The operation was not done; tetany and general convulsions eventually developed, and the child died unrelieved. I have noticed a remark by Dr. Sidney Ringer, in his *Handbook of Therapeutics*, which is the only reference I can find to the palate as a cause of laryngismus. He says:² "It may be useful here to advert to a condition not uncommon in infants. An infant in poor health frequently wakes up at night from 'a catch in the breath.' From some unexplained reason, it cannot for a time get its breath, and wakes up with a loud snore. This condition is altogether different from that of laryngismus stridulus, and the fault appears to lie in the soft palate, not in the larynx; moreover, it is not due to enlarged tonsils, as this 'catch in the breath' occurs in children of tender age, long before the morbid condition of the tonsils takes place."

I must say that I have not since seen any case with such an amount of elongation and thickening of the uvula, although, having examined a considerable number of cases, I have nearly always found the soft palate considerably congested, and I would strongly urge everyone to examine the fauces in all cases of laryngismus. It is just possible that the treatment which I have adopted in every case since, that of cold sponging, so strongly advocated by Dr. Ringer, has been the means of preventing such an aggravated condition developing, and I can strongly endorse what Dr. Ringer says of its good effects. An important part of the treatment, however, is diet and fresh air. Most of these children are hand-fed and breathing bad air; they get not only too much starchy food, but also a deficiency of albuminates and fats.

The hygienic surroundings are usually bad. It is a condition much more common in the early part of the year than at any other time (Dr. Gee says from January to the end of June), and more common among boys than girls. Several cases may occur in a family, the same causes operating in each case. The majority of such cases get well if the right treatment is adopted in time, but I would strongly advise an examination of the throat as a matter of routine in all cases of laryngismus, for occasionally the cause will be found there, and if so may easily be removed.

NOTE ON A POSSIBLE MEANS OF ARRESTING THE PROGRESS OF MYXEDEMA, CACHEXIA STRUMIPRIVA, AND ALLIED DISEASES.

By VICTOR HORSLEY, B.S., F.R.S., F.R.C.S.,

Surgeon to the National Hospital for the Paralysed and Epileptic, Assistant
Surgeon to University College Hospital, Professor of Pathology in
University College, London, etc.

It is believed, probably, by most practitioners and pathologists of the present day, that the diseases known as myxœdema, cretinism, cachexia strumipriva are the result of want of function of the thyroid gland. This position, at any rate, is that which received most support from the committee appointed by the Clinical Society under the chairmanship of Dr. Ord to inquire into the subject, and it has been endorsed by everyone who has paid personal attention to the point with the exception of Professor H. Munk and Dr. Drobnik. For the purposes of this brief note I shall assume that the view of the majority is correct.

Quite recently a very valuable paper has been written on the prominent early symptom which follows total ablation of the thyroid, namely, tetany, by Dr. Anton von Eiselsberg, Assistant in Professor Billroth's Clinic. In this monograph (entitled *Ueber Tetanie im Anschluss an Kropf-operationen*, Wien, 1890), Dr. Von Eiselsberg, after a masterly examination of this dangerous phenomenon, gives the records of an elaborate and careful series of experiments upon cats, from which he confirms the opinion referred to above in the fullest manner, and adds many exact results to the literature of the subject. I particularly wish, however, to draw attention to the cases in which he repeated and extended Professor Schiff's fundamentally important observation on the effects of transplantation of the gland into the peritoneal cavity, etc.

In 1886, I referred in this JOURNAL¹ to Professor Schiff's pioneering investigations. That observer found that in dogs "thyroidectomy loses its danger, and an essential amount of its effect, if one previously introduces and fixes in the abdominal

cavity other thyroid glands from an animal of the same species."²

Dr. von Eiselsberg, pp. 23, 24, 25, describes a number of similar experiments in the following manner: In nine animals extirpation of one (the left) thyroid gland was performed, the lobe kept warm in normal saline solution, and quickly transplanted either into a fold of mesentery or into the subperitoneal tissue. At dates varying up to three weeks the other half was removed from the neck. Of the nine animals eight died of typical symptoms of loss of the thyroid. *Post-mortem* examination showed in these eight fatal cases that the transplanted gland had not healed *in situ* or was degenerated. The ninth animal, however, survived, and increased in weight. It was killed, and a *post-mortem* examination revealed the fact that the gland transplanted into the peritoneal cavity had organised, was vascularised, and in no way degenerated. In four more cases the transplanted gland was placed between the fascia and the peritoneum. Of these, in three cases the transplantation failed, owing to the necrosis of the graft, and of course the animals succumbed. In the fourth case, however, the animal was perfectly well (and had grown) three months and a half after the extirpation. It was killed, and, on *post-mortem* examination, the gland was found in functional activity in the abdominal wall, highly vascularised, etc.

These results show conclusively that the transplanted gland, if it can be got to live after the grafting, will, in its new situation, provide for the needs of the body as well as if it were in the neck, and consequently saves the life of the animal. It seems to me that these observations of Professor Schiff, and of Dr. von Eiselsberg, are of especial value, as they suggest to my mind that possibly the diseases mentioned before, namely, myxœdema, etc., may be treated with success by transplanting thyroid tissue into the patient. In the first place these diseases are hopelessly incurable with present remedies, and consequently anything possibly remedial not endangering life is justifiable. The transplantation of a thyroid gland from one of the lower animals into the peritoneal cavity, or into the subcutaneous tissue might be followed by the successful growth of the grafted gland, and so bring about the arrest of the disease process by reason of the restoration of the lost function. Performed under strict aseptic conditions the operation would be without risk or practically inconvenience.

A far more difficult question is that involved in Professor Schiff's dictum, and which experiment will solve, namely, What kind of gland would be best for the purpose? Doubtless one from an anthropoid ape; but the infrequency of opportunity and very considerable expense would afford some obstacles (not, however, insurmountable by any means) to this proposal.

I have elsewhere shown that the thyroid gland of the sheep very closely resembles in anatomical characteristics that of man, and further that the sheep, of all animals as yet experimentally investigated in the present question, resembles man most in the duration and character of its symptoms after thyroidectomy. I would propose, therefore, when opportunity offers, to try transplanting a portion of the thyroid gland from the sheep. By a portion, I mean that possibly the grafting of one lobe or even half, would be more successful than an attempt to transfer the whole gland; and moreover, if the operation were successful, no doubt the imbedded piece would hypertrophy to meet the requirements of compensation.

A point of practical difficulty would arise when one attempted to gauge the success of the operation, although doubtless the development of the grafted gland, or the reverse, its atrophy, might to some extent be estimated by palpation. The real plan, however, would obviously be that of watching the symptoms very closely, and if no improvement resulted at the end of two or three months, the operation should be repeated.

From experimental evidence, I would venture to suggest that the progress of the anæmia would be the best indication of relief. I may perhaps be allowed to take this opportunity of correcting ideas which have been attributed to me concerning the relation of the thyroid gland to so-called blood formation, and for which I have been in consequence adversely criticised.

Attention undoubtedly in the past has been too much given to the origin of the corpuscular elements of the blood as easier of observation than the source of the components of the plasma; and, indeed, the expression hæmopoiesis, or blood formation, has provisionally been limited to speaking of the corpuscles.

In 1885, I pointed out that marked anæmia followed loss of the thyroid gland, and that this anæmia included a fall in the number

² *Handbook of Therapeutics*, 11th edition, p. 70.

¹ Brown Lectures, 1885.

² Transl., p. 440, *Revue Médicale de la Suisse Romande*, 1884.

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 ℥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 ℥ij given hypodermically, a mixture containing tinct. digitalis ℥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 $\frac{1}{10}$ 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.