Effect of Dietary Magnesium on Secretion of Serum Lipoproteins in Hyperlipoproteinemic Rabbits[1]

D. A. Werderitsh, K. Hess, D. Sanford, K. R. Safranski, and D. J. Morré.
Department of Biological Sciences
Purdue University, West Lafayette, IN 47907.

Abstract

Hyperlipoproteinemia was induced in rabbits by diets and ethanol. Golgi apparatus were disoriented and large accumulations of lipid appeared in smooth endoplasmic reticulum (SER) of the apical cytoplasm. When the diet was supplemented with magnesium, cholesterol levels were significantly lowered. The increased magnesium also appeared to maintain functional hepatic Golgi apparatus as well as result in a reduction in lipid deposits in the SER. An involvement of lysosomes in the latter was indicated.

Introduction

Two pathways are involved in the secretion of serum lipoproteins by the liver (8). 1) Protein synthesis is in the rough endoplasmic reticulum with modification and glycosylation in the Golgi apparatus. Secretory vesicles leave the distal face of the Golgi apparatus, carrying their contents to the cell surface where the lipoprotein is discharged into the capillary space. 2) The proteins are synthesized in rough endoplasmic reticulum with lipid addition in the smooth endoplasmic reticulum. Vesicles bud off the smooth endoplasmic reticulum and empty their contents at the cell surface into the blood stream. The proportion of lipoproteins following this route has not yet been determined. It is assumed that these lipoproteins are less glycosylated than those following the first pathway.

Hyperlipoproteinemia can be induced with high fat diet and ethanol (1,4,5,6,9). Magnesium was selected to ameliorate the effects of such a dietary regimen in rabbits since there is evidence of magnesium deficiency in human alcoholics (3) as well as experimental animals maintained on atherogenic diets (5,6,9). Early atherosclerotic lesions induced by atherogenic diet are diminished (or retarded) by increasing dietary magnesium (5,6,9).

The present study investigated the effects of atherogenic diet and alcohol on the liver cell, particularly the secretory mechanism. This study also shed light on the modifying role of increased dietary magnesium on these altered secretory patterns.

Materials and Methods

New Zealand male white rabbits were maintained in separate cages on three different diets. Group A, received standard rabbit pellets and water, *ad libitum;* Group B, atherogenic diet (#170060, Teklad) and 40% ethanol, *ad libitum;* Group C, atherogenic diet enriched with magnesium

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as magnesium oxide to ten times standard dietary levels and 40% ethanol, *ad libitum.*

Blood was collected from the ear vein each week. Total serum cholesterol was determined by the direct serum method (7).

Animals were sacrificed after nine weeks. Gross observations were made and liver samples from each were prepared for electron microscopy. Fixation was overnight in cold 1% osmium tetroxide buffered with 0.1 M sodium phosphate at pH 7.0. Samples were acetone dehydrated and embedded in Luft's epon. Sections were post stained with lead citrate.

Results and Discussion

Hyperlipoproteinemia was discernible after one week of an atherogenic diet and ethanol (Fig. 1), reaching a high and plateauing in five weeks. Although all the rabbits on these diets exhibit increased levels of serum cholesterol, the serum of those receiving the magnesium enriched atherogenic diet had 200 mg % less cholesterol than those without magnesium.

Growth of rabbits on the atherogenic diet and ethanol was retarded. The coats of these rabbits was ruffled and unkempt, but much less so in the rabbits receiving the magnesium enriched diet. The liver was caseous in texture, had a brownish color and fractured easily. These symptoms could have been the result of the diet, alcohol intoxication, or, in the one group, magnesium deficiency.

Thin sections of control liver (Fig. 2) had ultrastructural characteristics typical of mammalian liver with lipoprotein bearing secretory vesicles originating at the Golgi apparatus.

