should be considered in view of the recovery of other types of adenoviruses from the cerebrospinal fluid of children suffering from certain neurological illnesses(15). This possibility is further strengthened by the observation by Russell(16) that in one form of hydrocephalus in young children there is gross dilation of the third and lateral ventricles, the fourth being normal in size, a phenomenon not unlike that found in the hydrocephalic mice as described above.

Summary. A strain of polyoma virus isolated during serial IC passages of sarcoma 180 in 1-day-old Swiss mice and newborn hamsters produced only hydrocephalus in white Swiss mice and neoplasms in (C_3 H + A K R) F_1 mice. It is postulated that the hydrocephalus was due to the inammatory response produced by this strain of polyoma virus.

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Electron Microscopy of Monkey Liver After Exposure of Animals To Pure Oxygen Atmosphere.* (31004)

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Electron microscopic studies of the livers of rats exposed to pure oxygen atmospheres at reduced pressures indicated that mitochondrial alterations occurred within a few days, persisted for a few weeks and then disappeared(1). Biochemical evidence for altered mitochondrial function was also obtained in the same group of animals(2,3). To determine whether observations in rats were applicable to other species, particularly primates, monkeys were exposed to pure oxygen atmospheres up to 3 weeks and their livers examined electron microscopically.

Material and methods. Male monkeys (Rhesus *Macaca mulatta*) were exposed in an altitude chamber to an atmosphere consisting of essentially 100% O_2 at a total pressure of 380 mm Hg. Surgical or needle biopsies were obtained on two monkeys on each of days 2, 3, 6, 8, 9, 15 and 22 of the oxygen exposure, and on days 10, 20 and 30 post

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TABLE I. Atmospheric Conditions.

	Ground level	O_2 exposure
Barometric pressure (mm Hg)	749.1 ± 1.6	380.0 ± .0
Temperature (°C)	25.7 ± .1	26.4 ± .3
Relative humidity	39.4 ± 2.5	59.3 ± 2.4
Oxygen (% of total pressure)	20.95	99.21 ± .25
Carbon dioxide (% of total pressure)	.03	.25 ± .09
Nitrogen (% of total pressure)	78.08	.38 ± .10

exposure. The biopsies were performed under general anesthesia using sodium pentothal while still exposed to the specific atmospheric conditions. The specimens were fixed in 1% phosphate buffered osmium tetroxide or in glutaraldehyde followed by osmium tetroxide, then dehydrated and embedded in an epon-araldite mixture. Sections were made with a diamond knife on an LKB Ultrotome, stained with lead citrate and examined with a Hitachi HS-7 electron microscope. As controls, monkeys of the same weight, sex and species were kept on the same diet in a normal atmosphere at ground level in the same chamber and cage arrangement as the oxygen exposed animals. The relative humidity, temperature and light periods were as close to the experimental conditions as possible. These animals were examined 2 at a time, on days 10, 21, 31, 38 and 45 of their confinement to the chamber. Table I shows the atmospheric conditions during the 2 experiments. All animals were kept in individual cages measuring 41 cm in length, 51 cm in height, and 31 cm in width, adequate for a monkey weighing 3.5 to 4.5 kg.

Results. The normal monkey liver appears quite similar to human liver. In contrast to rat liver, mitochondria are somewhat less numerous and more irregular in shape, with fewer but longer cristae. Long parallel profiles of endoplasmic reticulum are in clusters but these generally are smaller and less numerous than in the rat. Microbodies contain little or no crystalline nucleoid in keeping with the uricase activity lower than in rats. Lysosomes are more numerous than in young rats but about the same as in most young adult humans. Golgi zones, bile canaliculi and cell borders are the same in monkeys as in rats and man.

Beginning as early as after one day of oxygen exposure, the amount of glycogen and rough endoplasmic reticulum are less than in control livers. Irregular and fragmented smooth endoplasmic reticulum is increased (Fig. 1). Mitochondria are somewhat more varied in their size and shape within the same cell, but some mitochondria in controls were as oddly shaped as in the exposed animals. Pericanalicular autophagic vacuoles were seen after 3 days' exposure but never more than one or two per cell on a section (Fig. 2). These, too, were occasionally seen in controls. The other structures all remained normal although more mitochondria were seen with a dumbbell shape.

These nonspecific changes which never were severe reached a maximum between 3 and 9 days with autophagic vacuoles most numerous at 9 days (Fig. 3). After this they began to wane and the variations seen after 2 or 3 weeks were no greater than between various cells in the control specimens and the number of lysosomes was not increased (Fig. 4). However, spiral polyribosomes were most numerous at 15 days. In animals kept in ambient air for several days after exposure the livers appeared the same as the controls. During the exposure the animals' appearance, feeding and behavior were normal; all the animals gained weight and had normal rectal temperatures. Liver tissue of each specimen, routinely prepared for light microscopy, was also normal as were one micron sections of epon-araldite embedded material stained with PAS and toluidine blue.

