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Efficiency and Advantages of Calcium Gluconate as a Therapeutic Agent.*

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Until a few years ago the progress of calcium therapy was seriously hindered by the physical and pharmacological properties of practically all calcium salts. Many are hygroscopic; practically all are nauseatingly salty-bitter to the taste; many are not well borne by the gastro-intestinal tract; and when their solutions are placed under the skin, severe, local, inflammatory reactions, leading even to actual necrosis, almost invariably follow.

Recently there has appeared 'Calcium-Sandoz," a calcium salt of gluconic acid—an oxidation product of glucose. This preparation is tasteless, soluble in water to the extent of 3% at room temperature; at higher temperatures it is 20-30% soluble. It contains 13% CaO, or 9.3% Ca. Physiologically and pharmacologically it has been found equivalent to $CaCl_2$ in equimolecular concentrations. Its medium lethal dose for mice and rabbits is much less than that of the chloride, the mannitol sulfate, and the mixture of the chloride and urea. When injected intra- or subcutaneously, or intramuscularly it causes no such severe local reactions as do the other calcium preparations just mentioned.[1] Clinically, subcutaneous and intramuscular injections are reported as relatively painless and followed by no local reactions. It has been used in the treatment of bronchial asthma, spasmophilia, pruritus, urticaria, mild tuberculosis, etc.[2, 3, 4]

These reports suggested testing calcium gluconate for preserving the lives of completely parathyroidectomized dogs, and comparing it with calcium lactate for local irritant effects. For the first purpose 9 dogs were thyroparathyroidectomized. Immediately after the operation calcium gluconate was administered according to the method of Luckhardt and Goldberg[5] except that instead of giving orally

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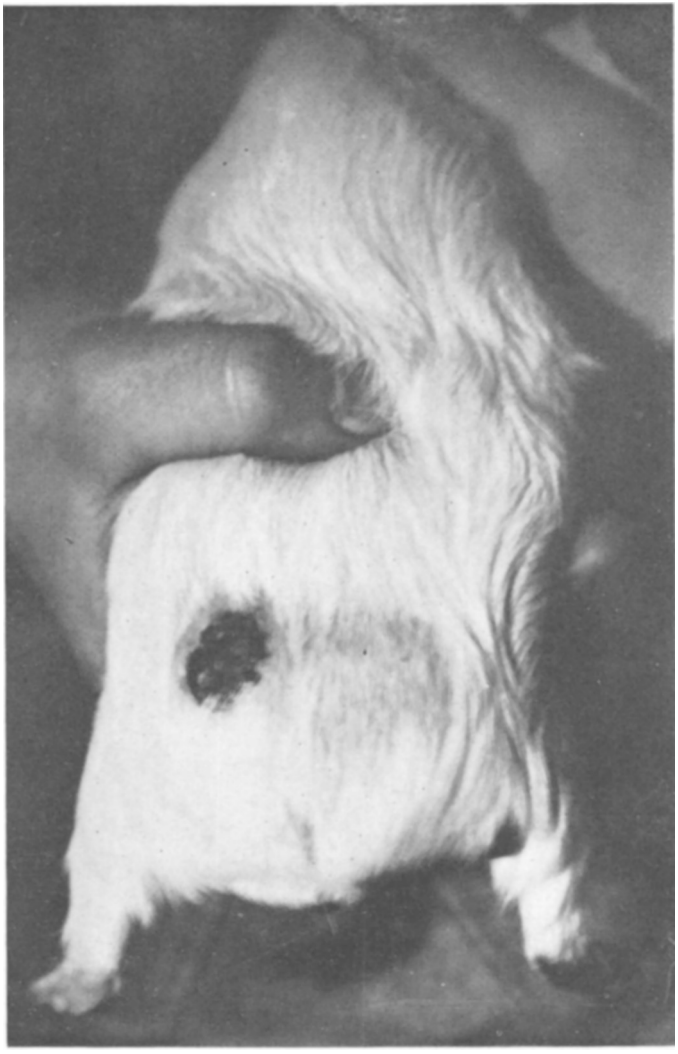
[1] Rothlin, *Schw. Med. Woch.*, 1927, 17.

[2] Kottmann, *Schw. Med. Woch.*, 1927, 18.

[3] Zimmerman, *Aertzl. Rundschau*, 1928, 7.

[4] Schaffler, *Deutsche Med. Woch.*, 1927, 42.

