A case of gastric tetany, with an account of the microscopic appearances found in the medulla and spinal cord / by Walter K. Hunter, M.D., B.Sc., Assistant Physician, Royal Infirmary ... from Dr. Lindsay Steven's Wards in the Glasgow Royal Infirmary.

Reprinted from Glasgow Hospital Reports, 1899.

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A CASE OF GASTRIC TETANY, WITH AN ACCOUNT OF THE MICROSCOPIC APPEARANCES FOUND IN THE MEDULLA AND SPINAL CORD.

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From Dr. Lindsay Steven's Wards in the Glasgow Royal Infirmary.

TETANY in the adult is a somewhat uncommon disease, and a case of tetany ending fatally is distinctly rare. The fatal cases, when they do occur, seem to be chiefly cases of what has been called "gastric tetany," meaning by that cases in which the tetany-convulsions have been associated with a chronic gastric disorder. Not more than 50 such cases have, so far as I know, yet been put on record, and the mortality among these is said to have been as high as 75 per cent.

I do not, however, propose to enter here on any discussion as to the nature of gastric tetany, as the subject has recently been very ably reviewed by Dr. Trevelyan in the *Lancet* for 24th September, 1898, and those wishing a general survey of the subject I would refer to that paper. But I wish to put on record what seemed to be almost undoubtedly another case of this disease, and I shall also take the opportunity to describe the microscopic appearances found at the post-mortem examination in the medulla and spinal cord.

The history of the case is, unfortunately, rather scanty, owing in part to the patient's mental condition while under

our observation, and in part to the fact that we could find no relation or friend of the patient who seemed to know any particulars of either her personal or her family history. As to its being a case of tetany there can be little doubt, for the convulsive movements were characteristic of those seen in that disease. We are, however, without any definite knowledge as to the condition during life of the patient's digestive apparatus. But the post-mortem appearances of the stomach strongly suggested a gastric disturbance of considerable duration, and the history of headaches and of being "somewhat addicted to drink, though not recently," may also be taken as evidence in favour of that view.

The condition of the kidneys found post mortem made one consider the possibility of the convulsions being uraemic in origin. Diseased kidneys, by preventing elimination of poisonous material, might quite well determine the onset of convulsive movements. But then the convulsions in this case were so characteristically those of tetany that we should not be justified in regarding them as entirely due to uraemia. Moreover, Dr. Trevelyan, in the paper already mentioned, draws special attention to the fact that it is not at all uncommon to find nephritis associated with cases of gastric tetany. The possibility of the case being one of antipyrin or antifebrin poisoning seems very remote, for I am informed on good authority that neither of these drugs has ever been known to produce such symptoms as seen in this case.

