Neurological Section.

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Dr. F. W. MOTT, F.R.S., President of the Section, in the Chair.

Pathological Changes in Voluntary Muscles in General Diseases.

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INTRODUCTION.

THE subject of our investigation has been the pathological changes in voluntary muscles in various general diseases, and we have purposely avoided the examination of muscles affected as the result of nervous lesions, with the exception of a very few cases, since this has already been fully dealt with by neurologists and others.

We were prompted to undertake this piece of work, since comparatively little seems to have been done on it by people in this country, and in foreign literature, with the exception of one or two writers, we have been unable to find very much concerning the changes which may occur in muscle in general conditions.

We propose to bring before you this evening a short abstract embodying the most important of our results. The full account of our work we hope to publish elsewhere. It would greatly increase the length of this paper without adding appreciably to its interest, did we attempt to summarize all the results obtained by other workers, but we are in no way unmindful of them, and we shall refer to them briefly under the various sections dealt with where they can be placed directly in comparison with our own.

Our work has been carried out in the pathological departments of St. Thomas's and Charing Cross Hospitals. We have investigated the histological changes in muscles from 153 different cases, including both

those from human subjects and from animals, which had been experimented upon. In all cases we have confined our attention to voluntary muscles. As a routine we have made sections from the biceps, rectus abdominis, and pectoralis major in each human case. In a very few cases other muscles were also examined. In all cases the muscles were fixed in formalin and cut in celloidin, since this was found the most satisfactory method, and the sections were stained with hæmalum and eosin. Other methods of cutting and staining will be referred to later.

For convenience of description we propose to deal with the subject under the following headings:—

(1) Muscle in wasting diseases.
(2) Muscle in acute diseases.
(3) Fatty changes in muscle.
(4) Glycogen in muscle.
(5) Amyloid changes in muscle.

Muscle in Wasted and Cachectic Conditions.

Muscles from forty-five cases were examined, all of which showed more or less wasting. The cases examined were as follows:—

	Cases
Malignant disease	19
Chronic pulmonary tuberculosis	4
Diabetes mellitus	2
Marasmus	1
Actinomycosis	1
Exophthalmic goitre	1
Prolonged suppuration	1
Chronic metal poisoning	1
Tuberculous meningitis	1
Ulcerative colitis	1
Cirrhosis of liver	1
Spina bifida	1
Pernicious anæmia	1
Paraplegia	1
Perigastric fistula with pulmonary tuberculosis	1
Animals (experimental)	8
	45

It has been found that, on the whole, most of the more wasted muscles to the naked eye show well-marked changes microscopically, but this cannot be by any means laid down as a rule, for there have been several cases in which, although macroscopically the muscles were markedly atrophied, the sections showed practically a normal condition. Nor can it be foretold from the naked-eye appearance of the muscle what kind of change is likely to be met with under the microscope—

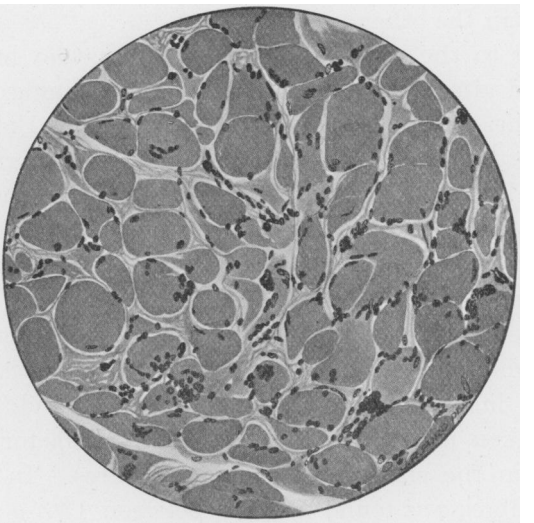

FIG. 1.

Muscle from a case of chronic pulmonary tuberculosis, showing the increase of fibre nuclei and their aggregation into darkly staining masses.

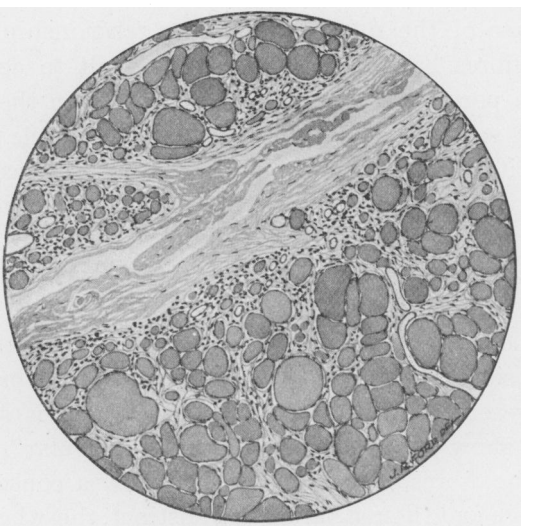

FIG. 2.

