In the case of a soap solution containing 3 per cent. of KNO_3 the results of the electrical and optical methods of measurement agree for thicknesses greater than 450 $\mu\mu$. At thicknesses between 450 and 200 $\mu\mu$ the ratio is generally above unity, being in some cases as large as 1·28, but there is no clear indication that its value increases as the film thins, and when the thickness corresponding to the black is reached the ratio is again unity.

The paper concludes with a discussion as to the cause of the increase of electrical conductivity in thin films. The authors point out that it may be attributed either to a modification of the chemical constitution of the film brought about by its tenuity, or to the formation of a pellicle on the surface. They prove that the experimental results cannot be explained by the formation of a pellicle only, but that they are consistent either with the former or with a combination of both causes. To discriminate between them it will be necessary to carry out observations in gases other than air, and an apparatus specially designed for this purpose is being constructed.

II. "Organic Oximides: a Research on their Pharmacology." By H. W. POMFRET, M.D., F.R.C.S., late Berkeley Fellow at the Owens College. Communicated by Sir WM. ROBERTS, F.R.S. Received March 6, 1893.

(Abstract.)

Organic oximides may be concisely defined as "bodies containing the chemical group $=N\cdot OH$ attached to a carbon atom."

These bodies may be broadly divided into two classes: (*a*) Those whose preparation involves the use of hydroxylamine; these are known as "oximes," whence the generic name "oximide" is derived. (*b*) Those which are prepared independently of hydroxylamine. These latter may be obtained by the aid of nitrous acid, and have been termed "isonitroso-" bodies. This group $=N\cdot OH$ must be distinguished from the true "nitroso-" group $-NO$. The oxime group is bivalent, being regarded as a compound of trivalent nitrogen with the monovalent radical hydroxyl. The true nitroso-group is monovalent, two "affinities" of the nitrogen being taken up by oxygen.

There is furthermore an essential structural difference between the bodies forming the subject of this research and the nitrites. In the nitrites the nitrogen is attached to oxygen, whereas in these oximido-bodies the nitrogen of the oxime group is attached to carbon, and the larger group "$C=N\cdot OH$" may be considered present.

For example

CH_3	CH_3
|	|
CH	CH_2
||	||
$N{\cdot}OH$	$O{\cdot}NO$
Ethylaldoxime.	Ethyl nitrite.

It is this larger group, $C{=}N{\cdot}OH$, which has been called the "oximido-" group.

The ultimate object of this research was to correlate this structural relationship with the pharmacology of these bodies, and to discover how far they may possess any pharmacological type which can be isolated and referred to the presence of the group $=N{\cdot}OH$.

Representative members were selected for pharmacological investigation from several series of the oximido-bodies. From the fatty aldoximes were taken—ethylaldoxime, propylaldoxime, isobutylaldoxime and œnanthaldoxime; acetoxime was chosen to represent the ketoximes; isonitrosoacetone to represent the isonitrosoketones; benzaldoxime and salicylaldoxime to represent the aromatic bodies. I had previously investigated the pharmacology of quinonoxime (paranitrosophenol, $C_6H_4{\cdot}O{\cdot}NOH$).

It may be said at once that the physiological actions of these substances recall in many points the properties of nitrites. When oxidised at the body temperature decomposition takes place, and very soon the presence of a nitrite can be demonstrated.

This decomposition consists essentially in the separation of hydroxylamine from an aldehyde or ketone. In other cases the intermediate production of hydroxylamine has not been proved, but an immediate oxidation of the whole molecule and severance of nitrous acid has appeared possible.

Before analysing the experimental results of the actions of these oximido-bodies, it was necessary to define the actions of their corresponding aldehydes and ketones.

Ethylaldehyde, $CH_3{\cdot}COH$.
Propylaldehyde, $CH_3{\cdot}CH_2{\cdot}COH$.
Isobutylaldehyde, $(CH_3)_2{\cdot}CH{\cdot}COH$.
Heptylicaldehyde, $C_6H_{13}{\cdot}COH$.

The action of these fatty aldehydes on voluntary muscle is chiefly evidenced in two ways—contracture and loss of irritability and contractility. A primary stimulation is always seen in observations with minimal stimuli, but becomes more and more transient in equivalent dilutions as the series of aldehydes is ascended.

In muscle tracings a primary increased range of contraction is

seen when dilute solutions are used; but the dilution must be increased with the atomic weight of the aldehyde.

There is a primary shortening of the latent period which also varies as the primary stimulation. This same action is also reflected in the muscle curves, where the abrupt ascent and increased height, whilst always to be seen as initiatory effects, are found to become more transient. At the same time the descending arm of the curve always shows the rigidity of contracture, and that in increasing degree.

As the group of aldehydes is ascended, muscle-nerve preparations show a gradually increasing loss of irritability in the nervous path, both absolutely and also slightly in comparison with a similar loss of irritability in the muscle itself.

A primary slight exaltation of irritability in the nervous path also becomes a little more evident, and, since the nerve trunks have shown no such action, the nerve endings must be the seat of such primary stimulation.