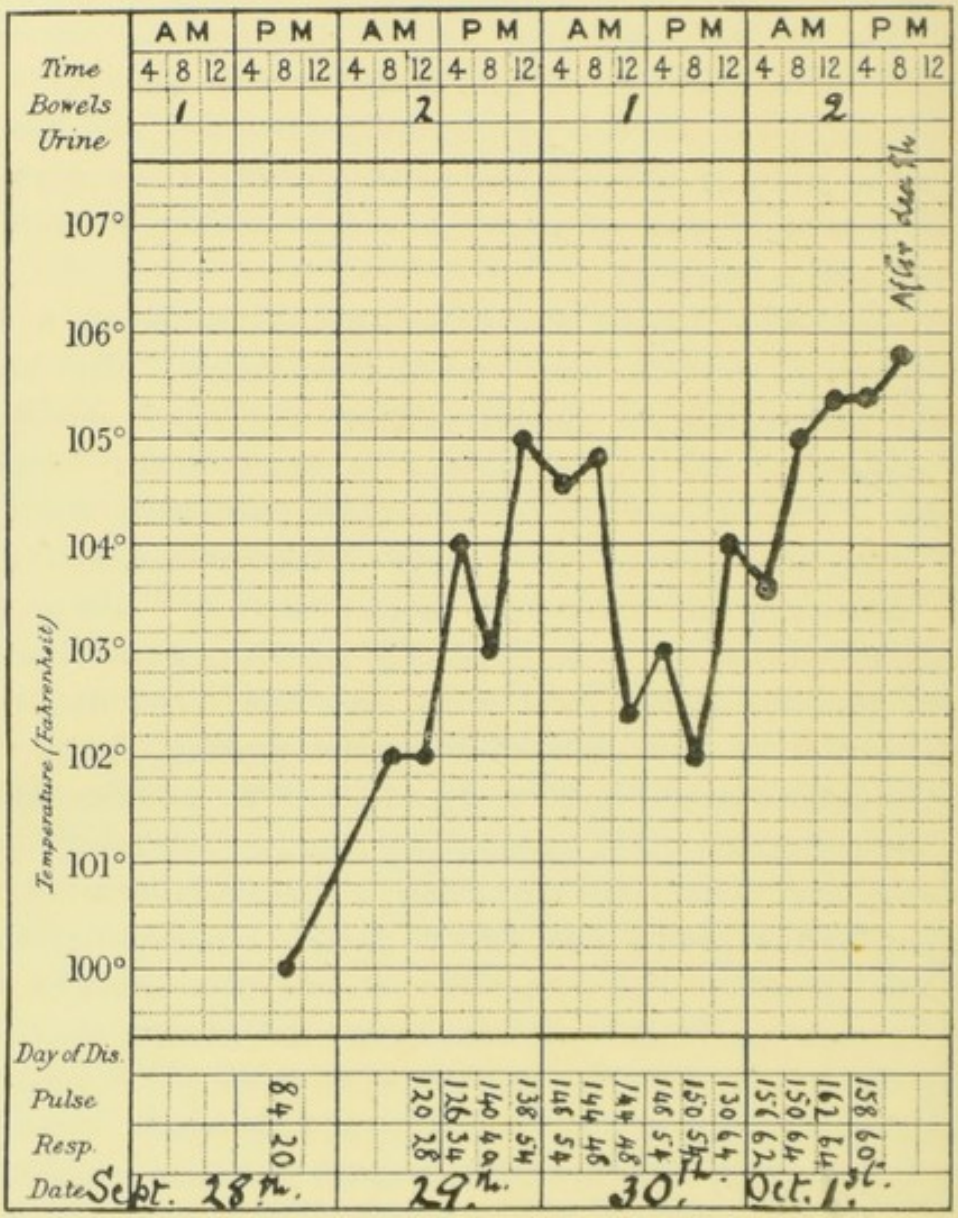
I. D., aet. 41, a domestic servant, was admitted to ward viii. of the Glasgow Royal Infirmary on 28th September, 1898, at 6 P.M., said to be suffering from some unknown form of poisoning. She had been in the habit of taking powders for the relief of headache, and two of these powders were brought to the infirmary by her friends. There is some doubt as to their nature, but the chemist in Arbroath from whom she had obtained powders since 1892, reports that they frequently supplied her with antipyrin, and that on subjecting one of the two powders to chemical tests they found it to consist of ten grains of antifebrin, which they say she must have obtained in Glasgow.

She had been in Glasgow for a fortnight before her admission, looking for a situation. On the morning of the 24th September she vomited and complained of headache. The headache continuing, she took a powder on the morning of the 25th. On the evening of the 26th, as she was still feeling giddy and unwell, she took a second powder. The next day she was delirious, and in the evening she was thought to be unconscious, and a doctor was sent for. He did not, however, see the patient until the 28th, and having heard the story of the powders, and regarding the symptoms as perhaps indicative of some form of poisoning, he ordered her removal to hospital.

