It appears that the oxidases can be produced in cells grown in a medium containing either a mixture of aminoacids without tryptophan, or with NH₄⁺ ions as nitrogen source and D-glucose as carbon source. It is possible that tryptophan, at relatively high concentrations in the growth medium, may act as a competitive homologue for the formation of the active sites in the enzyme protein. H. M. HENDERSON*

Department of Biochemistry,

University of Leeds.

* Present address: Department of Chemistry and Chemical Engineering, Constantine College of Technology, Middlesbrough, Yorks.

¹ Turner, J. M., and Happold, F. C., Biochem. J., 78, 364 (1961).

- Turner, J. M., and Happold, F. C., *Biochem. J.*, **78**, 364 (1961).
 Henderson, H. M., *Biochem. J.* (in the press).
 Pogell, B. M., *J. Biol. Chem.*, **232**, 761 (1958).
 Wada, H., Morisuc, T., Nishimura, Y., Morino, Y., Sakamoto, Y., and Ichihara, K., *Proc. Imp. Acad. Japan*, **35**, 299 (1959).
 Morisuc, T., Morino, Y., Sakamoto, Y., and Ichihara, K., *J. Biochem.* (*Japan*), **48**, 28 (1960).
 Wada, H., and Snell, E. E., *J. Biol. Chem.*, **236**, 2089 (1961).
 Scott, T. A., and Happold, F. C., *Biochem. J.*, **82**, 407 (1962).
 Dawes, E. A., Dawson, J., and Happold, F. C., *Biochem. J.*, **41**, 426 (1947).
 Lowry, O. H., Boschrouch, N. J. Farr, A. L. and Bandall, B. J., *J. Biol.*

- Lowry, O. H., Roschrough, N. J., Farr, A. L., and Randall, R. J., J. Biol. Chem., 193, 265 (1951).
- ¹⁴ Mueller, J. H., and Johnson, E. R., J. Immunol., 40, 83 (1941).
 ¹⁴ Cole, S. W., and Onslow, H., Laneet, ii, 9 (1916).
 ¹⁵ Hopkins, F. G., and Cole, S. W., J. Physiol., 29, 451 (1903).

PHYSIOLOGY

Reflex Innervation of the Ankle Joint

In spite of its obvious importance in postural physiology and lower limb surgery, no specific study of the innervation of the ankle joint in relation to mechanoreceptor reflexes elicitable therefrom has been reported previously. For this reason, we have examined the innervation of 58 ankle joints in the cat with macroscopic, microscopic and neurophysiological techniques similar to those used previously in this laboratory for the knee1, temporo-mandibular2 and laryngeal^{3,4} joints.

Extrinsic innervation. The articular tissues on the posterior aspect of the ankle joint (capsule, ligaments and fat pad) have the densest innervation—through articular branches of the long saphenous, posterior interosseous and anterior tibial nerves; from the intramuscular nerves in the flexor digitorum muscle; and from a nerve plexus in the deep posterior fascia of the lower leg. The anterior aspect of the joint is supplied from the anterior tibial nerve. The medial aspect (and the deltoid ligament) is supplied from the posterior tibial nerve. The lateral aspect (and the related collateral ligaments) is supplied from the anterior tibial and interosseous nerves.

Articular nerve endings. Microscopic examination (with gold chloride, frozen silver and methylene blue techniques) of the terminations of the articular nerves in the tissues of the ankle joint reveals the endings to be similar in type to those in the knee joint¹, although different in their relative proportions. Myelinated afferent fibres of medium size $(6-12\mu)$ in the articular nerves terminate in Type I and Type II corpuscles that are located on all aspects of the fibrous capsule of the joint. In the ankle, however, the Type II end-organs are relatively more numerous than in the knee joint¹, so that the numerical relations of the Type I and Type II corpuseles are more like those in the temporo-mandibular joints². Type II corpuscles are present also in the posterior fat pad at the back of the ankle joint, as is the case with the other joints^{1,2}. Myclinated afferent fibres of larger diameter (up to 17μ) in the articular nerves innervate Type III corpuseles, which are confined to the joint ligaments (as in other joints^{1,2,5}). Plexuses and free nerve terminals, present throughout the fibrous capsule, fat pad and the walls of the articular blood vessels at the ankle, constitute the Type IVa variety of articular nerve ending, and are supplied by small (less than 5μ) myelinated and unmyelinated afferent fibres in the articular nerves. Type IVb endings, confined to the

tunica media of the articular blood vessels, probably represent the terminations of unmvelinated, post-ganglionic sympathetic vasomotor fibres in the articular nerves.