Wasted muscle showing variation in shape and size of fibres. Increase of interstitial tissue and presence of large pale-staining fibres.

i.e., whether the fibres, interstitial tissue, &c., are likely to be affected, the one more than the others.

With regard to the muscle-fibres themselves, they have been found to show marked alterations in shape, size, and staining reactions, and, on the whole, these changes have been especially marked in the more wasted cases. Almost every variation from the normal cylindrical shape of the fibres was present. The size of the fibres varied to a similar degree. In many sections there were some very large isolated fibres, which took a very much paler stain than their neighbours. The above changes are well shown in figs. 1 and 2.

The diameter of the fibres in cross-section has been measured by means of the micrometer in a large number of sections; fifty fibres were measured in each section, and the largest and smallest noted. The average taken in each section does not satisfactorily express the real variations in the size of the individual fibres. In normal muscle the size of the fibres was found to vary between 13·3 μ and 33·3 μ, the normal average being 23·6 μ. The muscles measured in each case were the pectoralis major, biceps, and rectus abdominis. There was very marked variation in the size of the fibres in the muscles of this group of cases.

In the majority of the very wasted muscles a marked feature is the large increase of the nuclei. The true relationship of these nuclei to the muscle-fibres has been somewhat difficult to determine, owing to the extreme peripheral position of the nuclei in the fibres, but the examination of several preparations of teased muscle seems to prove that the majority of these nuclei lie beneath the sarcolemma, and so belong really to the fibres rather than to the interstitial tissue. This increase of nuclei was seen in thirty out of the forty-five cases comprising this group. Another marked change connected with the nuclei in several cases was their arrangement; they were found to be aggregated into irregular, darkly staining masses, and, for the reason mentioned above, we considered that these were the actual fibre nuclei. This change was present in nineteen of the cases, and is shown in fig. 1. Some sections show the nuclei arranged in irregular masses near the periphery of the fibres, and these fibres show a considerable amount of hyaline change and their striation is indistinct, the whole in transverse or oblique section closely resembling multinucleated giant cells, such as are seen in tuberculosis and certain chronic inflammatory conditions. False giant cells of this type are shown in fig. 3. Many of the above changes have been already observed by Durante and others. In two

cases certain of the nuclei were placed at or near the centres of the fibres instead of at the periphery.

In many cases abnormality in striation of the fibres was a marked feature, the transverse striation was often very indistinct and sometimes absent, and in others a longitudinal striation was in evidence. In twenty-five out of the forty-eight cases examined there was a very noticeable increase of the connective tissue. This is seen in fig. 2. In two instances, one a case of carcinoma of the breast and one of exophthalmic goitre, small lymphorrhages were noticed.

In the cases examined it does not appear that any one particular voluntary muscle is more liable to any special change in wasting con-

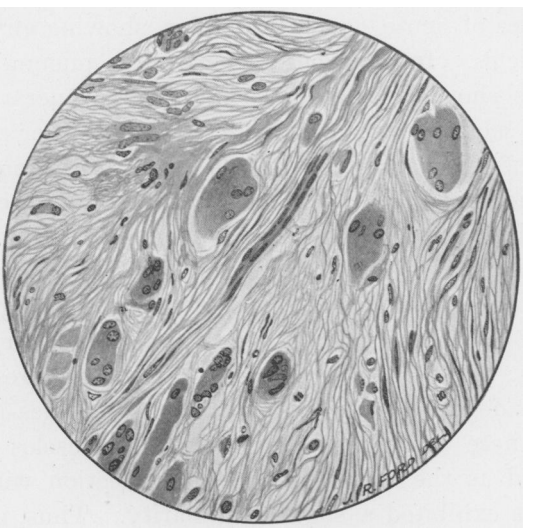

FIG. 3.

Muscle undergoing fibrosis, showing the presence of pseudo-giant cells.

ditions than other muscles in the same individual. For instance, sometimes the rectus will show the most marked changes, whereas in other cases of the same disease the biceps may be the muscle most affected.

MUSCLE CHANGES IN ACUTE DISEASES.