On admission patient was first regarded as being a case of poisoning, and she was treated accordingly. But more careful observation of the symptoms, cast much doubt on this diagnosis, and pointed rather to some definite organic disease. The patient lay for the most part with the eyes wide open and staring, the pupils being of medium size, and responding to light and accommodation. There was spasmodic contraction, with occasional twitchings and tremors, in the muscles of the face, arms, and legs. The lips were compressed, and in a state of constant tremor. There were also convulsive twitchings in the other facial muscles, and a very characteristic *risus sardonicus*, coming and going, fully exposing the teeth, and importing a distinctly smiling expression to the profile view of the face. A marked trismus was also present. The irritability of the facial muscles and their nerves was much increased, and percussion over the facial nerve, especially on the left side, produced a contraction of all the muscles on that side of the face.

There was marked spasm in both arms, these being adducted at the shoulders, flexed at the elbows and slightly flexed at the wrists. The hands assumed the attitude characteristic of tetany. There was flexion at the metacarpo-phalangeal joints, with extension of the phalanges, adduction of the thumbs and contraction of the thenar and hypothenar muscles. The irritability of these arm muscles was also greatly increased, any attempt at straightening the arms

leading to violent muscular contractions, which also spread to the muscles of the front of the chest. Twitchings were also present in the toes. The toes were flexed and the feet extended and inverted in the position of talipes equino-varus. The electrical reactions were not tested.



As to patient's mental condition, she seemed only partially to understand what was said to her. She attempted to reply to questions, but her answers were rather disjointed statements and not easily made out. During the first night of her residence in the ward she was very restless, lying with her eyes wide open, picking at the bed-clothes and

frequently talking to herself. Indeed her appearance was that of a person in the incipient stage of delirium tremens. The next day patient passed into a state of stupor, and this gradually increased till some twenty-four hours before death, when the coma became complete, and patient had to be fed by the nasal tube. As coma deepened the twitchings lessened, though the rigidity of the muscles still continued.

No definite information could be obtained in regard to sensation.

Examination of the other systems of the body revealed little worthy of note. There was no *tache cérébrale*, and no retraction of the abdomen. There was no rash, and the only abnormality of the skin was the presence of one or two brown stains on the abdomen. The heart, lungs, liver, and spleen seemed quite normal. The urine and faeces were passed in bed, the motions being loose, but without any abnormal appearances. A specimen of urine drawn off by catheter had a specific gravity of 1026, and it contained a small amount of albumen. The temperature, as will be seen on the chart, began to rise on the evening of admission, and it ran a high course. The pulse, too, became very rapid. The respirations were noted to be somewhat irregular and sighing, but never definitely to assume the Cheyne-Stokes character.

The patient died on 1st October, exactly three days after admission.

At the post-mortem examination the body was noted to be well developed, though somewhat emaciated. The pericardium contained about half an ounce of clear serum. The heart's muscle was soft and pale, and in places showed evidence of fatty degeneration. Small haemorrhages were seen immediately beneath the endocardium. The orifices and valves were normal.

The lungs were slightly emphysematous, but otherwise healthy.

The kidneys (8 ozs.) had their capsules closely adherent, and these, when stripped off, left a granular surface, evidently due to early interstitial nephritis. Microscopic examination

showed the appearance of a well-marked parenchymatous nephritis, as well as the interstitial change.

The liver, pancreas, and spleen were healthy.

The uterus was slightly larger than normal, and its mucous membrane was greatly congested.

The stomach was distended, and its mucous membrane soft and thin, due in part to atrophy and in part to digestion. The small intestine seemed healthy throughout. Microscopic examination of the stomach showed great atrophy and disintegration of the mucous membrane, there being few healthy epithelial cells made out.

The brain, spinal cord, and their membranes, to the naked eye, appeared quite healthy, unless for some slight congestion of the vessels. The pons, medulla, and cord were examined microscopically. They were fixed in formol (10 per cent. solution), transferred to alcohol, and cut in celloidin. Sections were stained (1) with theonin, (2) with haematoxylin and eosine, and (3) with osmic acid (1 per cent. solution). A careful examination was made of numerous sections taken from various levels of the cord, medulla, and the pons, and the only points in which these sections differed from the normal were (1) that the ganglion cells throughout the pons, medalla, and cord, contained a large amount of yellow pigment, and (2) that the majority of the vessels showed well-marked hyaline degeneration.