[5] Luckhardt and Goldberg, *J. Am. Med. Assn.*, lxxx, 79. See also Compere and Luckhardt, PROC. SOC. EXP. BIOL. AND MED., 1924, xxi, 526.



PIG 1. One cc. of calcium gluconate 10% (Sandoz) injected under the skin on the right side, and one cc. of calcium lactate 5%, on the left side 6 days before the photograph was taken. The solutions were sterile and aseptically administered.

1.5 g. per kg. per day, which is the calcium lactate dosage used by these authors, an equimolecular dose, *i. e.*, 3 g. per kg. per day, given in 3 doses, of the gluconate was found necessary to keep the animals free from tetany. Four to 6 days after the operation the animals were then tested for parathyroid deficiency by withholding the calcium gluconate until marked signs of parathyroid tetany ensued. Calcium gluconate injected intravenously (10 cc. of 10% solution)

almost invariably controlled the attack within 5-15 minutes and sometimes sooner.

Of the 9 animals 2 died of an accident while the stomach tube was being passed, one lived 11, the other 4 days after the operation; a third died after 13 days from a severe attack of distemper; a fourth was found dead on the fourth day with signs of acute tetany, while being tested, by withholding the calcium, for parathyroid deficiency. Of the remaining five, 2 are still living, now in the latent stage of tetany for more than 4 months. The other 3 lived for more than 50 days after operation, *i. e.,* all had survived the acute stage for 15-30 days and were no longer regularly medicated. They succumbed to acute attacks of tetany, which killed the animals in the absence of the writer. All showed a very marked diarrhea which was only partly controlled by substituting part of the gluconate by $CaCO_3$.

In order to compare the local irritating effects of calcium gluconate with that of calcium lactate an experiment was devised which we thought somewhat better controlled than those of Rothlin[1] for a similar purpose. Eight guinea pigs were given aseptically subcutaneous injections in equal amounts of equimolecular sterile solutions of calcium gluconate and calcium lactate. The sites of injection varied in the different animals but *each* animal received *both salts,* one on each of the corresponding sides of the body. The doses injected in the various animals varied from 1 to 3 cc. Two additional pigs were similarly treated except that the salts were administered intramuscularly. One of these was found dead 2 days after the injections. In all of the remaining 9 except one, the site of the injection of the lactate showed within 24-48 hours marked induration, followed, in a few days, by severe ulceration. In all of these 8 animals the site of injection of the gluconate showed very little if any discoloration, and never any induration or inflammation. The one exception made to the 9 above was injected under the skin of the lateral walls of the thorax, and there appeared no reaction at either site of the injection, but a very large area of severe necrosis and ulceration of the whole ventral surface of the thorax and upper abdomen. Apparently the calcium lactate had gravitated promptly to the most dependent portion and produced its necrosis at that place.

Conclusions: 1. Since on the basis of the experience of many investigators of parathyroid tetany it is possible to state that the average period of survival of complete parathyroidectomy in dogs is about 3-5 days, we feel justified in concluding that calcium gluconate (Sandoz) is fully as efficient in preserving the lives of com-

pletely parathyroidectomized dogs, in equimolecular doses, as is calcium lactate. 2. In comparing the experience of investigators using calcium lactate for the control of tetany with ours, it *seems* warranted to state that calcium gluconate in the doses administered appears to have a more marked tendency to produce a severe diarrhea in parathyroidectomized dogs than does calcium lactate. This effect may offset the advantage of tastelessness as compared with bitter calcium lactate. 3. We are able to confirm the finding of Rothlin, and others that calcium gluconate is practically non-irritating when administered subcutaneously and intramuscularly, whereas calcium lactate in equivalent equimolecular doses similarly administered to the very same animal causes severe inflammation and necrosis.

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Cutaneous Maximous Reflex in Experimental Hypothyroidism.

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In the normal rabbit, light tactile stimuli applied to the dorsum, causes a marked reflex contraction of the cutaneous maximous muscle. This response is especially marked if the stimulus is applied near the tail. In the cretin this reflex completely disappears but can again be elicited if the rabbit is treated with thyroid substance. The disappearance of this reflex is a reliable sign of cretinic degeneration.

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Changes of Structure and Lipin Content of Central Nervous System in Ether Anesthesia.

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The present investigation is part of a study of the reaction of the myelin sheaths of the nerve fibers under different pathological conditions. In order to avoid the criticism brought forward against

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