Figure 1. Interstitial Cardiac Mast Cell (Patient 1 [×4700]), with Extruded, Membrane-Free Granules with Altered Matrix (Arrows).
Some granules are in the process of being released from this undamaged mast cell. All cytoplasmic granules also show swelling, altered matrix, fusions of granule membranes, and formation of intracytoplasmic degranulation channels. Dense lipid bodies are unaltered (open arrows).

left and right ventricles and a decreased left ventricular ejection fraction.

Anaphylactic degranulation of human mast cells has been studied in isolated mast cells from the lungs.[7,8] These studies have shown degranulation channel formation and intracytoplasmic altered granule matrices, which ultimately dissolve before opening of channels to the cells' exterior. Rarely, extrusion of altered, nonmembrane-bound granules through plasma-membrane openings was also seen. Images diagnostic of anaphylactic degranulation of human mast cells in vivo are extremely rare. They must be extremely rapid events, and have been recorded with certainty only in skin specimens stimulated either by scratching a lesion of urticaria pigmentosa[9] or by intradermal injection of C5a.[10] In both instances, actual granule extrusion was recorded.

We present these two cases to document the unequivocal occurrence of degranulation of mast cells in human heart tissues in vivo. The degranulation mechanism includes the extrusion of altered, membrane-free granules to the cells' exterior, as well as intracytoplasmic solubilization of granules and degranulation channel formation. Although these are difficult images to capture in vivo, in vitro studies with isolated human pulmonary mast cells clearly associate these morphologic events with the rapid release of histamine.[7,8] Although the precise triggering mechanism, among the many possible ones, cannot be determined by morphologic analysis alone, the identification of these morphologic events suggests a role for mast cells and their release reactions in the pathogenesis of otherwise unexplained cardiac disorders.

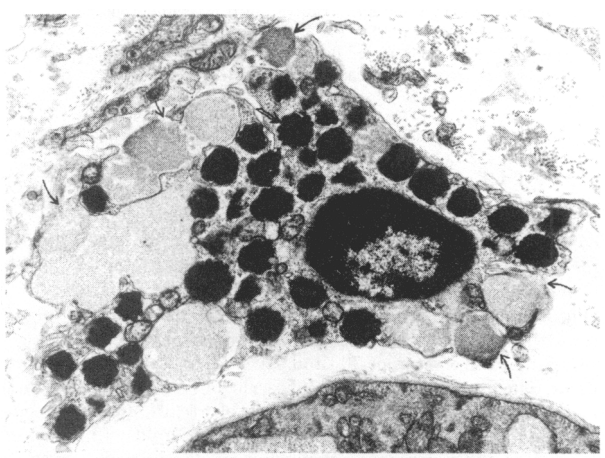

Figure 2. Interstitial Cardiac Mast Cell (Patient 2 [×8550]), with Extrusion of Membrane-Free, Swollen Granules with Altered Matrix Patterns from Multiple Openings in the Plasma Membrane (Arrows).
Many typical cytoplasmic granules show no alterations (open arrow).

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ENTERIC HYPEROXALURIA AND UROLITHIASIS

To the Editor: Patients with small intestinal disease, jejunoileal bypass, or ileal resection may have hyperoxaluria and calcium oxalate urolithiasis as a complication.[1-3] The cause of the hyperoxaluria in these conditions, collectively known as enteric hyperoxaluria, has now been shown to be hyperabsorption of oxalate from the bowel due to complexing of calcium by the malabsorbed fatty acids in the gut[4] and increased colonic permeability to oxalate caused by both bile and fatty acids.[5]

Recently we showed that patients with recurrent calcium-stone formation had malabsorption of ascorbate from the gut, which in turn resulted in increased conversion of ascorbate to oxalate at this site and subsequently in hyperoxaluria. In addition, we showed that the intravenous administration of ascorbate to these patients and normal subjects did not increase urinary oxalate output in either group.[6] We investigated ascorbate metabolism in three patients with enteric hyperoxaluria: Patient 1, a 57-year-old man in whom 82 cm of ileum was resected and right hemicolectomy performed; Patient 2, a 52-year-old woman in whom 30 cm of jejunum and 50 cm of terminal ileum remained after resection; and Patient 3, a 30-year-old man in whom 68 cm of jejunum was anastomosed to the left colon during bowel resection. All patients had a 5- to 10-fold increase in fecal fat excretion and multiple episodes of renal colic, with an average of three attacks per year, and required renal surgery two to four years after bowel resection.