All degrees of pigmentation were seen in these ganglion cells, ranging from cells with only a few yellow granules to those whose plasma was entirely filled with the pigment (see plate). There were very few cells without some pigment, and at least 50 per cent. had as much as half their plasma filled with the pigment. In a small proportion of cells the yellow pigment was scattered throughout the cell, giving, under the low power, the appearance of a yellow ground-substance containing chromatic granules (Nissl bodies). In these cells the Nissl bodies were often paler than normal, and the cell altogether presented somewhat the appearance of a "ghost cell" with a yellowish colouration of its plasma (cells *j*, *k*, *l*, *m*). But by far the greater number of cells

had the pigment granules collected together into one part of the plasma, the rest being filled with well-stained Nissl bodies (cells *b*, *c*, *d*, *e*, *u*). And it is to be noted that in these cells the presence of large masses of pigment did not seem to affect the staining of the Nissl bodies, for, even when only a few of these bodies remained, their staining was quite intense (cells *o*, *p*, *r*, *s*). In the majority of the cells the pigment granules seem first to be deposited as a compact little mass at one pole of the cell. This pigment mass seems gradually to increase in size, displacing, as it does so, the adjacent Nissl bodies till, ultimately, the whole cell plasma is filled with pigment and no Nissl bodies remain. At the part of the cell where pigment and Nissl bodies join there was a certain overlapping of the two elements, and there the Nissl bodies seemed smaller in size, as if the invading pigment was breaking them up (cells *b*, *d*, *i*). With a lower power ($\frac{1}{6}$th inch) the dividing line between pigment and Nissl bodies seemed sharply defined, but with the higher power ($\frac{1}{12}$th inch) the above-mentioned fragmentation of the chromatophile elements could usually, though not always, be made out. It could not be said that the Nissl bodies at this line of contact were individually more deeply stained than at other parts of the cell, and so I did not recognize in these cells the "sclerozed zone" as described by Bevan Lewis. Neither could I find any cells corresponding to Bevan Lewis's first stage of pigmentation—cells slightly swollen, and staining deeply. Certainly some cells stained fairly deeply but they did not seem swollen, indeed they seemed quite normal.

It was difficult to determine with any certainty the effect of the pigment on the cell nucleus. But as far as I could make out the nucleus suffered in much the same way as did the Nissl bodies. That is to say, the nucleus seemed unaffected till actually invaded by the pigment granules, or, till the whole cell plasma was replaced by pigment, when the nucleus could sometimes be seen faintly outlined towards the centre of the cell (cells *j*, *n*). Probably, however, the nucleus was sometimes obscured by the surrounding

pigment, for in some cells where there was no appearance whatever of a nucleus, a few well-stained chromatophile elements were still to be seen in the cell plasma (cells *o*, *p*, *r*, *s*).

Very few cells were found presenting what might be called a primary chromatolysis, for the disappearance of the Nissl bodies in the vast majority of cells seemed to be due to the invading deposit of pigment and to no other cause.

As to the nature of this yellow pigment, little seems to be known. Under a high power it is seen to consist of numerous small granules, closely packed together in the cell plasma. These granules do not blacken with osmic acid, though they stain deeper than does the plasma of the cell, and for this reason, osmic acid staining is a very excellent method of demonstrating the individuality of the granules (cells *v*, *w*, *x*, *y*). Neither do the granules dissolve with ether, showing again that they do not represent a fatty degeneration.

As to the condition of the vessels in these sections, little requires to be said other than that throughout the whole pons, medulla, and cord they presented a well-marked hyaline degeneration. The change was most marked in the arteriols, but it was also seen in many of the larger arteries. All three coats of the vessels were found affected, but the degeneration was usually most obvious in the media, where often no appearance of muscle fibres was to be seen. The condition corresponds to atheromatous change found in larger vessels. No haemorrhages were noted, and in none of the vessels could it be said that their lumen had become obliterated.

