On the Appearance of Absorbed Fat Droplets in the Nuclear Envelope. By Sanford L. Palay. (*From the Laboratory of Neuroanatomical Sciences, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda.*)*

INTRODUCTION

Since Watson (17) first reported that the nuclear envelope is continuous with the endoplasmic reticulum, numerous observers have noted examples of such continuity in the cells of several tissues (2–4, 8, 9, 12–14, 19). Connections between the membranes of the endoplasmic reticulum and the cell surface have also been demonstrated in several cell types (2, 3, 7–9, 19). In 1955 Palade (8) first formally set forth the concept that "the membrane limiting the cavities of the endoplasmic reticulum appears to be continuous with the cell membrane and the nuclear membranes," at least intermittently. This hypothesis implies the corollary that the cavities of the endoplasmic reticulum are continuous with the extracellular space and with the perinuclear cisterna, at least intermittently. As might be expected, demonstrative examples of the complete continuity from cell surface to nuclear envelope are not readily encountered, because of the inherent limitations of studying by means of thin sections a system so diverse and pleomorphic as the endoplasmic reticulum. In 1957, however, Epstein (3) published a micrograph of the cytoplasm from a Rous sarcoma cell in which the unbroken continuity of the limiting membrane of the endoplasmic reticulum could be traced within one field from its junction with the cell surface on the one hand to the nuclear envelope on the other. Thus morphological continuity from the extracellular space right through the cavities of the endoplasmic reticulum to the perinuclear cisterna has been demonstrated in at least one cell type. Diagrams picturing this condition have been published by Novikoff and Podber (5), Robertson (15), and Siekevitz (16), although Robertson has expressed doubts concerning their validity.

The present report is a brief description of findings which support the concept of continuity.

Materials and Methods

Blocks of tissue containing the full thickness of the intestinal wall were obtained from the jejunums of 21 fasted and 15 fat-fed Sprague-Dawley rats, according to the procedures given in detail in two previous publications (10, 11). After fixation in osmium tetroxide and embedding in methacrylate, the blocks were cut into thick sections for study with the phase contrast microscope and into thin sections for electron microscopy. Micrographs were made with the RCA-EMU-2E or 3B electron microscope.

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OBSERVATIONS AND DISCUSSION

Particulate fat is absorbed from the lumen of the small intestine by filtering between the microvilli of the striated border and inclusion within small pinocytotic vesicles at the bases of the intermicrovillous spaces of the epithelial cells (11). From these superficial vesicles the fat droplets pass into the endoplasmic reticulum, both granular and agranular, filling the apical two-thirds of the cell. The cisternae of the Golgi complex became distended with fat droplets. At the lateral margins of the cell, the droplets are discharged into the intercellular spaces of the epithelium.[1] The pathway of the fat droplets thus follows the devious channels of the endoplasmic reticulum from the apical surface of the epithelial cell to its lateral surface. The droplets may, therefore, be considered as physiological markers of the continuity, however transient, among the units of the reticulum and between the reticulum and the cell surface. In the same fashion the appearance of fat droplets in the perinuclear space of the nuclear envelope constitutes evidence of the physiological continuity between the endopasmic reticulum and the nuclear envelope.

Figs. 1 and 2 demonstrate fat droplets lying between the two leaves of the nuclear envelope. These two micrographs were made of sections of intestinal epithelium obtained from rats 30 minutes and 3.5 hours after administration of corn oil. The fat droplets are 60 to 200 mμ in diameter and occupy distended portions of the perinuclear cisterna. They are the same size and density as the other droplets present in the endoplasmic reticulum of the same and neighboring cells, and in the intercellular spaces of the epithelium. There seems to be no reason for doubting that their previous history is also the same, that is, they represent droplets of absorbed fat, taken up by pinocytosis and passed through the cavities of the endoplasmic reticulum. Fat droplets are only rarely found in the nuclear envelope. Those pictured in Figs. 1 and 2 are the only examples we

[1] Recent evidence (1) from studies with doubly labeled tracers indicates that only 20 to 50 per cent of dietary glycerides appearing in the thoracic duct lymph have been completely hydrolyzed during digestion and absorption.

have discovered in a study of the intestinal epithelium from 36 animals, either fasted or fat-fed. The rarity of this observation may be accounted for, first, by the relatively small volume of the nuclear envelope compared with the total volume of the endoplasmic reticulum, and, second, by the fact that the major traffic of fat droplets tends towards the lateral surfaces of the epithelial cells (11).

The appearance of absorbed fat droplets in the nuclear envelope lends further support to the concept that the envelope is properly a part of the cytoplasm (17, 18), and that the perinuclear cisterna within it is continuous with the lumen of the endoplasmic reticulum. Until now this concept has been based upon the frequent observations of morphological continuity between the nuclear membranes and the endoplasmic reticulum (2, 3, 8, 12, 16), and upon the appearance of ribonucleoprotein granules encrusting the cytoplasmic side of the envelope in many cell types (6, 8). The present observation, furthermore, suggests that the content of the nuclear envelope, like that of the endoplasmic reticulum, is fluid enough to allow unobstructed passage of particulate material.

Finally, this observation, together with the previously reported study of fat absorption (11), demonstrates the *physiological* integrity of the endoplasmic reticulum from the cell surfaces to the nuclear envelope. A body introduced into the reticulum at one point can be transported to any other point without leaving the system. Although the reticulum can be dispersed or fragmented at any one moment, or at any one spot; although a particular configuration can be evanescent, the system retains its reticular pattern by virtue of the labile or persistent interconnections among its several units.