The changes which have been described in voluntary muscles in acute diseases, especially by Durante, consist mainly in the *hyaline* and *granular* degenerations, *irregularities in size and shape of the fibres*, some degree of *multiplication of the nuclei*, and less commonly *fragmentation* and *vacuolar degeneration*.

We have examined the muscle from forty-two cases of acute disease. In twenty-four of these no change of any kind was noted; in the remaining eighteen cases the changes were for the most part extremely slight and consisted mainly of a certain amount of hyaline and granular degeneration. In four of these eighteen cases the muscles showing the above changes were the seat of acute inflammation themselves. Eight cases were either those of diphtheria in the human subject or animals in which diphtheritic toxæmia had been experimentally produced. The changes noted in these cases will be dealt with in the section relating to fatty degeneration. Four cases were those of animals poisoned by phosphorus; two of these showed marked fatty degeneration and will also be described more fully in the next section. Thus, there only remain six cases of acute general infection showing any change in the voluntary muscles. In a rabbit dying from a pneumococcal infection all the muscles showed some degree of fatty degeneration, and several fibres in these sections were also hyaline. Five other cases of animals dying from a pneumococcal infection, also one case of broncho-pneumonia, one of lobar pneumonia, and two cases of empyema in the human subject, were examined without finding any change. Three guinea-pigs and one rabbit died from an acute infection with the *Bacillus proteus*. The muscles of the rabbit showed a marked degree of hyaline and granular change; the muscle of one of the guinea-pigs showed in every section a few granular fibres; those from the second guinea-pig presented a marked degree of fatty degeneration; those of the third guinea-pig were slightly granular, but there was no fatty change. The muscles of a guinea-pig which had died as the result of an acute infection with the vibrio of chicken cholera exhibited a slight granularity. Thus, no case of acute disease in the human subject, except three of diphtheria, showed any abnormality.

Fatty Change in Voluntary Muscle.

One hundred and twenty-six cases were examined for fat. They include examples of various kinds of acute and chronic conditions. Sections of the muscles were cut on the freezing microtome, stained with Scharlach R, and counterstained with hæmalum. We deal with this subject under the following headings:—

(1) Changes in the amount of interstitial fat.

(2) Presence of fat droplets and pigment in the neighbourhood of the muscle-fibre nuclei.

(3) True fatty degeneration of muscle.

(1) *Interstitial Fat.*

In normal muscle there is, as a rule, very little fat in the interstitial tissue, in many sections none at all may be seen, or at most a few fat cells lying near the vessels—i.e., in those places where the interstitial tissue is relatively considerable in amount. In a few sections collections of fat cells were seen lying between the individual muscle-fibres, but this is not often met with.

We found the fat cells lying between the fibres to be enormously increased in the following cases, and the increase was so marked that

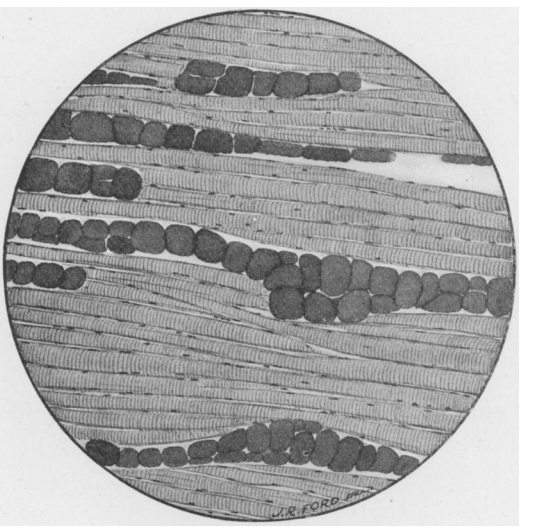

FIG. 4.

Muscle from case of diabetes, showing excessive amount of interstitial fat.

it was readily seen in the stained sections with the naked eye, and microscopically was most striking. Fig. 4 illustrates this from a case of diabetes. It has been found excessive in :—

	Cases
Diabetes mellitus	9
Senile gangrene with glycosuria	2
Pancreatic lesions (carcinoma 2, fibrosis 1)	3
Cirrhosis of liver (Cammidge +)	1
Mastoid abscess	1
Diphtheria	1

The interstitial fat was also increased in nine other cases, but to a much less marked extent than in the above. One case of diabetes

failed to show an excessive amount of fat, but this was the only exception.