These, then, are the morbid appearances found on examining the tissues of this case of tetany, and it now remains for us to consider what is their interpretation. The changes in the vessels indicate a degeneration, due most likely to the presence in the circulation of some toxic substance, the nature of which is unknown to us. Can it be that the pigment in the nerve cells has a similar explanation, and that this pigmentation of the cell is

a degenerative change? Such a view has been advanced. But another explanation, namely, that the pigment is the result or evidence of functional activity in the cell, is the one which seems to have obtained the more support. Bevan Lewis tells us that a deposit of yellow pigment is a constant appearance in healthy ganglion cells, and that it indicates a state of physiological activity rather than a pathological degeneration. He also points out that in the ganglion cells from cases of senile atrophy there is diminution of this pigment, while in cases of mania and epileptic insanity, where there was great motor excitement, the pigment is on the other hand excessive. He considers, therefore, that the pigment in ganglion cells is a sign of by-gone functional activity. If this, then, be so, the excessive amount of pigment in the ganglion cells of this case simply means that there has been a hyperactivity in their corresponding muscle fibres; and of this hyperactivity of the muscles the above report gives ample illustration. According to this view, then, tetany must be due to some poison which has a specially stimulating action on motor nerve cells, the activity of these ganglion cells being represented by an increase in their yellow pigment, and their hyperactivity by an excessive amount of this pigment as in the cells described above. But if this yellow pigment in the cell is evidence of by-gone activity, it must also mean a present incapacity, for we have seen that the pigmentation in many of the cells was so extreme as to entirely displace the Nissl bodies. Now, much importance is attached to the presence of these Nissl bodies, for they are thought to represent the functional potentiality of the cell, either in the form of nutrition, or as energy, or as both these combined. Whichever it may be, it seems sufficiently clear that the loss of the Nissl bodies must affect the function of the cell, be it that of a trophic centre or of a motor centre. And so it may be that, after all, this excess of pigment does represent the fatal lesion.

This extreme pigmentation of the ganglion cells is to all intents and purposes just another form of chromatolysis, by means of which the cell becomes a pigmented cell in place of becoming a "ghost cell." And careful examination

of large numbers of cells by means of high powers points to the pigment granules being formed from, or deposited as a result of, the fragmentation of the Nissl bodies. If there be any truth in this view—and I only suggest it, having no proof of it—the difference between the pathological anatomy of tetanus and tetany would lie in the different degeneration in the ganglion cell. In the one we have a chromatolysis producing a "ghost cell," in the other another form of chromatolysis producing this pigment cell. And so if pigment in the cell does represent hyperactivity of the cell it also represents its atony.

As to where this poison in cases of tetany may come from, and as to how it gets at the ganglion cells, I have nothing to add to what will be found in the paper by Dr. Trevelyan already referred to. I have, however, greatly to regret that, for completeness, I did not examine the cells of the cerebral and cerebellar cortices. The necessity of so doing now appears much greater than at the time of the post-mortem examination, although I do not anticipate that any changes found in these cells could have greatly changed one's views as to the pathology of tetany.

In conclusion, I have to acknowledge my indebtedness to Dr. Steven, by whose permission, and at whose instigation, I publish this case. I am also indebted to Dr. Workman for access to the post-mortem room journal. I myself, however, am responsible for the account I give of the various microscopic examinations.

DESCRIPTION OF PLATE.

Cell *a*.—Normal ganglion cell.

