The growth-rate is almost trebled compared with that obtained in the unsupplemented bread; an observation which is closely similar to those made by Rosenberg, Rohdenburg and Baldini[4]. It should be emphasized that our observations have only been concerned with growth, and the effect on other aspects of development needs to be investigated.

J. B. Hutchinson
T. Moran
J. Pace

Research Association of British Flour-Millers,
Cereals Research Station,
St. Albans.
April 27.

[1] Widdowson, E. M., and McCance, R. A., Medical Research Council Special Report No. 287 (London, 1954).
[2] Hutchinson, J. B., Moran, T., and Pace, J., *Proc. Roy. Soc.*, B, **145**, 270 (1956).
[3] Rosenberg, H. R., and Rohdenburg, E. L., *Arch. Biochem. and Biophys.*, **37**, 461 (1952).
[4] Rosenberg, H. R., Rohdenburg, E. L., and Baldini, J. T., *Arch. Biochem. and Biophys.*, **49**, 263 (1954).
[5] Harper, A. E., Benton, D. A., and Elvehjem, C. A., *Arch. Biochem. and Biophys.*, **57**, 1 (1955).
[6] Moore, S., and Stein, W. H., *J. Biol. Chem.*, **192**, 663 (1951).

Anticoagulant Action of Neodymium 3-Sulpho-*iso*nicotinate

Although it has long been known that the rare-earth metals interfere with blood clotting both *in vitro* and *in vivo*, it was not until 1950 that Vincke and Sucker[1] described, in neodymium 3-sulpho-*iso*nicotinate, a compound that was sufficiently soluble and free of toxic effects for clinical use. It is given by intravenous injection in 2·5 per cent solution and was at first regarded as a prothrombinopenic agent on the basis of a prolonged one-stage 'prothrombin' time. Recently, using newer techniques, Beller and Mammen[2] have reported that neodymium acts by reducing factor VII and factor X, leaving prothrombin normal. We have meantime been studying, independently, the mode of action of this salt, using in particular the blood thromboplastin generation test[3], with the following results.

In intravenous doses of the order of 5 mgm./kgm. in man and rabbits, it led to impairment of intrinsic blood thromboplastin generation by inhibiting, in the circulating blood, two thromboplastin constituents normally present in serum, namely, Christmas factor (*PTC*, factor IX) and factor X[4,5]—and also to reduction in factor VII (*SPCA*, stable factor) activity. It is this action on factor VII (which, it is now recognized, plays no part in blood thromboplastin formation) that is responsible for the prolonged one-stage 'prothrombin' time. These effects were demonstrable in four hours and lasted for twenty-four hours or slightly longer. With this dosage there was no alteration in the antihæmophilic globulin activity of the plasma, and the whole-blood clotting time in glass remained normal. With larger doses of 50 mgm./kgm. in animals, however, in addition to the above effects, the whole-blood clotting time was greatly prolonged and the activity of antihæmophilic globulin was reduced. In neither case was there any interference with prothrombin measured by the two-stage method, or with the thrombin–fibrinogen reaction. The action on factor VII and the serum thromboplastin factors was not prevented by oral premedication in humans with vitamin K_1 in 50-mgm. doses. In fifty-four injections in twenty patients no toxic effects were encountered.

Bergsagel[6] has shown that calcium interacts with Christmas factor at an early stage in the formation of blood thromboplastin. Since calcium and neodymium are similar in their chemical properties but are not, of course, biologically interchangeable, it is possible that neodymium acts as an antimetabolite of calcium by displacing it from combination with one or more of the protein factors in coagulation, although to date we have no evidence that excess of calcium will prevent the action of neodymium *in vitro*.

R. B. Hunter
W. Walker

Department of Pharmacology and Therapeutics,
Queen's College,
Dundee.
May 1.

[1] Vincke, E., and Sucker, E., *Klin. Wschnschr.*, **28**, 74 (1950).
[2] Beller, F. K., and Mammen, E., *Arch. für Gynäkologie*, **187**, 319 (1956).
[3] Biggs, R., and Douglas, A. S., *J. Clin. Path.*, **6**, 1, 23 (1953).
[4] Walker, W., and Hunter, R. B., *Nature*, **173**, 1192 (1954).
[5] Koller, F., communication to European Congress of Hæmatology, Amsterdam (1953).
[6] Bergsagel, D. E., *Brit. J. Hæmat.*, **1**, 2, 199 (1955).

Trans-Synaptic Atrophy in the Cerebral Cortex

The disappearance of neurones from the primate lateral geniculate body after de-afferentation has been clearly demonstrated[1], and less dramatic trans-synaptic degenerative changes have been described elsewhere in the central nervous system, for example, in the cortex of the piriform lobe after degeneration of the olfactory tract[2]. Hitherto, however, attention has been focused on the perikaryon, and the role of afferent input in preserving the normal dendritic organization of neurones has apparently never been studied.

We have examined the pyramidal cells in the pre-piriform cortex of the rat after removal of the olfactory bulb, which is known to be the main source of afferent fibres to this region[3]. Comparison of the two sides of rat brains subjected to unilateral olfactory bulb resection has revealed no obvious differences in the nuclei or perikarya of the pyramidal cells, apart from a slight reduction in size, in material stained with buffered thionin, or in the fibre plexuses in material prepared by the Holmes–Silver impregnation technique. In Golgi–Cox preparations, however, a marked reduction in the number of dendritic branches arising from the pyramidal cells on the operated side has been consistently observed during the examination of a large number of neurones in three brains.

This change is very conspicuous a hundred days after operation on forty-day old rats. It is readily observed in the plexiform layer, the second of the five layers into which the pre-piriform cortex has been subdivided[4]. This layer contains the dendrites of the pyramidal cells as they pass to synapse with the axons of the lateral olfactory tract, which spread out over the surface of the piriform lobe. Typical examples of normal and atrophic pyramidal cells that appeared to be completely stained are shown in Fig. 1; their silhouettes were traced under the micro-projector. We conclude that the normal pattern of dendritic organization of the pyramidal cells in the pre-piriform cortex is dependent upon the integrity of their afferent input.