In the liver of rabbits receiving atherogenic diet (Fig. 3), Golgi apparatus were sparse; those still recognizable were diminutive and disorganized. Secretory vesicles when present were void of lipoprotein particles. Near the apical portions of cells large accumulations of lipid were found in association with smooth endoplasmic reticulum. The rough endoplasmic reticulum of the cell was swollen, the lumina contained granular material of moderate electron density.

When the atherogenic diet was enriched with magnesium, the Golgi apparatus in liver thin sections (Fig. 4) conformed more closely to the typical image. Some lipoprotein particles were visible in secretory vesicles. Near the apical portion of the cell were numerous autophagic vacuoles and lysosomes containing large residual bodies. The lipid deposits in the smooth endoplasmic reticulum are greatly reduced. The rough endoplasmic reticulum remained distorted and swollen.

These observations suggest that an atherogenic diet accompanied by ethanol disrupts the secretory mechanisms in the liver. Large amounts of dietary magnesium appear to restore or maintain some normalcy to the secretory mechanism. The large number of autophagic vacuoles and lysosomes in the livers of animals receiving the magnesium-supplemented diet implicate the lysosomal apparatus in the restoration or maintenance process.

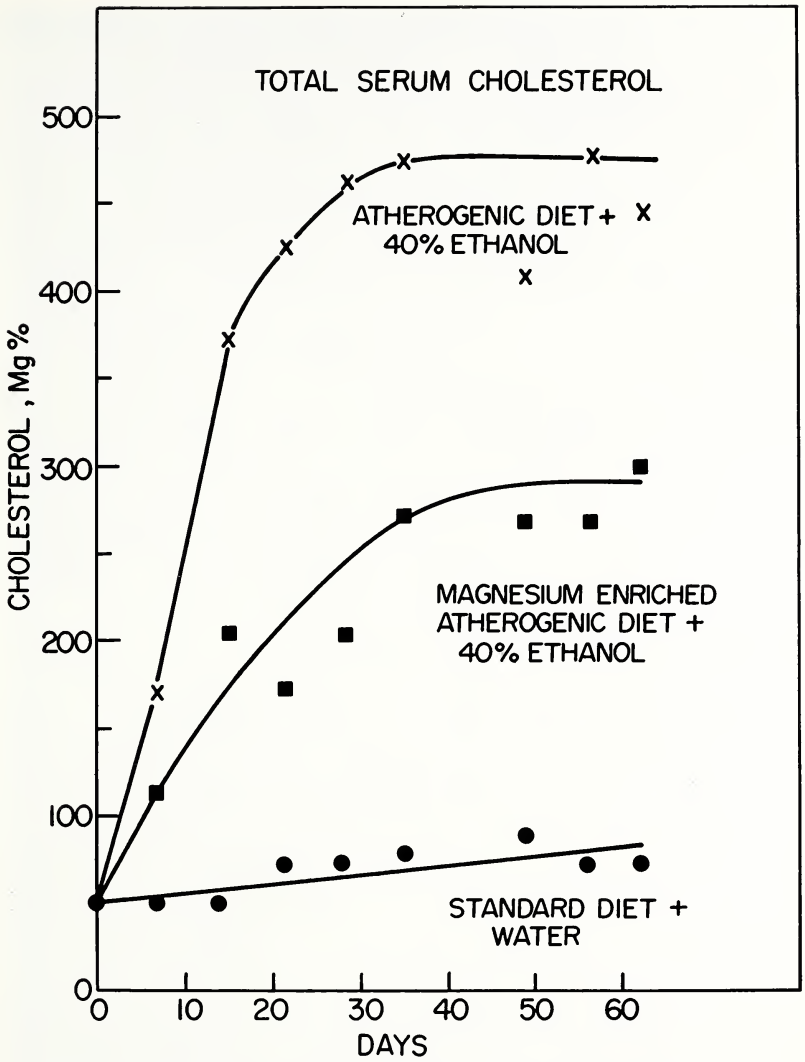

FIGURE 1. *Total serum cholesterol determined weekly using the direct serum method.*