The total fat in the muscle was measured in several cases by means of Soxhlet's ether apparatus; the accompanying table shows the percentage of fat in the dried muscle. This list clearly shows that the muscles of diabetics, and probably those from cases of gangrene associated with glycosuria, possess an abnormally large amount of interstitial fat. The quantitative estimation of fat was only undertaken as a means of controlling the histological findings, and was not meant as an incursion into the field of chemical pathology. Dr. Paul Haas has very kindly given us some valuable help in connexion with this part of our work.

PERCENTAGE OF FAT IN DRIED MUSCLE.

	Per cent.
Group I.	
Diabetes mellitus (5 cases)	26·44
	38·53
	13·65
	41·13
	10·66
Senile gangrene with glycosuria (2 cases)	32·10
	34·23
Average	28·11
Group II.	
Carcinoma of pancreas	13·10
Cirrhosis of liver	20·56
Average	16·83
Group III.	
Mastoid abscess	10·00
Cardiac failure	6·13
Carcinoma of stomach	8·45
Actinomycosis	3·06
Carcinoma of œsophagus	14·72
Diphtheria	12·00
Chronic pulmonary tuberculosis	12·00
Myasthenia gravis	25·00
Average	11·42

(2) *Fat and Pigment near the Nuclei.*

In a fair proportion of our cases we found near the muscle nuclei, and situated mainly at their poles, coarse fat droplets. This gave the muscle an appearance somewhat like that seen in cardiac muscle in the condition known as brown atrophy, although of course in these cases it is well known that the condition is due to pigment and not

to fat. In our cases small quantities of brown pigment as well as fat were sometimes found to be present. Fig. 5, taken from a case of carcinoma of the œsophagus, illustrates this condition.

The above change was seen in 50 per cent. of the cases examined, and it is doubtful whether it has any pathological significance. It is almost constant in the muscles of old people, rare in children, and was only found in a very slight degree in one out of thirty-eight animals examined.

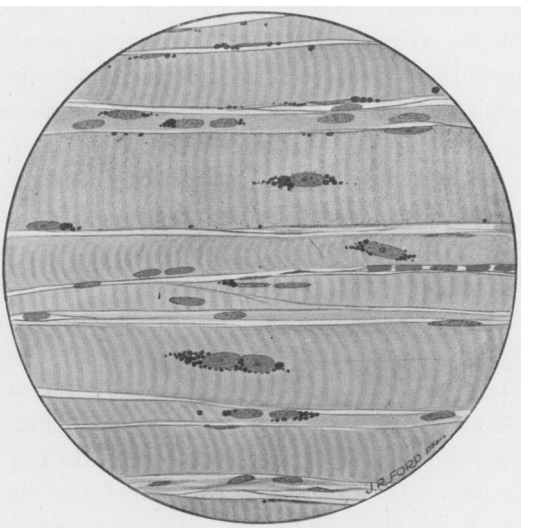

FIG. 5.

Muscle from a case of carcinoma of œsophagus, showing the presence of fat and pigment at the ends of the nuclei.

(3) *True Fatty Degeneration in Muscle.*

This condition is said to be commonly met with by several foreign authorities; Durante, in Cornil and Ranvier's "Manual of Pathological Histology," says that it occurs in general infective diseases, after poisoning by phosphorus and arsenic, in muscles which have been subjected to pressure by tumours, &c., also in infective myositis, myelopathies and myopathies; but he apparently denies that it may occur as a result of peripheral nerve lesions, and he therefore thinks it is a process due to the result of cachexia or of the general infective disorder rather than to the actual amyotrophic process. Lorenz draws attention to a granular degeneration and thinks that the granules are first protein in character and later become converted into fat. Others have stated that fatty

degeneration commonly occurs in wasted muscles in chronic pulmonary tuberculosis and in various other conditions.

