of red corpuscles. I drew attention, however, at the time to the probability that the thyroid gland in some measure acted on effete products in the plasma, and that, in the absence of such action, the anæmia might in part be secondary. It may be reasonably urged that this is not logically the question of "blood formation," and in one sense it is not, but in another and broader one it is.

We run, it seems to me, a danger of narrowing our views if, while yet aware of the constantly-changing metabolic processes which the blood not only subserves but participates in, we look to one set of organs—so-called "blood-forming"—for production of such a highly complex and ever-changing fluid tissue. It is always difficult for an incomplete experience to generalise without becoming vague, and I am thoroughly conscious that what I wish to express may not be evident to my readers. Perhaps it will be clearer if I add that, from the standpoint now advocated, the blood plasma not only, of course, is reinforced by digestive products absorbed through the alimentary system, but that, while giving up components on the one hand, it is added to and altered on the other by practically every tissue it passes through, by some more, by some less. We have only to consider closely the phenomenon of secretion to recognise the probable truth of this.

Among the tissues which more especially influence the blood plasma, I would, as in 1885, put the thyroid gland among the first, and I believe it operates more especially on the precursors or relatives of the mucinoid bodies. In this sense it seems to me to deserve the epithet of "blood-forming." Failing to do its duty, clearly the gravest disorganisation of the blood as a whole—for of course the corpuscles are not independent of the character of the plasma bathing them—would result. Hence the anæmia.

I would now refer back again to the corpuscles. I do not yet see reason to doubt my former conclusions, namely, that the embryonic tissue in the gland is truly hemacytopoietic, and the grounds for those conclusions need not be repeated here; but of course they have yet to be further tested by further research, and substantiated or rejected as the case may be.

Finally, since the common term "blood-forming," however much one may object to it, is not likely to fall into disuse, I may remark that, if we temporarily adopt with a protest the terminology usually conveyed by it, the views above expressed embody its meaning in suggesting that the thyroid "forms" both plasma and corpuscles, and that in addition the latter suffer if the plasma becomes abnormal by failure of the proper function of the gland.

ON TWO CASES OF POISONING BY ANILIDES (EXALGINE AND ANTIFEBRIN).¹

By T. JESSOPP BOKENHAM, M.R.C.S., L.R.C.P., L.S.A.,
AND
E. LLOYD JONES, M.B., B.C.(Camb.).

CONSIDERING the large number of artificial drugs which have recently come into general use, and the imperfect state of our knowledge as regards their exact physiological action, it is somewhat surprising that more mishaps have not occurred as a consequence of their use. Although acetanilide (antifebrin), antipyrin, and similar drugs are very largely prescribed, and are even used by patients on their own responsibility, yet there seems, judging from the English journals, to have been a considerable immunity from alarming toxic effects. This being the case, we feel that no apology is needed for recording the two following cases.

CASE I.—M. L., a girl, aged 24 years, had myelitis, with great pain in the back and limbs. There was no elevation of temperature. On June 3rd it was decided to give exalgin (methylacetanilide) with a view of relieving the pain. From this date until June 8th the drug was given in doses of gr. ij ter die. The dose was then doubled, but as even this amount failed to give relief it was further increased on June 10th to gr. vj ter die, and continued until June 17th, when symptoms of poisoning first set in. At 10.30 A.M. on the 17th the lips and cheeks were noticed to be blue, the pulse was small and compressible, but not rapid, temperature being normal. Though there were no very urgent symptoms the drug was discontinued, and brandy $\mathfrak{z}$ ij was ordered every hour. The patient stated that the medicine made her feel "sick and

giddy," that her sight was indistinct, and that there was a feeling of weight at the epigastrium. At 3.30 P.M. a few inhalations of amyl nitrite were given; this considerably emphasised the blueness, and caused marked dilatation of the vessels. It was thus evident that the whole of the circulating blood was profoundly changed. The cyanosis continued to increase, and at 3.45 P.M. the patient vomited, after which it became still more marked. At 4.10 P.M. her nails, lips, and cheeks were deeply cyanosed; frothy saliva was escaping from her mouth; she was delirious, and appeared to recognise no one. Her feet were not blue nor cold. Temperature 99.8° F.; pulse 144, very small, regular, compressible. The amount of stimulant was increased, and liq. strychninæ $\mathfrak{m}$ ij given hypodermically, a mixture containing tinct. digitalis $\mathfrak{m}$ x being also given by the mouth. She began to improve, and at 9 P.M. her condition, save for slight cyanosis, was fairly normal. She slept well at night, and had no further untoward symptom.

As regards this patient's previous condition it should be stated that her bowels had been opened only by purgatives and had not acted on June 14th, 15th, or 16th. She had not menstruated for some months.

CASE II.—K. B., a lady, aged 43, very subject to migraine, was seized with a severe attack shortly after rising on June 5th. She had been for some months much relieved by antipyrin on these occasions, but latterly this had failed; acetanilide, however, in doses of 5 grammes, had generally been successful in relieving the pain.

