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# Oral cornstarch therapy: is persorption harmless?

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**Abstract.** Sediments prepared from freshly voided urine of four patients with glycogenosis Ia, or leucine-sensitive hypoglycaemia, on oral cornstarch therapy contained starch granules, evidence for persorption i.e. the incorporation of undissolved starch particles. In these patients, amyluria was more marked than in untreated controls. While cornstarch therapy is successful and causes few side-effects, the possibility of late adverse reactions to persorbed starch should not be disregarded.

**Key words:** Cornstarch – Maize starch – Persorption – Glycogenosis type I

## Introduction

Almost a decade ago, uncooked corn (maize) starch was added to the therapeutic arsenal for the control of chronic hypoglycaemia in children [2]. It became an immediate success and is now routinely prescribed for patients who profit from the slow and protracted release of glucose from the ingested polyglucose compound [3]. Oral cornstarch has complemented, and sometimes replaced the cumbersome nocturnal nasogastric feeding of glucose in patients with glycogenosis type I [13, 14]. It has also found its use in the treatment of leucine-sensitive hypoglycaemia, glycogen synthase deficiency [unpublished] and of infant dumping syndrome after fundoplication [5].

It is widely held that the ingestion of tens of grams of "raw" starch, one or several times a day for weeks, months and years carries no risk except perhaps that of caloric overfeeding which, of course, can be avoided by careful planning of diet. In fact, its apparent safety made this simple, effective and inexpensive dietary agent especially attractive.

Yet one wonders whether the potential harm caused by the persorption of starch, i.e. the passing of solid particles from the intestine into the blood stream has been duly considered. As we show below, starch granules were detected in freshly voided urine of patients with glycogenosis Ia or leucine-sensitive hypoglycaemia taking starch orally, and thus persorption was demonstrated.

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## Patients

Three of the four patients (cases 1–3) had glycogenosis Ia, diagnosed by glycogen measurement and enzyme assays on liver biopsy, one had leucine-sensitive hypoglycaemia (case 4). All received uncooked cornstarch Maizena, suspended in a cold drink or sprinkled over semisolid food, during regular meals. Patient 1 (B.K., male, 25 years) had been weaned, at age 22.5 years, from nocturnal nasogastric glucose feeding to frequent meals supplemented by 140 g of starch per day. He voided urine 3 h after ingesting 30 g of starch. Patient 2 (P.D., male, 8 years) receives 80 g of starch daily. He voided urine a few h after ingesting 10 g of starch. Patient 3 (S.S., male, 22 months) is given 85 g of starch per day, in six doses. He voided urine 3 h after ingesting 6 g of starch, and 2 h after 12 g. Patient 4 (I.M., female, 8 years 3 months) receives 45 g of starch per day, in four doses. She voided urine 2.5 h after ingesting 10 g of starch.

Controls were 11 children aged 1 year 7 months to 15 years 10 months, seen in the outpatient clinic and selected at random, and one healthy adult male aged 23 years. None was on oral cornstarch therapy.

## Methods

Urine samples were obtained from patients and from controls at the same location, using identical materials and avoiding the use of rubber gloves. The laboratory bench was kept meticulously clean. Freshly voided urine was collected in glass and cooled; 20 ml were then centrifuged in capped tubes at 3000 rpm for 10 min at 4°C. The supernatant was decanted, the sediment stirred, one drop of it mounted between glass slides, and 3–4 slides were examined for each proband under the microscope not later than 1 h after voiding. Cornstarch granules were identified, and counted, in polarized light by their typical birefringence (Maltese crosses), their blue-black staining with iodine (0.5 g of iodine dissolved in 100 ml of 1.5 g potassium iodide in water), and by comparing their form and staining with that of native Maizena cornstarch granules suspended in water.

## Results

We examined a total of five freshly voided urine samples from the four patients. In every sediment, starch