In this our results differ considerably from those of other workers. In five cases of chronic pulmonary tuberculosis examined it was found only once, and then only in two fibres of one of several sections taken from the pectoral muscle. In twenty-five cases of malignant disease it was found only once in a single fibre of one section from the rectus abdominis. In one fibre of a muscle from a case of cardiac failure. In one out of ten cases of diabetes a few fibres in most of the sections showed this change. A case of slowly progressive paralysis of unknown origin[1] involving all the muscles of the body, and ending in paralysis of the bulbar type with resulting broncho-pneumonia, showed some degree of fatty change in all sections. The acutely inflamed pectoral muscle of a rabbit which had received an intrapleural injection of a virulent culture of the pneumococcus showed a few fibres presenting this type of degeneration. The muscles of another rabbit dying as the result of an acute pneumococcal infection showed a slight degree of this change. We have examined a large number of muscles which were the seat of acute inflammatory change, and also the muscles from a considerable number of rabbits, guinea-pigs and mice dying from pneumococcal infection, and four cases of pneumococcal infection in the human subject, but have never found true fatty degeneration present except in the above two cases. In all these cases the fatty change was a very slight one; but in a certain proportion of the cases examined an entirely different condition obtained. True fatty degeneration was present in a most marked degree, obvious in the majority of the fibres in all sections examined, and presenting an appearance quite comparable to that seen in cardiac muscle in acute diphtheritic toxæmia. The muscle of a girl dying of a severe anæmia, which did not conform to any recognized type, showed this change to a marked degree; and also to a still greater extent did the muscles obtained from a case of infective purpura; one of these muscles is shown in fig. 6. On the other hand, two cases of pernicious anæmia, one of acute lymphæmia, one of myelæmia and one of lymphadenoma presenting the severest possible type of secondary anæmia, showed no trace of this change.

Following these results an attempt was made to determine the effect of the injection of a specific hæmolysin into a guinea-pig. Two experiments were performed; in one of these marked fatty change was

[1] For the inclusion of this case we are indebted to the kindness of Dr. Turney under whose charge the patient was during life.

produced in the soleus and anterior thigh muscle. Three cases of diphtheria in the human subject were examined. Of these one showed the enormous increase of interstitial fat alluded to above, but no other change. The other two cases, in which the interstitial fat was normal in amount, showed true fatty change in a marked degree.

Following these observations we examined the voluntary muscles of certain animals dying as the result of inoculation with diphtheria toxin and with cultures of the diphtheria bacillus. To summarize briefly the results, we may say that in animals dying after an interval of less than twenty-four hours, fatty change in the voluntary muscles is very rare;

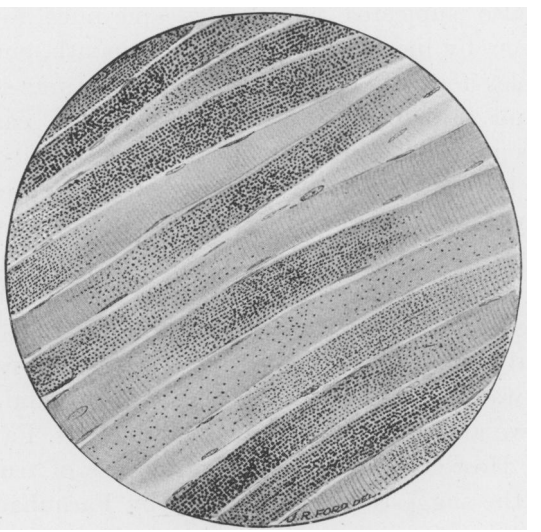

FIG. 6.

Section from case of infective purpura in a girl aged 19, showing well-marked true fatty degeneration.

but in the case of animals dying after a longer interval, it is almost constant.

In this connexion we would recall Dudgeon's experiments as described in his contribution on the "Pathology of Acute Diphtheritic Toxæmia."[1] In the course of his investigation he examined the tissues of many animals dying as the result of experimental inoculation with diphtheria toxin. In a few of these, sections of the voluntary muscles were examined, the results being uniformly negative. In all these cases, however, the inoculated animals died within twenty-four hours, and

[1] *Brain*, 1906, xxix, pp. 227-64.

thus the results are in close agreement with the experiments noted above, in which two guinea-pigs dying within eighteen hours after inoculation showed in one case no fatty change in the voluntary muscles, in the other only the very slightest degree of such change.

Sidney Martin records a case of a man, aged 19, dying from diphtheria on the twenty-seventh day of disease, in which the right and left vasti muscles and the palatal muscles showed scattered fatty change.

Mallory describes two cases of diphtheria in the human subject in which the skeletal muscles showed fatty change, and gives a plate showing the condition in the psoas magnus in one of them. He does not, however, state the duration of the illness in either case.

We have also subjected guinea-pigs and mice to the action of phosphorus given by inoculation and by the mouth, and examined the voluntary muscles for fatty change, at the same time staining sections of the liver and cardiac muscle in certain of the cases as controls. In two animals in which death occurred within twenty-four hours the voluntary muscles showed no fatty change, but a mouse which died on the fourth day after receiving repeated doses of phosphorus showed well-marked fatty change in all the voluntary muscles examined.