A short time before this date, thinking that the introduction of a bromide atom into the molecule would render acetanilide more powerful as an analgesic, one of us had obtained a specimen of monobromacetanilide from Schuchardt, of Götting. Having used this body with personal benefit, the patient was given two powders (0.25 gramme in each) to use for the next migraine. At 10.30 A.M. the patient took one of these powders, and, getting no relief, at 11 A.M. took a second. At about this time she noticed her lips were rather blue, but laid no stress on it. Finding the headache no better, at 11.30 she, of her own accord, took 0.5 gramme of acetanilide, and repeated this dose at 12.15 and 1 P.M.; headache not relieved. She had a good appetite for lunch, but it was noticed that she was very cyanosed, and she confessed to feeling "almost intoxicated, and very giddy." She took some whisky and lay down, but the headache became worse. At about 3 P.M. her clothes "felt tight, and the pressure almost suffocating." She tried to undress, but was seized with pain in the left shoulder starting from the cardiac region, and extending to the tips of the fingers. She was quite unable to call anyone to help her, and lost consciousness. When found soon after, however, she was conscious again, feeling only giddy; the headache persisted, and the pain in the arm returned with every attempt at movement.

At 5 P.M. her condition was as follows: The pulse was 108 and easily extinguished; the respirations 24, somewhat shallow; the temperature was 99° F.; heart's action feeble, and a mitral systolic murmur at apex; mental condition perfectly normal; arm still painful on movement, and a tendency to close the eyes unless speaking. On being questioned as regards this closure of the eyes, she answered that it was only because it "wasn't worth while keeping them open"—not because she was drowsy. She felt hungry and thirsty, and took some tea with bread and butter. The cyanosis was said to be less intense than in the afternoon.

At 7 P.M., the heart being very weak, nitro-glycerine $\mathfrak{r}_{10}$ grain was given. Great dilatation of vessels was produced, with increase of cyanosis. The heart sounds were feeble; there was no murmur. Alcohol, strychnine, and digitalis were now given at frequent intervals, and the cyanosis diminished.

At 11 P.M. the temperature was 100.2° F.; pulse 120, soft; respirations 28. Faintness was induced by the least movement, and pain in the shoulder and arm was still present; headache no better; cyanosis much less. Next morning, at 11, the temperature was 99.4° F.; the patient had not slept during the night, but the cyanosis was almost gone, the headache was better, and the pulse stronger; hands distinctly puffy. A stimulant treatment was adopted through the day, and in the evening the patient was practically well. Urine was watched for albumen and blood residues, but none was found. No very marked anæmia followed the attack. It is to be noticed, also, that this patient became ill on the third day of normal menstruation. Bowels were perfectly normal throughout.

REMARKS BY MR. BOKENHAM.—The drugs used in these two cases, together with the symptoms produced, were much alike.

¹ Read in the Section of Pharmacology and Therapeutics at the Annual Meeting of the British Medical Association, held in Leeds.

The connection between the drugs will be clearly appreciated from a study of their graphic formulæ:

In each case the carbon atoms of the benzene ring have been omitted for the sake of clearness.

The condition of the blood in these cases reminded me of a similar condition produced in animals by Dr. Lauder Brunton and myself by the administration of nitrites, hydroxylamine, and some other nitrogenous bodies. In these the blood was found to contain much methæmoglobin, and in many cases to coagulate with a well-marked buffy coat. The heart, too, was much weakened, and it would seem that in all these cases the enfeeblement was due to the blood acting as but a poor nutrient medium to the heart substance. It is strange that there should not have been (in the second case) any marked affection of the mental condition.

As regards the condition of the patients which led to the change in the blood, it is very difficult to obtain any clue. In the first case, the antecedent constipation may have led to an accumulation of exalgine in the body sufficient to produce toxic effects. As, however, the drug is excreted for the most part by the urinary organs, and as these were unaffected, it is difficult to admit of this as being the true explanation. It is not possible that any such cause could have been at work in the second case, as the symptoms seem to have commenced soon after the first dose, which was a very small one. If the whole result is to be attributed to the bromine atom, in the case of the monobrom-acetanilide, there remains still to be explained the fact that no cyanosis followed its use by myself. The most attractive theory is that the toxic symptoms in each case were due to an unusual decomposition of the drug in the body; and, in the second case, it is very possible that menstruation may have been the means whereby some new substance accumulated in the blood, which reacted on the drug; or, to put the matter in another way, the accumulation of a substance (possibly of the nature of an albumose) in the body may have caused: (1) the menstruation; (2) the headache; (3) the unusual action of the drug. Mr. Jones has been unable to obtain exact evidence as to the time at which the menstrual nixus should have appeared in his patient. It is, of course, possible, though highly theoretical, that in her, too, the conditions which produce menstruation were present, but were prevented from acting in the ordinary way by her physical condition. It will not do, however, to press this point further than to bear it in mind as a possible cause of some cases of poisoning. Unfortunately, the condition of patients is not mentioned in other recorded cases. Popular beliefs, which are well known, as to the condition of a woman at the catamenial period, such as the inadvisability of her entering a dairy or touching fresh meat, etc., may have, after all, some foundation in fact.

