objective stimulus. In order to account for the discrepancy between the duration of this response and the duration of its stimulus, two general theories have been advanced. The *peripheral* theory holds that the post-stimulus persistence of vestibular nystagmus is dependent upon a continuation of the excitatory process (inertial movements of the endolymph, displacement of the cupula, or the like) which is initiated in the vestibular receptors by the objective stimulus. The *central* theory, on the other hand, holds that the post-stimulus persistence of this response is dependent upon the action of a neural mechanism located within the brain, which, once properly excited by a stimulus, however brief, continues to transmit effective impulses to the muscles involved in nystagmus until either this "after-discharge" mechanism becomes self-damped (perhaps through a gradual lengthening of the refractory phase of the constituent neurons) or until its activity is checked by the occurrence of an opposing stimulus.

In the hope of obtaining possibly more definitive evidence than has previously been advanced in support of either of these two rival hypotheses, the writer has undertaken a systematic comparison of the duration of objective stimulation of the vestibular receptors and the duration of the action currents thereby produced in the vestibular nerve. By means of a vacuum-tube amplifying apparatus developed by Dr. E. G. Wever and Dr. C. W. Bray, of Princeton University, for use in their investigation of the electrical phenomena of the auditory nerve, it has been found possible to make the passage of impulses along the vestibular nerve audible in a telephone receiver. The results thus far obtained from the study of the common painted terrapin (*Chrysemys picta*) indicate that, at least in this type of subject (selected because of particular accessibility of the vestibular nerve), the action currents probably never last for more than a fraction of a second after the cessation of objective stimulation. When the terrapin is accelerated on a manually operated turntable, there is audible in the receiver a distinct burst of discharge; and when the animal is retarded there is audible another similar burst of discharges, even though the maximum angular velocity attained be quite moderate. During prolonged rotation weaker discharges may be heard more or less continuously, due presumably to the more or less constant stimulation of the vestibular receptors through slight unavoidable variations in the speed of rotation. However, at the end of rotation, objective stimulation definitely ceases; and in no case has the passage of impulses been heard for more than approximately half a second after the subject has come to rest.

It is conceivable, of course, that effective impulses may continue to pass over the vestibular nerve (due to a continuation of the excitatory receptor process) for many seconds after the end of objective stimulation, without necessarily being detectable by the technique just described. However, if further investigation, with oscillographic recording and a more accurately controllable method of stimulation, confirms the results thus far obtained, it will be reasonably certain that the post-stimulus persistence of vestibular nystagmus is due, not to a concomitant persistence of receptor activity, but rather to sustained after-discharges from a neural mechanism located within the brain.

O. H. MOWRER,
National Research Fellow
PRINCETON PSYCHOLOGICAL LABORATORY

THE SPECIAL REACTIVITY OF PEPTIDES

IT is one purpose of the present note to point out that, whereas current theory seems to assume that most of the obvious transformations of amino-acids occur when these are present as such, some of these reactions may really take place much more readily as transformations of peptides.

For some time the writer has been interpreting the decomposition[1] of cysteine and cystine derivatives by alkalies as a reaction in which preliminary enolization allowed expulsion of the sulfur (with whatever might be attached to it) as a negative group. Theory and recorded fact seemed to agree as to the modifications of the amino- and carboxy- groups necessary to produce greatly increased reactivity. Peptides (and analogous compounds) were conspicuously more reactive than simple amino-acids, though less reactive (for reasons which will be explained elsewhere) than cyclic derivatives, such as diketopiperazines and hydantoins.

From the beginning it was assumed[1,2] that this type of reaction would be reversible. It has now been found possible[3] to add p-tolylmercaptan to α-acetylaminoacrylic acid to form S-p-tolyl-N-acetylcysteine, and this is now leading to a new cystine synthesis which will perhaps have a definite relation to the natural synthesis of cystine. The important point in the present connection is, however, that it is decidedly easier to add[3] mercaptans to benzoyl-dehydrophenylalanyl-glycine ester, which may be considered as a model of a dehydro-tripeptide. The addition as well as the elimination of sulfur derivatives thus occurs according to the principles already advanced. That is, it occurs more readily in a peptide which is at least a tripeptide, and in which the active portion of the molecule is not in a terminal position.