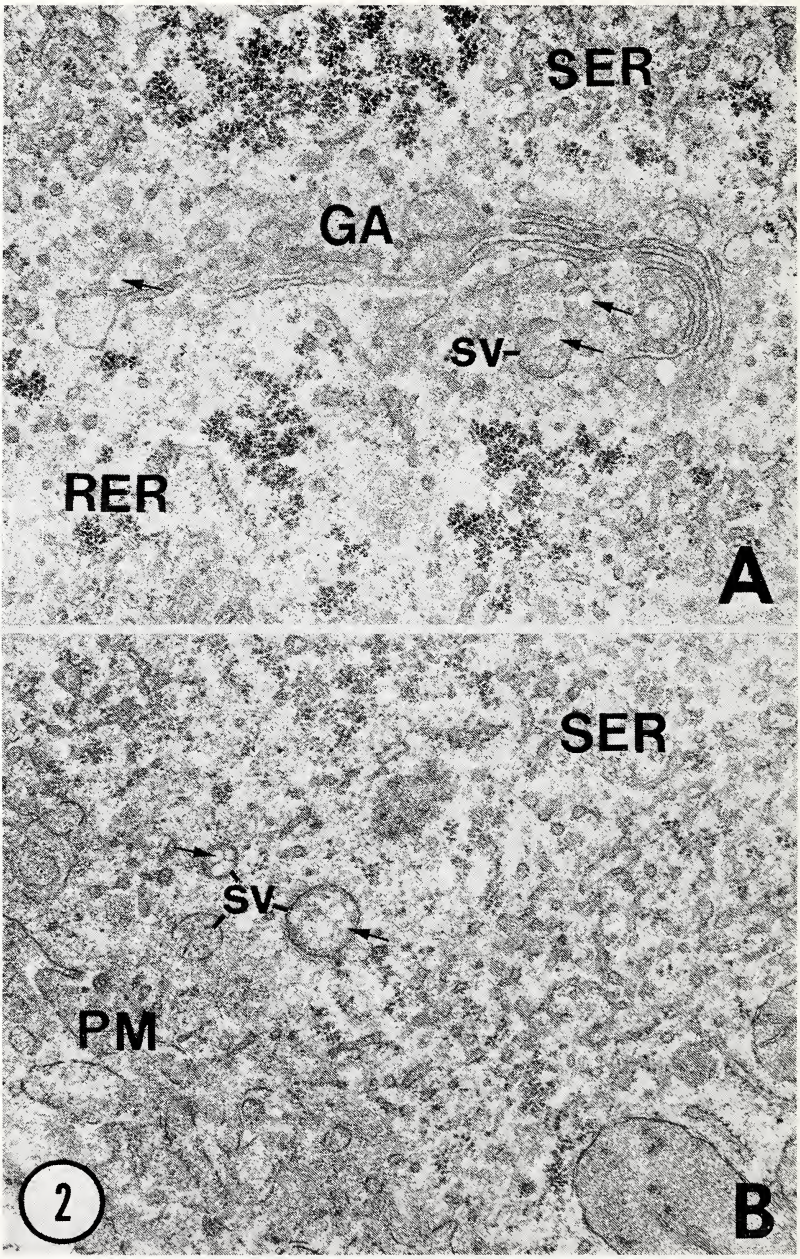

FIGURE 2. *Thin sections of liver from control rabbit.*

A. Golgi apparatus (GA) with secretory vesicle (sv) containing very low density lipoproteins (arrows). SER = smooth endoplasmic reticulum. RER = rough endoplasmic reticulum. X 23,800.

B. Secretory vesicle (sv) containing very low density lipoproteins (arrow) near the apical portion of the cell. PM = plasma membrane. SER = smooth endoplasmic reticulum. X 23,800.

