

vesico-abdominal fistula close within three weeks, but at the end of two months the only apparent communication between the bladder and vagina was by a pinhole opening to the left of the cervix, through which all the urine was discharged.

3. The radical character of the operation, in which I was not content to pare the edges of the divided cervix in the usual manner, but excised the portio entirely, thus removing all that remained of the uterus. The difficulty of avoiding the ureteric opening was also worthy of note.

4. The chill and rise of temperature immediately following the operation. I have been unable to find any satisfactory explanation of the phenomenon, but was impressed at the time with its resemblance to urethral fever in the male. There was absolutely no malarial element in the case. In this connection it should be stated that though I sought for some evidence from which I might decide whether the left ureter was occluded or not, I could find no definite information on this subject in any of the authorities consulted.

A CASE OF ANTIPYRINE POISONING, WITH THE FORMATION OF MEMBRANES IN THE MOUTH AND SYMPTOMS OF LARYNGISMUS STRIDULUS.

BY JULIUS L. SALINGER, M.D.,

ASSISTANT DEMONSTRATOR OF CLINICAL MEDICINE, JEFFERSON MEDICAL COLLEGE.

THE following case, illustrating the administration of antipyrine in small doses, with toxic effects of unusual occurrence, deserves to be recorded. The case is especially interesting, as the same symptoms occurred at three different periods following the taking of the antipyrine:

Mrs. W., æt. fifty-three, weight 212 pounds, very tall and of florid complexion; complained of pain in the loins in the region of the kidney. The pain was so severe as to make it impossible for her to lie on her back. The pulse was full and regular—about seventy-two in the minute. On cardiac examination no disease of the valves was found. The apex beat was full and bounding with a marked accentuation of the second sound. The examination of the urine gave the following result: sp. gr. 1026; reaction acid; color dark yellow; sugar none; albumin present; excess of urates. No tube-casts were found after repeated examinations under the microscope. There was no change in the amount of urine passed.

The patient had occasional periodic attacks of headache, unaccompanied by any gastric disturbance. The pain in the head was always in the frontal and parietal regions, and was very severe. A diagnosis of lithæmia with chronic contracted kidney was made. She was put on a

diet largely of fresh vegetables and milk, and all alcoholic and malt liquors were strictly prohibited. Drop doses of a one per cent. solution of trinitrin, pushed to its physiological effect, were ordered. The treatment seemed to improve the patient very much, and after two weeks she was able to lie on her back, and the pain in the region of the kidneys had entirely disappeared.

About this time the patient had an unusually severe attack of headache, and it occurred to me that the specific (?) for all headaches, especially of the lithæmic and gouty variety, antipyrine, was the indicated remedy. Accordingly, I prescribed five grains, to be taken every three hours, until the headache was relieved.

The first dose was taken about nine o'clock in the evening. Five minutes after taking the antipyrine the patient began to feel uneasy, complaining of flushes of heat, alternating with chilly sensations, principally along the spine, and in the face; the breathing became short and labored and almost immediately the lips and tongue began to swell. I was sent for in haste. On arriving I found the patient with lips swollen to almost three times their normal size; the tongue was already so swollen that it could be protruded only with the greatest difficulty. Her breathing was distressed, and very much resembled Cheyne-Stokes respiration. The pulse was quick, feeble, and irregular—about 160–168 in the minute. The temperature was 101.3°.

Spasmodic contractions of the muscles of the neck and face now commenced, but principally of the muscles of the larynx. The spasm was irregular in coming on, the intermission being from one to three minutes, and lasted about half a minute each time. During the spasm the patient would become blue in the face and would struggle for breath. Cold perspiration broke out all over the body. In the meantime the lips and tongue still continued to swell until the tongue became so swollen that it could no longer be contained in the mouth and protruded between the teeth.

I gave the patient a hypodermic of sulphate of morphine (gr. $\frac{1}{4}$) and sulphate of atropins (gr. $\frac{1}{16}$). The spasmodic contractions of the larynx decreased at once in both vigor and frequency, although there was still action of the muscles of the face and larynx for the next twelve hours—in fact, during the whole night. During these spasmodic contractions she lost control of the sphincters of the bladder and rectum, and urine and feces were voided involuntarily. On the following morning a reddish, elevated, erythematous eruption was noticed between the fingers and toes, in area at first no larger than a cent. There was no itching, the skin being covered with perspiration.

The patient lay in a comatose condition, being roused only with the greatest difficulty, immediately relapsing into her drowsy state when left undisturbed. The pupils were contracted to almost a pin-head in size. This contraction of the pupil could not be attributed to the hypodermic of morphia, for the pupil remained in this condition for the next six days.