[1] B. H. Nicolet, *Jour. Am. Chem. Soc.*, 53: 3066, 1931.
[2] B. H. Nicolet, *Jour. Biol. Chem.*, 95: 389, 1932.
[3] Unpublished results.

Thus two reactions, the decomposition and the formation of cysteine and cystine derivatives, occur more readily in the case of peptides. To these may be added a longer known third reaction fulfilling the same conditions—the racemization of peptides[4,5] by alkali. A further extension of the principle will now be considered.

Is "Oxidative Deamination" a β-Oxidation?

Oxidative deamination[6] of amino-acids to α-keto acids under biological conditions is an accepted concept. So is, to a considerable degree, the intermediate formation of a "dehydro"-amino-acid, which is, however, formulated as $RCH:C(NH_2)CO_2H$ (A) or as $RCH_2C(:NH)CO_2H$ (B), according to the tastes of the particular author concerned. The two types are tautomers. Type B is almost surely involved in the hydrolysis; but whether A or B is originally formed in the oxidation is a matter of much interest.

Some theoretical aspects of a reaction leading to the initial formation of Type A will now be discussed. In the first place, such a reaction could conveniently be regarded as a special case of β-oxidation; and such a view-point allows the drawing of certain conclusions which, it seems to the writer, may eventually allow a decision to be reached.

It is clear that the "oxidation" of hydrogen, even when it involves merely the transfer to an acceptor other than oxygen, involves the approach of the hydrogen atoms concerned to a more positive character. But the hydrogen of least positive character, and therefore that most subject to oxidative attack, is located on the β-carbon atom, due to the effect of the carboxyl group. This effect, while in the case of a free amino-acid relatively feeble, is still very real; and it should favor the formation of a dehydrogenation product of Type A.

But two types of modification of the amino-acid structure should favor such β-activation quite strongly. These are just those modifications which have been reported as affecting so strikingly the reactivity of the sulfur-carbon bond in cystine derivatives; and excellent examples would be, peptide formation on both the amino- and carboxy- groups. In other words, *if* oxidative deamination is essentially a β-oxidation, and occurs through a derivative of Type A, it can be predicted that it will occur most readily in substances which have at least the complexity of tripeptides, and that in these the middle member of the tripeptide chain will be the most susceptible to dehydrogenation.

So far as the writer knows, no clear-cut distinction on this basis has been made as yet, either theoretically or experimentally. A variety of "model" experiments in deamination have recently been reported in which charcoal, with or without air, or substances of quinoid type, have been used to induce the reaction. These experiments, which can not here be cited in detail, show glycine to be attacked with exceptional ease. This is certainly not β-oxidation; but neither is it clear that the type of deamination used in the body is here represented. On the other hand, Krebs[7] has managed to demonstrate oxidative deamination of the usually assumed type most convincingly, since he has also isolated derivatives of the expected α-keto acids; but the kidney tissue with which he induced the reaction contained such a complex of proteolytic enzymes that it has not yet been possible to decide whether or not peptides are attacked more rapidly than the simple amino-acids. It is perhaps a modification of his procedure which will settle the question.

The main idea of this portion of the present discussion is definitely this: In so far as oxidative deamination under more or less biological conditions attacks peptides more rapidly than simple amino-acids, and the intermediate members of peptide chains rather than the terminal members, in just that measure it will appear probable that the first stage of oxidative deamination is a β-oxidation, leading to an initial product of Type A.

BEN H. NICOLET

BUREAU OF DAIRY INDUSTRY
BELTSVILLE, MARYLAND

[4] H. D. Dakin, *Jour. Biol. Chem.*, 13: 357, 1912; H. D. Dakin and H. W. Dudley, *ibid.*, 15: 263, 1913.

[5] P. A. Levene and M. H. Pfaltz, *ibid.*, 63: 661, 1925; 68: 277, 1926.

[6] F. Knoop, Oxydationen im Thierkörper, Ahrens-Sammlung, neue folge, 9: 1931.

[7] H. A. Krebs, *Zeits. physiol. Chem.*, 217: 191, 1933; 218: 157, 1933.

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