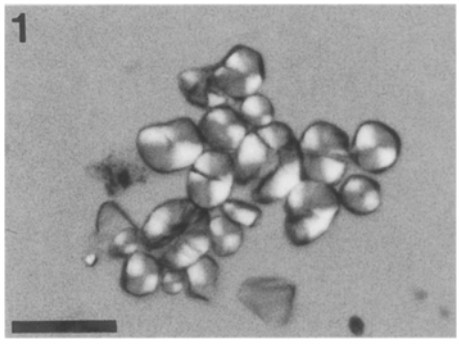


**Fig. 1.** Cornstarch granules in urine sediment of patient 3, under polarized light. Bar = 10 µm

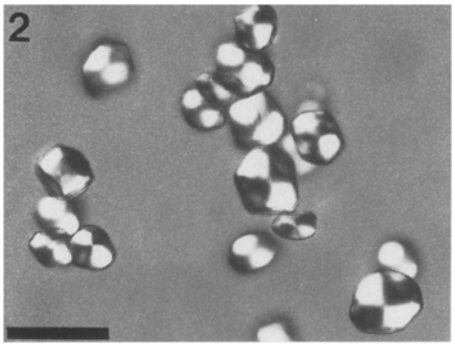


**Fig. 2.** Granules of a suspension of native Maizena cornstarch, under polarized light. Bar = 10 µm

granules were at once recognized under polarized light. Granules were birefringent (Fig. 1) and stained blue-black with iodine. They were identical with the granules in suspension of native Maizena cornstarch (Fig. 2). Each drop of urine sediment contained one to many dozens of granules. One urine sample of patient 2, collected on a separate day, was discarded because excessive amorphous urate made microscopy with polarized light impossible.

In contrast, the urine sediments of the controls contained far fewer starch granules, if any, which were seen only after a meticulous search. Sediments of seven controls contained no granules at all whereas in those of the other five, on average one to three granules per slide were identified.

## Discussion

Although the history of starch persorption [20] began almost 150 years ago, this seems to be the first observation of starch granules in the urine of patients on cornstarch treatment. As shown here, the patients' amyluria was in excess of that of the untreated controls.

The appearance of orally ingested starch particles in the chylus and blood stream was first reported in 1844 by Herbst [7] and soon confirmed and extended to other particular matter [20]. Reports variably stirred interest and scepsis, and twice the phenomenon fell into 50 years of oblivion, after 1845 and again after 1911, just as Verzar had shed his own scepticism by swallowing his own test portions of starch [16].

The term "persorption" was coined by Volkheimer [18]. Starting in 1960, he thoroughly studied the phenomenon in painstaking experiments in laboratory animals and a large number of healthy students [18, 21]. Persorption designates the incorporation of insoluble particles with diameters in the micrometer range from the intestine. Particles apparently perforate [17] the intestinal epithelium between neighbouring cells, the tips of the villi i.e. the desquamation zones and the crypts being the most likely transgression sites [19, 22]. Mechanical forces seem responsible for the transport, e.g. the kneading of intestinal contents, vascular pulsations, the movements of villi. Neostigmine and caffeine increase the rate of persorption, atropine and barbiturate slow it.

After incorporation, strach granules appear in the intestinal mucosa and submucosa and are removed via chyle and by the portal blood [21]. They have been found deposited in small blood vessels of lung, liver, brain, and also in the peritoneal cavity [18, 21]; they appear in cerebrospinal fluid and bile [21]. Enzymic breakdown has been signalled by observed structural changes in the starch granules, e.g. those recovered from peritoneal rinsings and from cerebrospinal fluid [21]. Unknown are, however, the degree of retention of intact granules in various tissues and the rate of their disposal by enzyme action [21]. After the ingestion of uncooked starch, granules invariably appear in urine [18], a fact discovered in 1906 by Rahel Hirsch [8, 11].

In a recent discussion on the management of type I glycogenosis [1], participants were unaware of the phenomenon of persorption. It was stated that 9 years after its introduction, adverse effects of cornstarch therapy were not known with the exception of transient diarrhoea, increased flatulence and excess weight gain [1]. As far as present day experience is concerned, this is certainly true. As to possible late side-effects, however, we believe that caution is in order. Once starch granules appear in urine, as observed in our patients, they must have crossed not only the intestinal epithelium but also other barriers such as vascular endothelia, basement membranes etc. While this phenomenon is highly interesting it is also somewhat disquieting, for starch granules are deposited in many organs, for an unknown time [18, 21]. They may cause microembolisation and give rise to starch granulomata, as seen in glove starch granulomatous peritonitis after laparotomy [4, 9, 15], and cause sensitisation as that seen in some patients with granulomatous starch peritonitis [6].

It may be argued that compared with the quantity of ingested starch the proportion of starch which is persorbed and retained must be small [16, 18, 21]. Yet, harmful effects of seemingly insignificant amounts of starch brought into the peritoneum, e.g. through vaginal exploration [10, 23] and condom use [12], have been reported. While cornstarch therapy retains its place in the management of chronic hypoglycaemia, the possibility of late occurring adverse effects should not be disregarded.

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