In their action on the spinal cord these fatty aldehydes produce a primary increase of irritability followed by a secondary depression. The intensity of this primary stimulation of the spinal cord seems scarcely to vary in the case of the lower three members, that is to say, ethyl-, propyl-, and isobutyl-aldehyde, whereas the potency of their secondary depressant action intensifies with their increasing weight. Œnanthol causes a more marked primary stimulation of the cord than would inferentially be expected, and may cause reflex convulsions in the frog.

Ethyl-, propyl-, and isobutyl-aldehyde all constrict the vessels of the excised sheep kidney. This action varies inversely as the atomic weight; thus, isobutylaldehyde constricts the vessels less than propyl-aldehyde and the latter less than the ethyl compound. Œnanthol first constricts and then dilates the same vessels. In the tortoise ethylaldehyde and propylaldehyde are again vaso-constrictors. The effect of pithing the cord in the tortoise has shown that both ethyl- and propyl-aldehyde have a local constrictory influence on the vessel walls, and it would appear that this action is reinforced during the period of exalted sensibility of the cord by a like influence exerted through the spinal centres. As the cord becomes depressed this central constricting influence is abolished, or even replaced by an influence antagonistic to the local constrictory action.

Isobutylaldehyde dilates the tortoise's vessels slightly, and the action increases somewhat as the circulation is continued. This vaso-dilating action of isobutylaldehyde is again exerted locally on the walls of the vessels, and is at first either uninfluenced by, or is slightly antagonised by, the spinal cord; later, a vaso-dilating influence is also exerted through the spinal centres.

Œnanthol also dilates the vessels of the tortoise, but, provided the spinal cord be intact, by no means so markedly as the vessels of the excised kidney. Pithing the cord balances the comparison, for then the tortoise's vessels are dilated by œnanthol to as great a degree as those of the excised kidney. Œnanthol has, therefore, its local vaso-dilating action inhibited by a central action exerted through the spinal cord.

All these fatty aldehydes have essentially the same action on the heart, the difference between them being simply one of degree. They all tend to slow the cardiac rhythm, and have a primary tonic and secondary depressant action. As the atomic weight of the aldehyde increases, weaker solutions are required to show the tonic effect, and the arrest in diastole is more quickly reached.

Ethylaldoxime, $CH_3 \cdot CH{:}NOH$.
Propylaldoxime, $C_3H_6{:}NOH$.
Isobutylaldoxime, $C_4H_8{:}NOH$.
Œnanthaldoxime, $C_7H_{14}{:}NOH$.

Contrasting now the actions of the fatty aldehydes with the actions of their corresponding aldoximes as observed by similar experimentations, it is seen how closely these latter bodies reflect the combined actions of a nitrite and aldehyde.

These fatty aldoximes depress the irritability of voluntary muscle. This depressant action is also possessed by nitrites and by aldehyde. Ethylaldehyde has also a slight primary stimulant action, but this in the aldoxime molecule is for the most part absent, being counteracted by the oxime group.

The aldoximes diminish the extensibility, the elasticity, and the range of contraction of voluntary muscle, actions also possessed both by aldehyde and nitrite.

Ethylaldoxime has rarely produced an initial increased range of contraction, which initial increase is a usual effect of ethylaldehyde, but might be annulled by nitrites.

The latent period is not affected by nitrites. Under the influence of both aldehydes and aldoximes there is a primary shortening of this period.

Again, these fatty aldoximes differ amongst themselves in their action on voluntary muscle exactly as do the corresponding aldehydes. As the series is ascended the action on voluntary muscle becomes more toxic, as seen firstly in the increasing degree of contracture, and secondly in the more rapid loss of irritability.

In their action on the spinal cord they present the same characters and variations as those possessed by the corresponding aldehydes. Comparison simply shows a more marked primary stimulation in the

case of the aldehydes. This might be explained by the fact of nitrites being purely depressant to the cord. The stimulant action of the aldehyde would in this sense be discounted by the $=N\cdot OH$ group of the aldoxime.

In the same way the experimental circulation of these aldoximes has shown their action to be that of the corresponding aldehyde modified by a local vaso-dilating influence.

Lastly, accelerated rhythm coupled with depression is the type of the cardiac action of all but very dilute solutions of nitrites, and perfusion experiments on the heart have shown that these aldoximes possess this nitrite type superadded to the action of the corresponding aldehydes. Accelerated rhythm is invariably produced, whilst the primary tonic effect is less marked.

Benzaldehyde, $C_6H_5\cdot COH$.
Salicylaldehyde, $OH\cdot C_6H_4\cdot COH$.

These aromatic aldehydes have the same type of action as their fatty homologues, but differ from them in their much more powerful toxicity and greater dominance of irritation, which is more especially seen in their action on the spinal cord and voluntary muscle.

They are both vaso-dilators, though such action is not very pronounced.

A solution of either of these aldehydes not stronger than 1 part in 30,000 parts has a marked action on the frog's heart. The rhythm is slowed whilst the amplitude of beat gradually diminishes, and the heart becomes arrested in diastole. Stronger solutions cause imperfect dilatation of the ventricle during diastole, with final arrest in systole.

