it seems inadequate to solve all cases. I would suggest that impurity of the acetanilid may be responsible for some accidents. Anilin is very poisonous and the presence of anilin compounds, due to imperfect purification, might produce symptoms of collapse from small doses. As stated in my work on "Materia Medica and Therapeutics" (Fifth Edition, page 10), "Toxic symptoms are especially apt to occur when acetoluid is present." In this connection, we may recall the fact that Ritser (*Pharm-Zeitung*, 1890, p. 306) has called attention to the almost constant presence of toluidin in commercial anilin. (Quoted from United States Dispensatory, 18th Edition.) To return, however, to the subject of acetanilid itself, and to its proper physiologic action: As pointed out by T. Lauder Brunton, in his Croonian lectures on the "Relationship Between Chemical Structure and Physiologic Action" of drugs (1892), acetanilid has the simplest structure of any member of the group of aromatic bodies, and is the nearest to anilin, since it merely consists of anilin in which one atom of hydrogen is replaced by acetyl. It may also be regarded as ammonia in which one atom of hydrogen is replaced by phenyl and another by acetyl, hence it is also known as phenylacetamide. Structurally, therefore, acetanilid is closely related to phenacetin; but it is less soluble in water, and is more toxic than the latter. In its medical actions, it appears to be almost identical with antipyrin; but the latter does not cause alteration in the red blood cells, with the formation of methemoglobin, as acetanilid and its congeners do. This action is due to the decomposition of acetanilid in the blood and the liberation of paramidophenol, or a similar derivative. This action also occurs, although more slowly, in the case of phenacetin and its allies, and is absent after antipyrin (as stated by Cushny). The toxic action of comparatively small doses of acetanilid is thus explained. Small quantities cause the formation of methemoglobin within the blood cells, which remain intact; but larger doses destroy the blood cells and set free the methemoglobin in the plasma. Part of this, in escaping through the kidneys, may excite nephritis; and set up albuminuria, hemaglobinuria, or hematuria.

Without pursuing this interesting topic further, I would merely express my cordial agreement with the views expressed in the article referred to, especially the following paragraphs:

"That the action of acetanilid is more pronounced on the blood than on any other part of the system is generally recog-

nized. Consequently, its effects on the circulation, respiration, temperature, and elimination are all probably secondary to the blood changes, etc."

In conclusion, I wish to emphasize your final word of warning as to the cautious use of the drug, especially when the personal idiosyncrasy, or degree of susceptibility, to the toxic action of acetanilid is unknown. Compounds, or mixtures, of acetanilid with soda, ammonia, or other comparatively harmless substances, should not be administered in large doses indiscriminately, simply because they are advertised as being "entirely free from depressing action on the heart and circulation."

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#### Too Few Physicians—Hardly.

*To the Editor.*—An article has been going the rounds of the daily press, purporting to be an interview with me, bewailing the prospective scarcity of physicians. No such interview was ever held. The only grounds that could ever have existed for such an article was that while I was talking to another physician, I congratulated the people that good, yes, first-class medical schools would have fewer graduates owing to the fact that preliminary requirements and the standard of teaching had increased to such an extent that numbers would not rush to these colleges as had been the case before the rise in requirements. It is quality and not quantity that is needed. I have stood for quality all my life. I endorse the sentiment in your editorial: "Too few physicians? Hardly."

Yours truly,

A. W. McALESTER.

#### "Epilepsy of Syphilitic Origin."

PITTSBURG, June 9, 1905.

*To the Editor.*—The statement of Dr. John T. Moore in *THE JOURNAL*, June 10, p. 1855, that "practically all authorities agree that epilepsy, coming on during adult life, unless directly traceable to injury, should be regarded as syphilitic in character" ought not to pass without protest. Certainly the possibility of syphilis should be carefully considered; but there are other causes, among them innocent arteriosclerosis certainly may be reckoned and it would be wrong to give prolonged antisyphilitic treatment in all cases of epilepsy in which the attacks first appear in adult life and which are not traceable to injury.

THEODORE DILLER.

#### Report of Acetanilid Mixtures.

BROOKLYN, June 8, 1905.

*To the Editor.*—Allow me, as a subscriber to *THE JOURNAL*, to add my word of approbation for the work of the Committee on Chemistry. The results of this investigation are most profitable to us all as practicing physicians, and perhaps the word of good cheer for this undertaking from many quarters will not be amiss. I only hope that this work may continue.

HARRIS MOAK.

#### Whereabouts of Mr. Orriss Wanted.

PRINCESS ANNE, MD., June 10, 1905.

*To the Editor.*—A Mr. A. W. Orriss is operating among physicians, exchanging old medical books for new ones. Will any one knowing the whereabouts of such a person kindly communicate with

CHAS. W. WAINWRIGHT, M.D.

### Association News

#### Additional Through Train on Canadian Pacific.

To accommodate a number of members who wish to go to the Portland session over the Canadian Pacific Railway, that road announces that a special sleeping car for physicians and their friends will be attached to their train leaving St. Paul at 9:05 a. m., Tuesday, July 4, reaching Banff, Friday at 7:06 a. m.; Vancouver, Saturday at 10:45 a. m., and Seattle via Victoria and Puget Sound at 10:45 Saturday evening or all-