perforation, and the latter seemed to be an unpredictable complication of peptic ulcer.

We would like to express our thanks to Professor F. H. Bentley and the surgeons of the Royal Victoria Infirmary for their kindness in allowing us to see their cases, and to Mr. H. Campbell for his help with the statistics.

REFERENCES

- Berson, H. L. (1942). *Amer. J. Surg.*, **56**, 385.
 Corlette, C. E. (1931). *Med. J. Aust.*, **2**, 587.
 Gilmour, J., and Saint, J. H. (1932). *Brit. J. Surg.*, **20**, 78.
 Griswold, R. A., and Antonic, R. F. (1941). *Ann. Surg.*, **113**, 791.
 Hinton, J. W. (1931). *Surg. Gynec. Obstet.*, **52**, 778.
 Jamieson, R. A. (1947). *British Medical Journal*, **2**, 289.
 Pearce, H. E. (1932). *Ann. Surg.*, **96**, 192.
 Tidy, H. (1945). *British Medical Journal*, **1**, 319.

DENTAL CAVITIES IN THE GOLDEN HAMSTER

BY

J. D. KING, Ph.D., F.D.S.R.C.S.

(From the Dental Research Unit, Medical Research Council, King's College Hospital Medical School, London)

The reported production of caries-like lesions in the molar teeth of the golden hamster (Arnold, 1942) has aroused new interest in the quest for experimental animals of value to workers in the dental field. Subsequent investigators assumed that the tooth cavities observed in animals receiving rations rich in carbohydrate, especially sucrose, were analogous to those found in human caries (Keyes, 1944; Dale, Lazansky, and Keyes, 1944; Orland, 1946; Sognnaes, 1948; Hurst, Firsbie, Nuckolls, and Marshall, 1948; Granados, Glavind, and Dam, 1948; Shafer, 1949; Mitchell and Shafer, 1949). On the other hand, I have shown that hamsters given wholemeal flour, wheatmeal bread, or white maize as their main dietary ingredient develop a form of parodontal disease associated with calculus deposition and food impaction leading to primary cavitation of the cementum and dentine of the tooth roots (King and Gimson, 1948-9; King, 1949).

Later disease phases include extension of the cavities into the pulp, followed by breakdown of the coronal dentine and enamel; but disintegration of the tooth crown, with the appearance of caries-like cavities, is essentially secondary to the initial root excavations which themselves result from the periodontal disturbances. The present note summarizes the first of a series of studies on the effects of replacing the cereal of such diets by refined or raw cane sugar, thus bringing the investigations more into line with those of the American workers.

Material, Methods, and Results

The experimental animals, all males, were obtained from two different sources, the approximate diets of the parents and of the offspring till weaning being as follows:

Medical Research Council Farm (M.R.C.).—Bread soaked in water, 16 parts; bran, 6; fishmeal, 3; whole wheat, 16; milk powder, full cream, 4; green foods, varied, *ad lib*.

Messrs. May and Baker (M. and B.).—Ground yellow maize, 55 parts; wholemeal flour, 15; ground linseed, 15; casein, 4; dried yeast, 5; milk powder, full cream, 5; salt mixture, 1. (The salt mixture comprised calcium carbonate, 5; sodium chloride, 5; iron citrate, 1; potassium iodide, 0.02.)

The hamsters were then given the following basal diet from weaning for an experimental period of six months: sugar, 65 parts; casein, 22 parts; dried live yeast, 0.5 part; alfalfa, 5 parts; sodium chloride, 1 part; peanut oil, 0.5 ml. daily. Each hamster received 10 g. daily of this diet

moistened with about 10 ml. of water, and in addition 5 g. of cabbage and 5 g. of carrot twice weekly. The animals from each stock were divided into two groups, one receiving the refined white cane sugar as used in this country and the other a specially prepared sample of raw sugar (pol. 96), the approximate percentage composition of these products being:

	Sucrose	Invert	Ash	Water	Organic Material
Refined	99.95	0.01	0.01	0.02	0.01
Raw	96.00	1.20	0.60	0.02	0.01

The fluorine contents of the two varieties of sugar, estimated according to the method described in the report to the Medical Research Council's Fluorosis Committee (1949, Memo. No. 22), were refined, 0.36 p.p.m.; raw, 0.3 p.p.m. F. Before mixing with the other dietary ingredients, the particle size of the sugars was rendered similar by grinding to powder form.