There was no urine voided in the next twenty-four hours, so that it had to be drawn off with a catheter. Only about five ounces were obtained. The examination of the urins gave the following result: sp. gr. 1.032; color dark red; reaction alkaline; albumin present in large amount; sugar none; sediment, urates in excess. There were no tubercles present.

The eruption between the fingers and toes gradually became better defined and soon assumed the well-known appearance of urticaria. The eruption was also found in large blotches upon the face, neck and arms. It was evident that the eruption began to itch now, as the patient kept up an almost constant scratching.

The comatose state lasted about thirty-six hours. The patient could not talk after coming out of her stupor, probably on account of the swollen condition of her tongue (which was enormous), lips, and pharynx. The patient communicated her wishes in writing. On the third day a white false membrane began to form on the tongue, lips, and pharynx. It began by a deposit of white, round spots, which united with each other and formed a white membrane, very much resembling diphtheritic membrane. When the membrane was removed by tearing moderate bleeding set in with almost immediate reformation of the membrane. She complained very much of pain on deglutition, and it was with the greatest difficulty that she was able to take food.

The temperature ranged between $101\frac{1}{2}^{\circ}$ and $103\frac{1}{2}^{\circ}$. The curious part about the temperature was, that it was always higher in the morning than in the evening, the lowest temperature usually being found between the hours of eight and twelve in the evening.

On the morning of the fourth day she began to spit up large quantities of phlegm. At first the expectoration consisted largely of mucus, but it soon changed to muco-pus, and on the fifth day large quantities of pus, tinged with blood, were ejected. From six to eight ounces were ejected during the next few days. The odor from this discharge was sickening, and all the windows and doors had to be kept open to obtain proper ventilation.

Looking into the mouth numerous abscesses varying in size, usually about as large as a chestnut, were seen in the gums, tonsils, and base of the tongue. I counted thirteen different abscesses. The pharynx and post-nasal space were very much inflamed.

The patient was in bed twenty-six days; when able to get up she was so weak that she had to be assisted in walking. She lost twenty-four pounds in weight. The fever disappeared gradually; there was less pus discharged, but the last symptom to disappear was the urticaria. Even after the last trace of urticaria itching of the skin persisted for some weeks.

She remained well for two months, gradually regaining strength. Another attack of severe headache came on, and the patient, not suspecting that the antipyrine was the cause of her last trouble, again took a five-grain powder, without my knowledge.

Precisely the same effect as with the first dose of antipyrine two months ago occurred. The flushes of heat and cold, with rapid pulse, and swelling of the lips and tongue, again occurred. The muscular contractions of the face and neck were not so marked this time.

The appearance of the urticaria was more marked than in the preceding attack. Prof. J. M. Da Costa saw her in this attack with me, and agreed that it was a case of antipyrine poisoning. The attack lasted sixteen days. The patient lost six pounds in weight. There was also in this attack an increase of albumin in the urine.

Three months later another attack took place, precisely similar to the preceding ones. This attack again followed the taking of antipyrine by

the patient for her headache. The symptoms were all milder, except the contractions of the muscles of the neck and larynx. These contractions had to be again controlled by administering a hypodermic of morphine and atropine. The eruption of urticaria between the fingers and toes was very marked. The patient was well again in ten days.

All the symptoms which this remarkable case exhibited have been noted before in instances of antipyrine poisoning, except the formation of the whitish-yellow membrane on the tongue, lips, and pharynx, and the multiple abscesses. To account for these would be a very difficult matter, except as a manifestation of sepsis. Urticaria has often been mentioned as occurring in cases of antipyrine poisoning, and it was this symptom more than any other which called my attention to the correct diagnosis of the case. The swelling of the lips and tongue is not a very usual symptom, still it has been noted in several instances.

Dr. Oscar Jennings, in the *Lancet*, 1888, reports a case of antipyrine poisoning characterized by swelling of the lips and tongue, so that for six hours his patient was in danger of suffocation. All of the other symptoms noticed in my case were present, except the formation of the membrane on the lips and tongue and the abscesses.

The patient whose case has just been narrated takes antifebrin, exalgin, and phenacetin with perfect freedom from attacks of the kind just described. In fact, phenacetin is the drug on which she now relies when her periodical headache occurs.

This case is certainly a warning against the indiscriminate use of antipyrine, especially by the laity. A drug which can produce such symptoms as those just enumerated is entirely too dangerous to be dispensed over the counter by druggists and other unauthorized persons.