In view of the exhaustive studies undertaken by Panton we did not consider it necessary to investigate the effect of arsenical poisoning.

The skeletal muscles obtained from a case of myasthenia gravis, which were forwarded to us from the National Hospital, Queen Square, and for which we are indebted to the kindness of Dr. Farquhar Buzzard and Dr. Hinds Howell, showed a marked degree of true fatty change.

In view of the suggestions put forward by Farquhar Buzzard as to the part played by the red and pale muscle-fibres respectively in this disease, we endeavoured to discover whether the red muscles in those animals in which fatty degeneration of the skeletal muscles had been experimentally produced showed any special susceptibility to this change. We were, however, unable to satisfy ourselves that any such difference between the two kinds of muscle existed.

Dealing now very shortly with the suggested relation of the presence of fat droplets in the immediate neighbourhood of the nuclei to true fatty change, we may say at once that we have been quite unable to satisfy ourselves that any such relationship exists. Durante, as stated above, considers that this nuclear charge is the precursor of a more general fatty degeneration affecting the whole fibre, but we have found no evidence of this. It is true that certain sections which show the one change show the other also, but considering the frequent occurrence of

the nuclear fat droplets this is to be expected. The following facts appear to us to prove the entire independence of the two processes :—

(1) The nuclear collections of fat are of frequent occurrence (50 per cent. of the cases examined). True fatty change is, however, very rare. Were the one change only an early stage of the other this marked disproportion would be very remarkable.

(2) The occurrence of nuclear fat was no more frequent in those cases showing true fatty degeneration than in the cases in which this change was absent.

Thus in those cases which occurred in adults a large proportion showed this change. In the cases in which true fatty change occurred in the muscles of young adults or children, the nuclear collections of fat were absent or only very slightly marked. In no case did the muscles of an animal in which fatty change had been experimentally produced show these collections. In some cases in which fatty change has occurred in the muscle-fibres we have noted the occurrence of fat phagocytosis by mononuclear cells.

Glycogen in Muscle.

Thirty-five cases were examined for the presence of glycogen granules in the muscle-fibres by Best's carmine method of staining. In each case the muscle was obtained fresh from the operating theatre at the time of operation, or in the case of animals immediately after death. Of these cases, glycogen granules were found present in the fibres in eleven instances, and were absent in the remaining twenty-four.

The results obtained (with one exception) do not admit of any conclusion being drawn as to the effect of disease on the presence or absence of glycogen granules in voluntary muscle-fibres. The exception referred to is the following : The leg muscles were obtained immediately after amputation from three cases of diabetic gangrene : in all of these a very marked excess of glycogen was present, but the small number of cases examined does not allow of any generalization being made. In many of the experimental cases on animals the liver was treated by the same method, and examined as a control, and in all sections showed the presence of glycogen. The distribution of glycogen granules in different fibres of the same muscle was noted to be exceedingly irregular, thus one fibre showed the presence of a large amount of glycogen, whilst in neighbouring fibres it was often entirely absent. This same irregularity was also noted in regard to the different muscles themselves from the

same case—one muscle might be found to contain glycogen while in another it was absent. It is not to be supposed that the presence or number of glycogen granules shown by this method of treatment affords an accurate indication of the actual amount of glycogen present in the muscle-fibres.

Amyloid Degeneration in Muscle.

Twelve cases were examined for the presence of any amyloid change, methyl violet being used as a stain; in all of these it was completely absent.

Conclusions.

(1) In wasting diseases the voluntary muscles show varying degrees of histological change bearing little relation to the actual degree of wasting present. These changes consist of alterations in the size, shape, and staining reactions of the fibres, increase in the fibre nuclei, and alteration in their arrangement, sometimes resulting in the production of false giant cells; and lastly of a relative increase of the interstitial tissue.

(2) In acute general diseases, muscle changes are extremely slight, consisting of some degree of hyaline and granular change, and in a certain small number of cases of fatty degeneration.

(3) Fatty changes. In certain disorders associated with an abnormal carbohydrate metabolism, there is a great increase in the amount of interstitial fat present. In many cases small collections of fat droplets are present in the neighbourhood of the fibre nuclei; these are common in advanced life, rare in children, and almost entirely absent in animals. They bear no relation to true fatty degeneration, and it is doubtful if they have any pathological significance. True fatty degeneration appears to be much less common than is usually stated, but occurs to a marked degree in cases of diphtheritic toxæmia, in certain blood disorders, and in poisoning by phosphorus.