Benzaldoxime, $C_6H_5\cdot CH{:}NOH$.
Salicylaldoxime, $C_6H_4<\begin{matrix}OH\\CH{:}NOH\end{matrix}$.

These two aromatic aldoximes have been found to scarcely differ in their physiological actions from their corresponding aldehydes. The powerful aldehyde influence almost completely obscures any action which might be attributable to the NOH group in their structure.

Progressive contracture and loss of irritability are the main features of their action on voluntary muscle. A primary stimulation of voluntary muscle, doubtful in the actions of the fatty aldoximes, is well in evidence in the case of those aromatic compounds, and in muscle-nerve preparations is seen equally well, should the stimulus have been thrown along the nerve or directly into the muscle fibres.

The results of subcutaneous injections of these two aldoximes have

indicated their action on the spinal cord to be paramount. The reflex irritability of the cord is greatly increased until the muscles of the limbs are thrown into tetanic convulsions.

The presence of the NOH group is, however, felt by the vessel walls of the excised kidney, and is revealed by the much more powerful vaso-dilating action exerted by salicylaldoxime than by salicylaldehyde.

Also in the action of these two aldoximes on the heart the influence of the NOH group is probably to be traced in the fact that no retardation of rhythm occurs as is seen in perfusion experiments with the aromatic aldehydes, though in all other respects the cardiac actions of these two classes of aromatics are identical.

Acetoxime, $(CH_3)_2{:}C{:}N{\cdot}OH$.
Isonitrosoacetone, $CH_3{\cdot}CO{\cdot}CH{:}N{\cdot}OH$.

I have investigated the physiological actions of these substances by the same methods as those employed for the previously described bodies, and have found their actions to closely resemble those of the fatty aldoximes. The structural difference is not borne out pharmacologically. Acetoxime more especially repeats the actions of propylaldoxime, and in the presence of this fact it is interesting to observe that the molecular weight of acetoxime is exactly equivalent to that of propylaldoxime.

Isonitrosoacetone finds its parallel intermediate to propylaldoxime and isobutylaldoxime, in some of its actions approaching the former, but, on the whole, being nearer to the latter.

In molecular weight isonitrosoacetone finds its exact equivalent in isobutylaldoxime.

Acetone, $CH_3{\cdot}CO{\cdot}CH_3$.

I have examined the actions of acetone on the isolated tissues and organs, and have found that, except in the case of voluntary muscle, these actions differ in little from those of propylaldehyde. Nervous depression is the cardinal feature of the general action of acetone on the frog. Injections have paralysed the spinal cord. In muscle-nerve preparations acetone quickly depresses the irritability of the nervous path.

It is in its action on voluntary muscle that acetone diverges most from the aldehydes. Pure acetone causes no contracture in muscle, and the muscle irritability is depressed rather than the contractility. In fact, the action of acetone on voluntary muscle I have found to closely resemble that of ethyl alcohol.

On the vessels of the tortoise and excised sheep's kidney, acetone has not been found to possess any action, beyond at times an equivocal constriction.

Acetone is almost innocuous to the frog's heart in all but very strong doses, when the only action is depressed systole with final arrest in diastole.

Seeing, therefore, the resemblance in action found to exist between a ketoxime and an aldoxime, and also between isonitrosoacetone and an aldoxime; seeing, further, the resemblance in action between the involved aldehydes and ketone, it must follow, as a corollary, that the influence of the oxime group must in each case be the same. This influence is that of a nitrite, as was also found to be the case in the aromatic aldoximes.

The only discrepancy arises in the actions of acetoxime and of isonitrosoacetone on voluntary muscle. They both give rise, when present in strong solution, to the development of some contracture, a phenomenon which cannot be ascribed to acetone.

During the course of this research it has been sought to explain the nature of muscle contracture, and it has been determined that the phenomenon is probably due to direct irritation of the nerve end plates, the irritant in the case of these oximido-bodies being an aldehyde, or, perhaps, more accurately, the COH group.

In support of this contention several facts may be here adduced.

It is an active process associated with an increased formation of heat.

Tracings show the onset and decline of contracture to be in relationship with the shortening and lengthening of the latent period.

The development of contracture is prevented by curare.

A primary increase of irritability in the nervous path of muscle-nerve preparations can be traced to the end plates.

This irritability, better expressed as exalted conductivity of the end plates, becomes more marked as the power of the aldehydes to cause contracture increases.

The decline of contracture is synchronous in its onset with the loss of conductivity through the end plates.

Experiments on the oxidation of acetoxime and isonitrosoacetone have led to the detection of an aldehyde—pyroracemic aldehyde, in the case of acetoxime, and acetylformic aldehyde in the case of isonitrosoacetone. This formation of aldehyde, should it take place in the tissues, would then be a sufficient explanation for their giving rise to contracture. On the other hand, it might be argued that the oxime group, whilst in all other respects giving rise to actions identical with those of nitrites, yet exerts a primary stimulant action on nerve centres and on the muscle end plates. Such an action this investigation has not disproved.