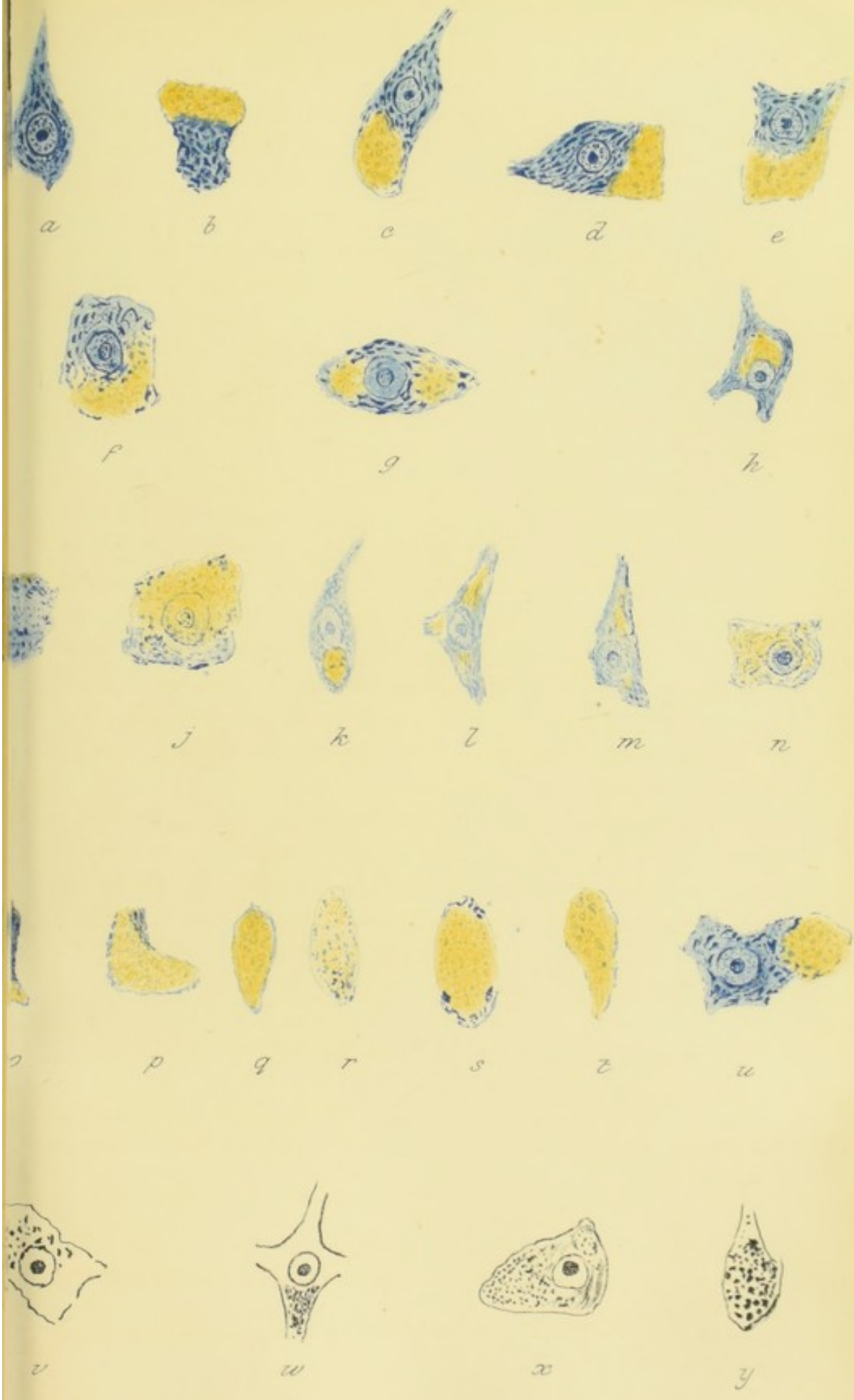
Cells *b*, *c*, *d*, *e*, *u*.—Normal cells, except for deposit of yellow pigment. The pigment is confined to one pole of the cell, and the Nissl bodies are deeply stained.

Cells *f*, *g*, *h*, *i*.—Pigment diffused throughout the cell, the Nissl bodies not so well stained, and in places fragmented.

Cells *j*, *k*, *l*, *m*.—Pigmented "ghost-cells."

Cells *o*, *p*, *q*, *r*, *s*, *t*.—Cells with plasma almost entirely filled with pigment; cells atrophied.