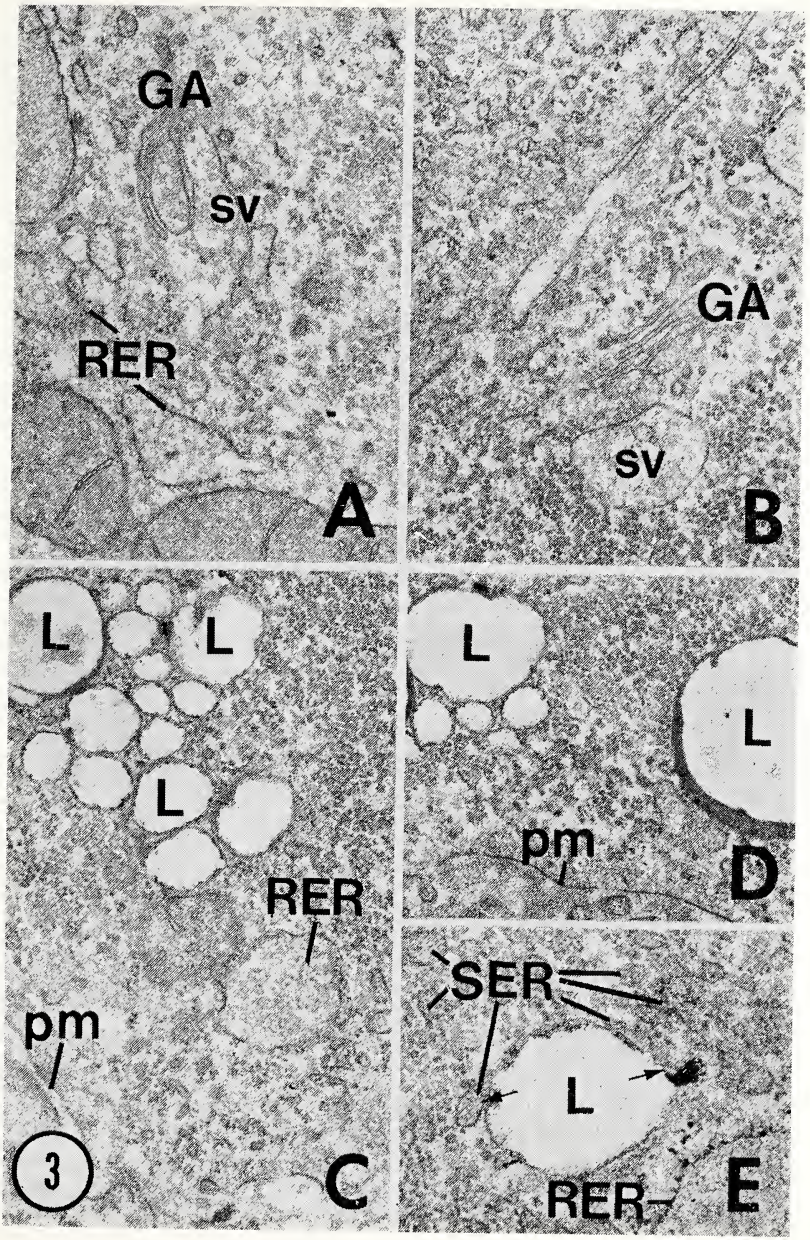

FIGURE 3. *Thin sections of liver from rabbit on atherogenic diet and 40% ethanol. A and B. Golgi apparatus (GA) irregular in appearance and secretory vesicles (sv) containing very low density lipoprotein particles were sparse. Note swollen rough endoplasmic reticulum (RER). X 23,800.*

C and D. Large lipid containing vesicles (L) in apical portion of cell. pm = plasma membrane. RER = rough endoplasmic reticulum. X 23,800 E: Lipid containing vesicle (L) showing membrane continuities (arrows) with smooth endoplasmic reticulum (SER). pm = plasma membrane. RER = rough endoplasmic reticulum. X 35,000.