(4) Glycogen. Of the many muscles stained for glycogen, it was only strikingly present in each of the three cases of diabetes examined.

(5) Amyloid change was not found in any case examined.

It only now remains for us to acknowledge our great indebtedness especially to Dr. L. S. Dudgeon, at whose instigation this work was undertaken, and whose help and advice throughout have been invaluable, and also to many others for their kind suggestions and assistance in providing us with material.

DISCUSSION.

Dr. F. E. BATTEN said he felt great admiration for the work the authors had done. He had examined muscle from children, the subjects of advanced tuberculosis in whom there was considerable wasting, and he would agree that there was a comparative increase in the interstitial tissue. But it always seemed to him that that increase of interstitial tissue was not a real but only a relative increase, owing to the wasting of the fibres; an entirely different condition from that met with under pathological conditions, such as the myopathies, where a true increase of the tissue was found. The authors exhibited a specimen that evening which he did not think they alluded to in their paper—namely, a muscle taken from a patient who was suffering from sarcoma. That muscle was a most peculiar one, and was in a condition which he did not think he had ever seen before. He thought that that muscle was infiltrated by some form of growth, and that it was not a condition merely secondary to growth elsewhere in the body. It might be argued that the cells in the interstitial tissue were not the cells of sarcoma; they might, however, be an inflammatory exudation between the fibres. He would like to hear what other members thought of that specimen.

Dr. FARQUHAR BUZZARD said he was no better able to criticize the paper than many of those present, as it was full of work carried out in a field of investigation which few had entered. Like Dr. Batten, he had investigated much muscle tissue, but chiefly in connexion with neurological conditions, and he had always found some difficulty in deciding how far muscle changes might be regarded as secondary to neurological processes, and how far they represented primary alterations in the muscles themselves. The paper they had heard would enable them to form better ideas on this question. So far as his own experience of investigations along these lines was concerned, he had found that in acute diseases generally the heart and diaphragm were more subject to fatty degeneration than the skeletal muscles. This result suggested that the fatty degeneration was not so much the result of the acute disease as the result of muscular action being continued right up to the moment of death under conditions which were unfavourable to normal metabolism. At any rate, the absence of changes in the skeletal muscles, which are kept at rest, suggests this interpretation. The authors alluded to another point—namely, the difference between their observations and those of other workers as to the prevalence of fatty degeneration. This difference might possibly be explained if it were shown that the other investigators had used the osmic acid method instead of the Scharlach stain used by the authors of the paper. It had been fairly well established that the two methods gave somewhat different results.

The PRESIDENT (Dr. F. W. Mott, F.R.S.) said that some years ago he was interested in the subject of the condition of muscle in disease, especially in association with general paralysis of the insane, in which disease great wasting

took place. But he was surprised to find there was very little change in the muscle-fibres, beyond an atrophic condition, a pallor of the fibres, and a little indistinctness of striation. But if the patient had had a series of fits, a very different condition of muscle was found. If the fits had been universal, there was found extensive fatty degeneration of muscle-fibres in all the muscles of the body, and the extent of that degeneration was proportional to the number of fits which the patient had had. He found also fatty degeneration of the heart muscle, but not so marked as in the voluntary muscles. This condition was also marked in the diaphragm. He found the same state of things present in status epilepticus, but he was doubtful whether this might not be due to the condition which caused the status epilepticus, or the fits in general paralysis; because he soon found that in general paralysis, as a rule, when the patients had fits they had some terminal or secondary microbial infection—pneumonia, broncho-pneumonia, or dysentery, which raised the temperature. So that there was a double cause; there was a condition of over-action of the muscle, or at least continual action of muscle under stress, conditions which would prevent the restoration of the substance used up. And the problem was a difficult one because many of these patients in whom he found fatty degeneration with status epilepticus, died with a temperature of 107° or 108° F. Still, he had seen cases die with very high fever and with marked changes in the nerve cells, as in status epilepticus, but if they did not have the fits they did not show fatty degeneration. Therefore he concluded that the continuous contraction of the muscles had something to do with the fatty degeneration. Dr. Buzzard had somewhat anticipated the remarks he had intended to make about the diaphragm. He had found that in pernicious anæmia and other diseases, as he said in his Croonian Lectures, the diaphragm of guinea-pigs poisoned with the toxin of *Bacillus botulinus*[1] showed fatty degeneration, although he found none in the skeletal muscles. And for the same reason he thought it was because the animal lay at rest, but would have to use its diaphragm two or three times as rapidly as under normal conditions. He therefore thought that excessive exercise in the muscles played a part in the fatty degeneration, and he suggested it would be well if the authors could undertake some experiments, such as those of Edinger, with regard to the effect of toxins and excessive exercise in animals in causing degeneration of the posterior columns. If they were to poison rats and then put them into a rotary cage in which they had continually to move, no doubt fatty degeneration would be found in their muscles. He also suggested that the authors should try the effect of carbon monoxide, because he thought the deficiency of oxygen might play an important part in connexion with these changes. One interesting fact in connexion with the muscles of general paralytics would interest Dr. Batten—namely, that he found muscle spindles beautifully intact in some of these cases where there was marked fatty degeneration of the other muscles. That was also rather in favour of the effect of excessive exercise being a factor in the production of