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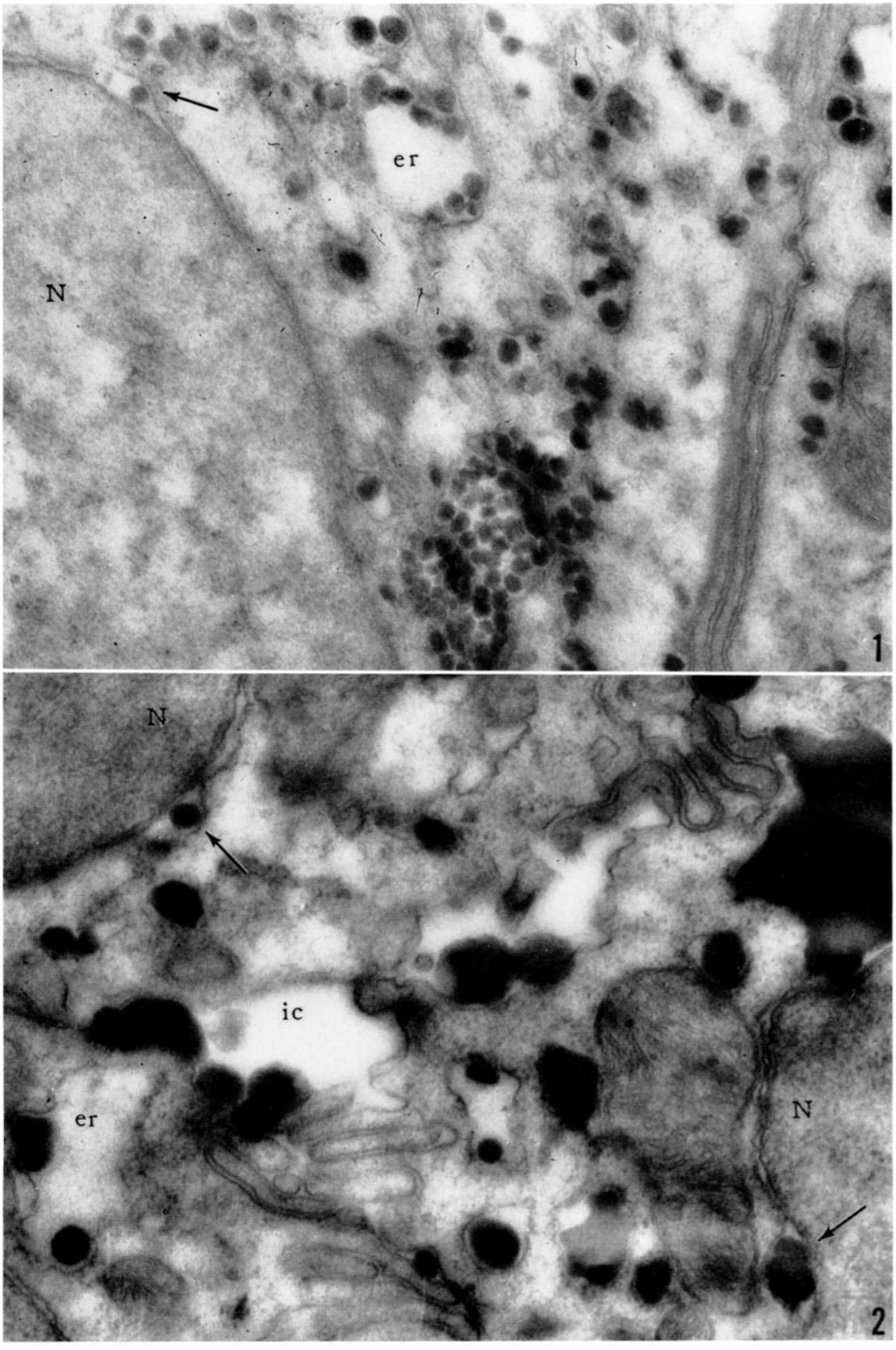
Explanation of Plate 214

Fig. 1. Portion of an intestinal epithelial cell from a rat 30 minutes after intragastric instillation of 1.5 ml. of corn oil. The nucleus (*N*) lies at the left margin of the figure and the highly folded, interdigitating lateral cell membranes of this cell and its neighbor course diagonally across the figure at the right. Crowds of fat droplets occupy the cisternae and vesicles of the endoplasmic reticulum (*er*). Two extracellular fat droplets lie between the two epithelial cells. Near the left upper corner of the figure a small fat droplet is located within the perinuclear cisterna (arrow). × 52,000.

Fig. 2. Portions of three intestinal epithelial cells from a rat 3.5 hours after intragastric instillation of 1.5 ml. of corn oil. The nuclei (*N*) of these cells are visible in the left upper, left lower, and right lower corners of the figure. The intercellular junction (*ic*) courses diagonally across the middle of the picture. Numerous fat droplets appear in this intercellular space. Other fat droplets are intracellular, enclosed within the endoplasmic reticulum (*er*). The nuclear envelopes of the nuclei at the left upper and right lower corners of the figure contain fat droplets (arrows). × 52,000.



(Palay: The nuclear envelope)