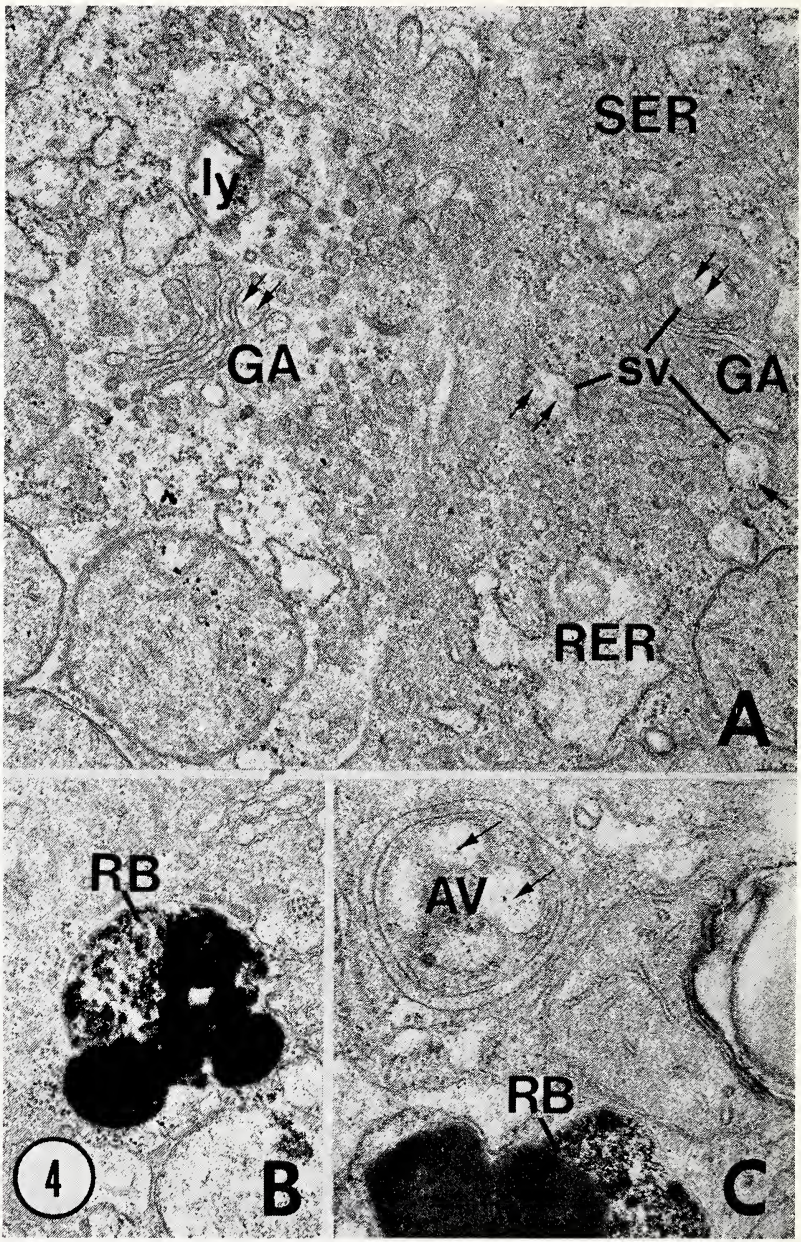

FIGURE 4. *Thin sections of liver from rabbit on MgO enriched atherogenic diet and 40% ethanol.*

A. Golgi apparatus (GA) more nearly normal in appearance with secretory vesicles (sv) showing some very low density lipoprotein (arrow) particles. Note the swollen rough endoplasmic reticulum (RER). ly = lysosome. X 32,800.

B. Lysosome containing residual bodies (RB) X 23,800.

C. Autophagic vacuoles (AV) containing lipoprotein material (arrow). Large residual body (RB) in lysosome. X 40,800.

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