The results given in Table I are based on the presence of definite tooth cavitation visible in radiographs magnified three times; in each instance they were confirmed by dissecting microscope examination ($\times 18$) of the tissues *in situ* with the aid of a fine exploratory broach.

TABLE I.—Incidence of Dental Cavities in Hamsters: Radiographic and Dissecting Microscope Observations

Stock Origin	Type of Sugar in Experimental Diet	Animals			Molar Teeth		
		Total Observed	Affected		Total Present	Affected	
			No.	%		No.	%
M.R.C.	Refined	20	8	40.0	240	14	5.8
	Raw	20	4	20.0	240	4	1.7
M. & B.	Refined	26	12	46.2	312	20	6.4
	Raw	22	10	45.5	264	15	5.7

It is evident that no firm conclusions can be drawn from these findings. In the M.R.C. stock groups those given the refined sugar seem to have been rather more prone to tooth destruction than those receiving the raw sugar, but in the M. and B. hamsters the effects of the two sugars were closely similar. It is of course possible that the stock (pre-natal and pre-weaning) diet may have influenced the issue, but even if this were so there is still no explanation of the apparent difference between the two main groups.

In other respects, however, the results were by no means sterile. On x-ray diagnosis, there was a general but not always consistent tendency for the upper teeth to be more affected than the lower: taking all groups together, the percentage incidence figures for the two jaws were 3.8 and 1.1 respectively. Histological examination of the material disclosed a much higher incidence of both maxillary and mandibular lesions but little difference in their proportionate distribution. By radiographic and by histological diagnosis the upper third and second and lower first and second molars, in that sequence, were the most prone to destruction. This observation is of interest in view of the similar distribution of calculus-induced parodontal disease in hamsters on high cereal rations (King, 1949), but assumes still greater significance when the histopathology of the present lesions is considered.

Decalcified serial sections were made from 48 teeth of the M.R.C. groups showing radiographically definite or suspected cavities. Histologically, 32 cavities were found, and in all but two the initial lesion was clearly sited in the cementum of the tooth root, whence it progressed into the dentine and often into the pulp; with involvement of the latter, secondary disintegration of the coronal dentine and

overlying enamel soon followed, simulating, but only in end-effect, coronal caries in man. In no instance could primary coronal cavitation be established. The animal cavities here, as in the cereal experiments, were invariably associated with progress of calculus-like material beyond the amelo-cemental junction, arousing inflammatory or other disturbances in the periodontal membrane and further facilitating the impaction of food debris. The most severe cavitation was generally found in those parts of the denture neighbouring on the openings of the salivary ducts, and excavation of an adjacent tooth root appeared to be largely dependent on extension of parodontal disease to that area. So far these findings have been confirmed in a further series of 146 sugar-fed hamsters by radiographic examination of all and by serial sections of 266 representative teeth. The precise mechanism of the cemental and dentinal breaches is now under active investigation.

Comment

It is of interest that root cavities may also result from calculus-induced parodontal disease in *ferrets* given diets containing relatively large amounts of bread or oatmeal (King, 1944; King and Glover, 1945), and in these animals, at least, identification of the calculus presents no difficulty. The amount of "calculus" obtainable by gently scraping teeth of affected hamsters is relatively small and determinations of its chemical composition have not yet been made. However, the presence of calcium in such scrapings has been shown histologically by Lillie's (1948) modification of the alizarin-red technique of Langeron (1933): the alizarin-positive hamster specimens compare well with similar preparations of human and ferret calculus. These observations—together with the manner in which the material builds up on the hamster's enamel cuticle, burrows into the gingival crest, pushes out the subgingival epithelium and forms a parodontal pocket, invades the periodontal membrane, and progresses along the cementum of the tooth root—strongly suggest the accretions' similarity to calculus in the ferret.

From these results and from others to be reported later it would seem that extreme caution should be exercised in interpreting tooth cavitation in the hamster as being analogous to human coronal caries arising in the enamel. This is not to decry the use of the hamster for dental research purposes, since for parodontal studies alone it is an animal of great promise. Indeed, it may be that some of the cervical and interstitial tooth cavities assumed to be of carious origin in man in fact result from parodontal disease, but much further investigation is necessary before this suggestion can be seriously entertained.