The 24-hour urinary ascorbate concentrations of these patients, though low, were within the reference range (>0.2 mmol per day). Each was given 2 g of oral ascorbate as a loading dose, and 24-hour urinary ascorbate and oxalate excretion was monitored as described previously.[6] The patients had significant ($P = 0.05$, Mann–Whitney nonparametric statistics) hypoexcretion of ascorbate (excretion expressed as a percentage of the loading dose: 6.4 percent in Patient 1, 6.1 percent in Patient 2, 0.4 percent in Patient 3; 19.9 to 29.3 percent in four normal subjects) and hyperexcretion of oxalate (2.35 percent, 0.74 percent, 1.35 percent, and 0.37 to 0.5 percent, respectively).

The ascorbate-induced hyperoxaluria in our patients may partly explain why renal oxalate excretion in such patients is not stabilized by a low-oxalate diet.[7,8] Treatment with high-dose calcium (3 g per day) and a low-fat diet normalized renal oxalate excretion in all three of our patients (<0.50 mmol per day; range before treatment, 0.92 to 1.07). Urinary calcium excretion after several days of high-dose calcium loading was less than 5 mmol per day (normal, <7.5). The biochemical changes have been paralleled by a marked reduction in stone formation in all three patients. Although oxalate excretion was controlled by high-dose calcium supplements, it is recommended that patients with hyperoxaluria, like those with recurrent calcium-stone formation, not receive high-dose ascorbate supplements.[6]

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SCIENCE OR SCAM?

To the Editor: Doctors throughout the United States are being approached to join the Clinical Advisory Board of a company called United Sciences of America. Here is an overview of its activities.

United Sciences is a multilevel marketing operation similar to that of Shaklee, Amway, and Herbalife. Distributors (called "independent associates") are recruited with a high-technology videotape that suggests that the company's products can help protect against heart disease and cancer. Independent associates are urged to use the products themselves and to persuade others to become independent associates; these, in turn, use the products and recruit more independent associates. When sales volume is sufficient, those near the top of the heap receive a percentage of the sales of those below them.

Anyone can become an independent associate by completing an application and paying $24.50 for a "Success System Kit" and manual. More than 100,000 have done so since January of this year, when the company began public operations. No knowledge of nutrition or medical care is required. According to the manual, United Sciences' nutritional products are "truly revolutionary" and "represent the basic elements of a highly effective program for optimal health." The manual also claims that the products constitute "the finest nutritional program ever developed" (despite the fact that no foods or dietary advice are involved). Independent associates pay $100 for a month's supply, which retails for $135. The company projects gross sales of $150 million this year and says it is the fastest growing business in American history.

Independent associates are asked to submit the names of doctors for United Sciences' Clinical Advisory Board. Hospital residents as well as office-based physicians are being solicited. When a name is received, the doctor is sent an information kit that includes the introductory videotape, a videotape about research findings, and applications to join as a research member or physician affiliate of the Clinical Advisory Board. Research members are expected to conduct research on their patients, whereas affiliates are merely placed on a mailing list for medical reports.

The applications ask how many referrals the doctor can accommodate. According to the plan, the company will refer users who have questions about United Sciences' products or who need general medical care. Some doctors have reported being asked by independent associates to sell the products to their patients or recommend that they buy them from an independent associate (with a commission to the doctor possible).

I doubt that United Sciences' products are "a highly effective program for optimal health." As far as I know, they were not tested before marketing. Moreover, an optimal health program should involve more than high-priced food supplements, protein powder, and candy bars.

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OCCASIONAL NOTES

MARKETING A NUTRITIONAL "REVOLUTIONARY BREAKTHROUGH"

Trading on Names

The fact that they have M.D.'s backing up the product is the biggest plus they have. . . . For decades the multilevel field [of marketing] has been the province of snake-oil salesmen, so the credibility provided by top-name medical people is invaluable.

THESE quotes are from "Big Plans," published in February 1986 in *Inc.*, the "magazine for growing companies." Who are "they," what is the product, who are the M.D.s, and are they really top-name medical people?

"They" are United Sciences of America, Inc. (USA, Inc.), of Carrollton (Dallas), Texas. The "product" is a nutritional supplement — in fact, four supplements. The M.D.s backing the product are members of the Scientific Advisory Board of USA, Inc.; most of them are highly recognized in their fields of expertise, but not in nutrition.

What intrigued me about USA, Inc., was a statement from its "Company Overview" of its corporate mission: "To provide all Americans with the potential of optimum health and vital energy through state-of-the-art nutrition." To accomplish this, "United Sciences of America, Inc., has drawn together into a single corporate entity the brilliant talents of world-renowned scientists, medical researchers and business experts to achieve a new national goal." The statement continued,

United Sciences of America, Inc.'s revolutionary program was born out of necessity: a dedicated response to the soaring dangers to our health from toxic pollution, stressful lifestyles and the loss of vital nutrients in food from "modern" farming techniques, mass processing and improper cooking.