No nerve endings of any type are present in the synovial tissue of the ankle joint-as is the case with all the other joints we have examined^{1-3,5}. Likewise, there are no Pacinian corpuscles in the articular tissues of the ankle (or other⁵) joints.

Mechanoreceptor reflexes. Neurophysiological studies^{4,5} show that the corpuscular end-organs are articular mechanoreceptors with differing behavioural charac-Type I corpuseles are slowly-adapting and teristics. Type II corpuscles are rapidly-adapting-both types having low thresholds. The Type III corpuscles are high threshold, slowly-adapting mechanoreceptors. The noncorpuscular Type IVa terminations provide the articular pain receptor system.

Passive movements of the skinned and tenotomized ankle joint in the intact, lightly anaesthetized animal activate the Type I and Type II corpuscles to produce reciprocally related polysynaptic reflex changes in motor unit activity in the log muscles, identified by multi-channel electromyography^{5,6}—dorsiflexion of the foot provoking gastroenemius facilitation and tibialis anterior inhibition. The motor unit responses are rapidly adapting from the Type II corpuscles, and slowly adapting from the fewer Type I corpuscles. The Type III corpuscles are not activated, except at the extremes of joint displacement. Painful stimulation of the capsular tissues of the joint activates the Type IVa endings to produce polysynaptic reflex spasm of both flexor and extensor muscles in the log.

The articular origin of the reflex responses in the leg muscles is confirmed by their suppression following articular neurectomy, local anaesthesia (with 1 per cent 'Lignocaine' solution) of the joint capsule, and electrocoagulation of the joint capsule. Similar reflex responses in the leg muscles can be provoked by direct mechanical stimulation of the joint capsule with varying intensities. With increasing barbiturate anaesthesia, the articular reflexes in the leg muscles are abolished before the monosynaptic stretch reflexes, elicited in the same muscles, disappear; and they can only be demonstrated at the early stages of such anacsthesia. The articular mechanoreceptor reflexes appear to operate polysynaptically through the y-motoneurone loop, contributing thereby to the co-ordination of limb muscle tone in posture and movement.

We thank Mr. Johanna Kitau for his assistance.

M. A. R. FREEMAN* BARRY WYKE †

Neurological Laboratory,

Royal College of Surgeons of England,

Lincoln's Inn Fields, London, W.C.2.

* Present address: Department of Orthopaedic Surgery, Middlesex Hospital, London.

Assisted by a grant from the Postgraduate Medical Federation of the University of London.

¹ Freeman, M. A. R., and Wyke, B. D., J. Anat. (Lond.), 98, 299 (1964).

² Greenfield, B. E., and Wyke, B. D., J. Anat. (Lond), 98, 300 (1964).
 ³ Kirchner, J. A., and Wyke, B. D., J. Anat. (Lond.), 98, 684 (1964).
 ⁴ Kirchner, J. A., and Wyke, B. D., Nature, 203, 1243 (1964).

⁵ Freeman, M. A. R., and Wyke, B. D., J. Bone Joint Surg. (to be published).

⁶ Freeman, M. A. R., and Wyke, B. D., J. Physiol. (Lond.), 171, 20P (1964).

Basal Metabolic Rate in Developing Renal Hypertension

THE development of renal hypertension in the rat, induced by means of partial occlusion of one renal artery and contralateral nephrectomy, has been reported to be associated with transient elevation of cardiac output¹. The experiments reported here were designed to test the possibility that this transient rise in cardiac output is due to a concurrent increase in metabolic rate.