Acetanilide had once an unexpected, though not alarming, effect on myself. During an attack of typhoid fever last year I was given large doses of acetanilide with the usual fall of temperature; one day, however, the drug failed to lower temperature, and the urine passed during that day was noticed, after standing for some hours, to have become dark chocolate coloured. This never occurred on any other occasion, and I certainly did not suffer from cyanosis. Here, too, it seems that the drug was decomposed in an unusual way.

In conclusion, it may be useful to state briefly the results obtained by experiments on animals. As regards acetanilide, Lépine produced in dogs trembling, "apathy," weakness, and fall of temperature, with loss of excitability of peripheral nerves. The arterial blood became, in some cases, of a dirty brown colour, loaded with methæmoglobin; the corpuscles were said, however, to be unaltered either in number or shape, and the serum was not tinged. Analysis of the gases of the blood showed great deficiency in oxygen. Large doses depressed the heart's action.²

As regards "exalgine," Binet³, working with methylacetanilide,

has observed in cats and rabbits similar changes in the blood, with much salivation.

Cyanosis is also a marked feature of poisoning by aniline: the base

from which all these bodies are derived.

CASE OF HEPATIC ABSCESS, SECONDARY TO SEVERE PELVIC PERITONITIS FOLLOWING UPON SALPINGITIS, WITHOUT DEFINITE SYMPTOMS DURING LIFE.¹

By JOHN LINDSAY STEVEN, M.D., F.F.P.S.G.(EXAM.)

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THIS case is one of great interest from many points of view; and although I cannot enter into detail with regard to the clinical aspects, yet, from the purely pathological standpoint, many most interesting considerations arise. Not the least interesting of these is the fact that a patient should be the subject of such exceedingly severe inflammatory changes in vital parts without their giving rise to symptoms which would at once direct attention to the organs mainly involved. Yet so it was in the present case; the patient from first to last made no complaint referable to the pelvic organs. The cause of the pelvic peritonitis is also another interesting problem which arises out of a consideration of the facts met with in the case, and the relationship of the hepatic supuration to the pelvic inflammation is well demonstrated.

I shall first of all give an account of the *post-mortem* examination, and then make one or two remarks with regard to the bearing of the different facts in the case. The patient was a domestic servant, aged 18, unmarried. The case during life was regarded as one mainly of phthisis pulmonalis, the patient having been admitted complaining of pain in the back and belly, and with a history of pleurisy of the left side on two occasions. There was no spit, but little cough, and a very distinct hectic temperature. No signs of disease could be detected in the apices, but there was marked dulness at the left back. The menstruation was regular, but latterly scanty and at times delayed. There was slight albuminuria, probably due to menstrual blood. There was no diarrhoea. There was no family history of tubercle.

Post-mortem Summary.—Pelvic peritonitis, with uterine catarrh and salpingitis; secondary pyæmic abscesses of liver and spleen; old pleurisy of left side, with fibrous condensation of left pulmonary base; double vagina—one rudimentary.

External Appearances.—A fairly well-nourished body. On opening the peritoneal cavity, it is found that the left lobe of the liver is adherent to the anterior abdominal wall, and that thick yellow pus issues from beneath the ensiform cartilage. The intestines are considerably distended; the pericardium contains several ounces of clear serous fluid; and the lungs, except at the extreme base on the left side, are quite non-adherent.

Chest.—The heart weighs 9 ounces, and, with the exception of some paleness and flabbiness of its muscular tissue, presents nothing abnormal. The right lung presents quite healthy characters. The left lung is very firmly adherent at the base, and its tissue in the lower lobe has undergone a fibrous transformation; elsewhere its tissue is healthy.

Abdomen.—The diaphragm is generally adherent to the liver and to the enlarged spleen, so that it is necessary to remove liver, spleen, and stomach *en masse*. The adhesions between liver and diaphragm are not very firm. On section of the liver it is found to be the seat of very numerous, large, ragged, abscess cavities containing a mixture of bile and pus. It weighs 70 ounces. One or two small abscesses are also seen in the spleen, which is more firmly adherent to the diaphragm than the liver is, and weighs 11½ ounces. The mucous membrane of the stomach is quite healthy, and the hepatic papilla is normal and pervious. The

² Hemoglobinuria has been recorded, however, as a symptom of acetanilide poisoning in human beings.

³ *Rev. méd. de la Suisse Romande*, April—May, 1889.

¹ Read at the Glasgow Medico-Chirurgical Society.