[1] *Brit. Med. Journ.*, 1900, i, p. 1588.

fatty degeneration. He was showing that evening specimens of a case of a man who had over 500 unilateral epileptic fits in three days. He did not discover what was the cause of the fits; they were unilateral, on the right side; and there was most extensive fatty degeneration of the muscles. He only took out for examination a piece of the thumb muscle on the right side and a piece from the left, and the difference was extraordinary. He found also most extensive fatty degeneration of the diaphragm, and some fatty degeneration of the heart; also, as he had found in cases of status epilepticus before, the convoluted tubules of the kidney contained large quantities of fat in the epithelium, as if the fat had got into the circulation and had been picked out from the blood by the epithelium of the convoluted tubules, leaving the glomeruli perfectly free. The case was interesting as supporting the idea he had entertained, that the fatty degeneration in status epilepticus was not due to the microbial infection or the fever, but was due mainly to the excessive activity under unfavourable conditions. He congratulated the authors upon this valuable piece of work; it was the kind of spade-work which was required, and it would be of great value to all who might go into the subject later to find what conclusions were deducible from the work of Dr. Topley and Dr. Jewesbury.

Dr. F. PARKES WEBER asked whether the authors had been able to bring out any relationship between prolonged disuse of skeletal muscles, such as in the case of a bedridden patient, and excess of interstitial nuclei (interstitial connective tissue elements) in the skeletal muscles.

Dr. TOPLEY, in reply, said that, with regard to Dr. Batten's remarks, they quite agreed that the apparent increase of interstitial tissue was in most cases much more a relative than a real increase, since the muscle-fibres themselves had atrophied. The most marked exception was the case Dr. Batten referred to. The patient had generalized sarcoma. The two muscles examined were the pectoral and the rectus abdominis, and there was no growth anywhere in the neighbourhood of either of those muscles.

In answer to Dr. Buzzard, they felt sure that if they had examined the heart and diaphragm in all their cases they would more often have discovered fatty degeneration, but they had purposely left out those muscles because they had so frequently been examined by others. The great difference between the heart and diaphragm and the voluntary muscles was a most striking point. With regard to the methods employed by others, they thought that almost all the workers referred to used osmic acid as a stain. Dudgeon had shown conclusively, in his contribution on the pathology of acute diphtheritic toxæmia, that the fine fatty change occurring within twelve hours in the cardiac muscle was, in many cases, well shown by Scharlach R, but not by osmic acid. The two stains certainly appeared to pick out different substances in some cases.

Dr. Topley exhibited a list showing the percentage of total fat in the voluntary muscles in a series of cases. The average in cases of true diabetes and of glycosuria with gangrene was 28·11 per cent. of the dried muscle.

In two other cases, one of cirrhosis of the liver, which during life gave a positive Cammidge reaction in the urine, and one of carcinoma of the pancreas, it was 18·3 per cent., whereas in eight other cases the average percentage was only 11·42.

They had not examined the tongue in any of their cases. They had examined only two cases of pernicious anæmia, neither of which showed any fatty change in the voluntary muscles. They had been most interested in the very instructive cases described by the President. The only case in their series which was at all comparable was one of acute tetanus, in which there was no fatty degeneration in any muscle examined. They had not had an opportunity of examining a case in which rapidly recurring fits had occurred shortly before death. They had examined several cases, in which pyrexia had been a marked feature, but they showed no sign of fatty change. So that Dr. Mott's suggestion that the muscle changes were due to exhaustion seemed the more likely.

In answer to Dr. Parkes Weber, a certain number of the cases examined had suffered from prolonged illness involving continued rest in bed, but they had not examined the muscles of patients who had been at rest for long periods, as contrasted with those who had not.