Cells *v*, *w*, *x*, *y*.—Stained with osmic acid to show arrangement of pigment granules.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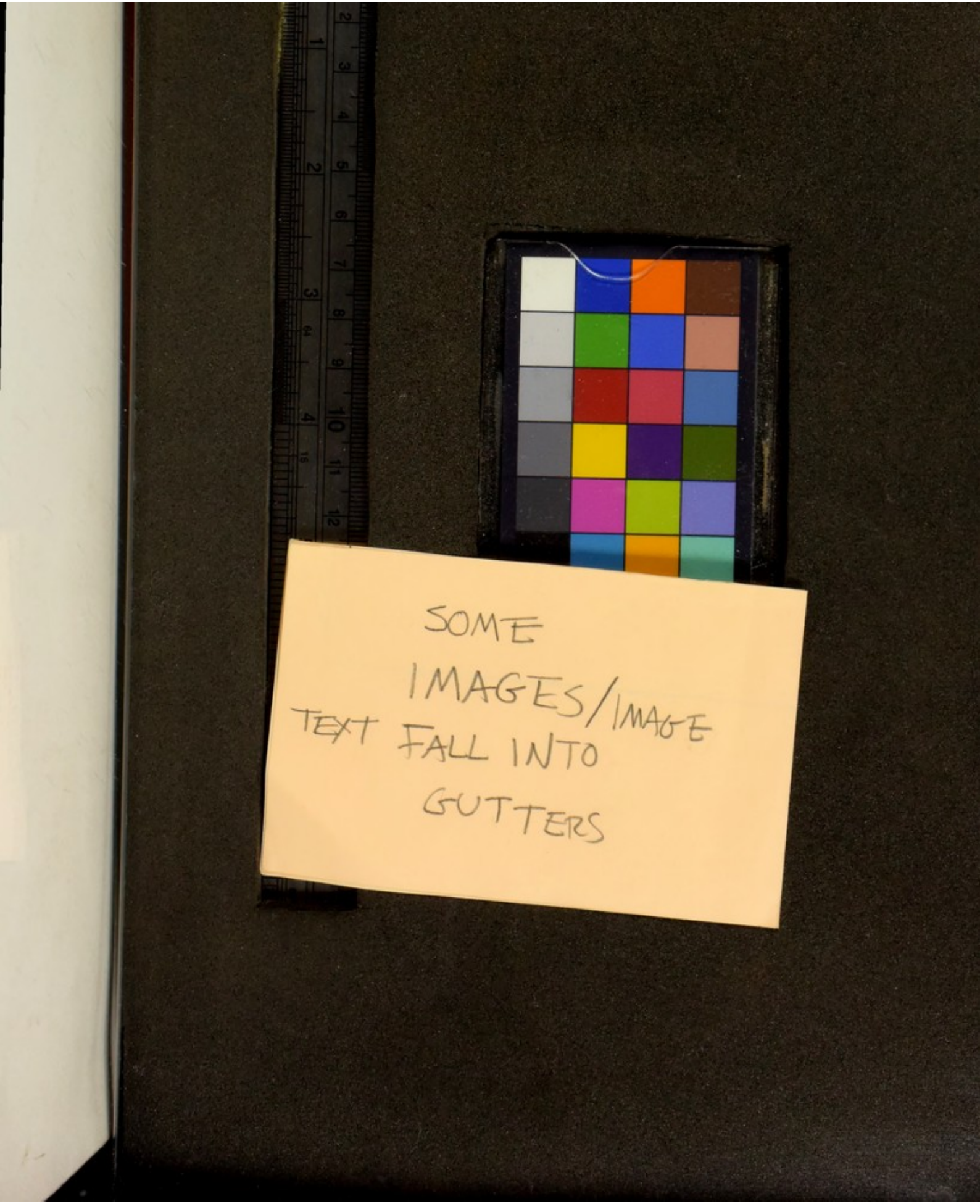
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