Summary

The relative incidence and distribution of dental cavities in hamsters are described, following experimental feeding of diets containing high proportions of refined and raw sugar.

In contrast to the findings of other workers, it was observed that the lesions arose in the cementum of the molar tooth roots, whence they progressed through the dentine to the pulp. Disintegration of the coronal dentine and enamel occurred as a secondary extension of the root cavities, and in no instance could primary cavitation of the enamel be established.

The lesions were associated with irritation and other disturbances due to penetration by calculus-like material and impacted food debris, and similar phenomena have been encountered in ferrets.

The differences between the hamster syndrome and enamel caries in man are discussed.

My thanks are due to Messrs. Tate and Lyle and especially to Mr. Philip Lyle and Mr. J. O. Whitmee, for the sugar supplies, and

to Mr. H. C. E. Powers, their chief chemist, for the general sugar analyses; to Miss J. Lenz for the fluorine estimations; and to Mr. R. Thorley for the histological preparations.

REFERENCES

- Arnold, F. A. (1942). *Publ. Hlth Rep., Wash.*, **57**, 1599.
 Dale, P. P., Lazansky, J. P., and Keyes, P. H. (1944). *J. dent. Res.*, **23**, 445.
 Granados, H., Glavind, J., and Dam, H. (1948). *Acta path. microbiol. scand.*, **25**, 453.
 Hurst, V., Firsbie, H. E., Nuckolls, J., and Marshall, M. S. (1948). *Science*, **107**, 42.
 Keyes, P. H. (1944). *J. dent. Res.*, **23**, 439.
 King, J. D. (1944). *Brit. dent. J.*, **77**, 213, 245.
 — (1949). *J. Path. Bact.*, **61**, 413.
 — and Gimson, A. P. (1948-9). *Brit. J. Nutr.*, **2**, 111.
 — and Glover, R. E. (1945). *J. Path. Bact.*, **57**, 353.
 Langeron, M. (1933). *Précis de Microscopie*, 5th ed. Masson, Paris.
 Lillie, R. D. (1948). *Histopathologic Technique*, p. 249. Blakiston Co., Philadelphia.
 Mitchell, D. F., and Shafer, W. G. (1949). *J. dent. Res.*, **28**, 424.
 Orland, F. J. (1946). *Ibid.*, **25**, 455.
 Shafer, W. G. (1949). *Science*, **110**, 143.
 Sognnaes, R. F. (1948). *J. Amer. dent. Ass.*, **37**, 676.

HYPERCALCAEMIA DURING VITAMIN D TREATMENT OF RHEUMATOID ARTHRITIS

BY

H. St.C. C. ADDIS, M.B., B.Chir., M.R.C.P.

AND

R. D. CURRIE, M.B., Ch.B.

(From the University Rheumatism Centre, Manchester
Royal Infirmary)

That excessive administration of vitamin D gives rise to toxic symptoms has been known since 1928, when their occurrence was reported in a baby treated with irradiated ergosterol (Hess and Lewis, 1928). Since that date many other reports have been published (Anning, Dawson, Dolby, and Ingram, 1948). The purpose of the present communication is to stress the dangers inherent in the employment of massive doses of vitamin D, the inadequacy of purely clinical control, and the absolute necessity for repeated laboratory control of such treatment. Two cases seen at the Rheumatism Clinic of the Manchester Royal Infirmary are reported in illustration of these points.

Case 1

A single woman aged 61 was admitted to the infirmary on September 8, 1949. She was extremely pale and apathetic, and complained of pain in the neck and knees with marked lack of energy.

After an attack of tonsillitis and erysipelas in 1942 she had developed a generalized polyarthritis accompanied by anorexia and loss of weight. Several courses of gold produced no improvement, and her condition remained unchanged until 1946. At this time some subjective improvement occurred following treatment from her doctor. Eighteen months before admission she first developed pain in the neck, which steadily increased in severity until it became her principal complaint. About this time she began to tire easily and to lose her appetite. These symptoms persisted up to the time of her admission to hospital, and were accompanied by loss of weight and by nocturnal frequency of micturition. The only significant point in the past history was "Bright's disease" at the age of 5 years.

On examination she was extremely pale and wasted. The skin was lax but the tongue moist. Subconjunctival calcification was present in both eyes. Pubic and axillary hair was scanty. Symmetrical tenderness and swelling were present in