Discussion. The mitochondrial changes which were striking in rat livers after animals were exposed to pure oxygen at 258 mm Hg or ⅓ atmosphere were minimal in monkeys exposed to even greater oxygen concentrations. The only morphological reflection of altered metabolic activity is in the appearance of increased smooth endoplasmic reticulum at the expense of the rough form. This can be an indication of damage ("toxicity"), but also could represent an increase in microsomal enzymes to meet the demands of the

altered oxygen tension which seems more likely. Possibly the difference between rats and monkeys is related to quantitative differences in the various pathways of cofactor (*e.g.*, NAD) metabolism. Whatever the mechanism producing the changes may be, the

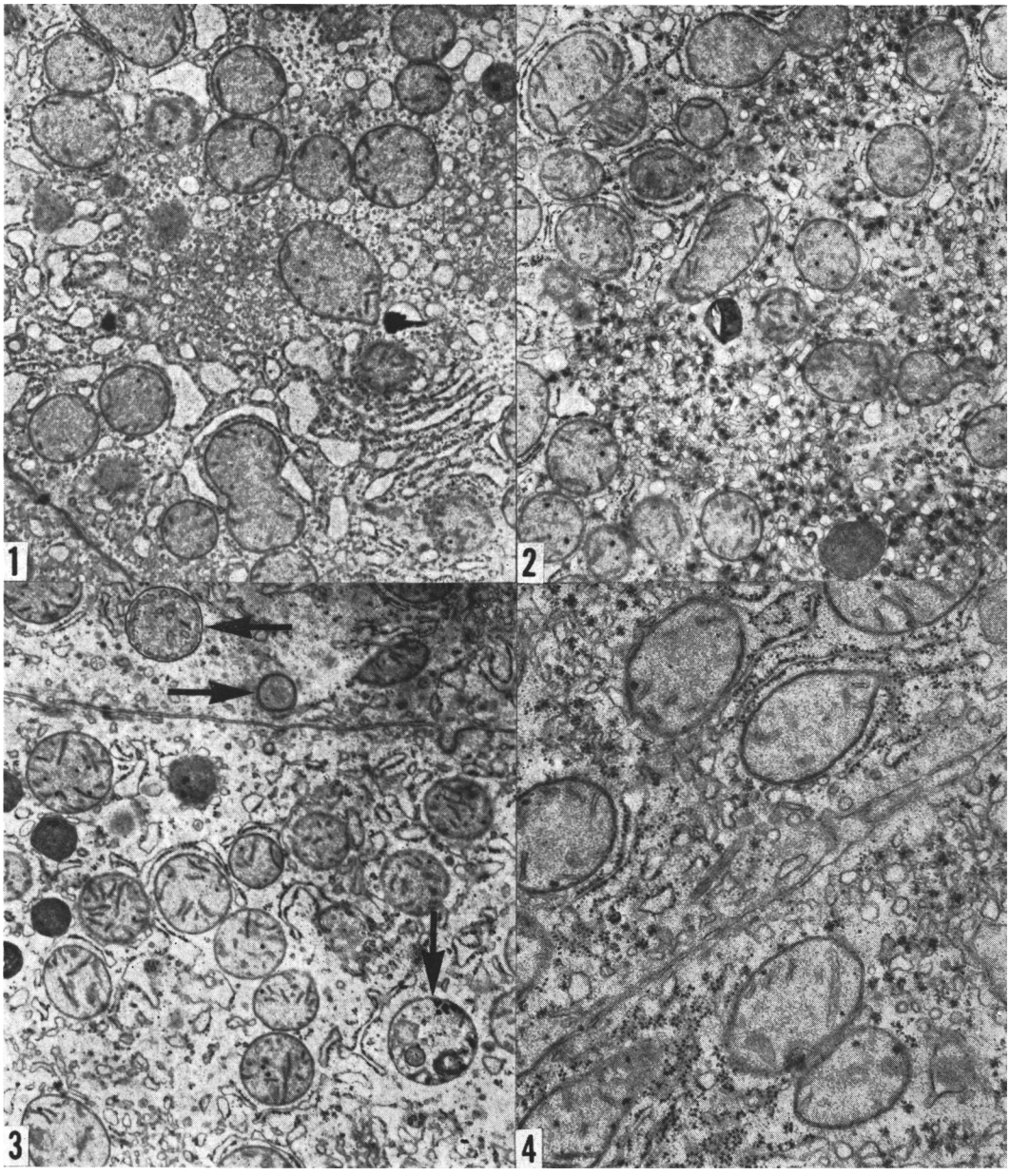

FIG. 1. Dilated cisternae and cluster of fragmental endoplasmic reticulum in liver of monkey exposed to oxygen for one day (× 11,000).

FIG. 2. Most of endoplasmic reticulum in small vesicles after 3 days' exposure to oxygen. A small autophagic vacuole is noted as the dark body in the center and a dumbbell-shaped mitochondrion is on the top (× 11,000).

FIG. 3. Autophagic vacuoles (arrows) were most numerous at 9 days' oxygen exposure. The endoplasmic reticulum is still largely fragmented (× 11,000).

FIG. 4. Normal appearance of organelles after 15 days' oxygen exposure. Spiral polyribosomes at bottom were more numerous than in the control (× 14,000).

livers of both rats and monkeys seem to become adapted quickly to the new circumstances and the structural integrity is restored. The changes in monkeys seem not only less striking than in rats but adaptation appears to occur more quickly even in the presence of oxygen inhaled under higher pressure. Presumably this might also apply to man but only study of human material can answer this with certainty. The major unanswered question is whether the liver during the period of becoming adapted is more sensitive to the damaging effects of volatile solvents which may enter the atmosphere in closed systems such as space capsules or of irradiation which may be encountered during open space flights.

Summary. Livers of monkeys exposed to pure oxygen at 380 mm Hg were examined electron microscopically. Only minimal nonspecific changes were observed; the most significant was an increase in smooth endoplasmic reticulum at the expense of the rough form and glycogen. The changes, which appeared as early as 24 hours and were gone by 2 weeks, are considered an adaptive response rather than a sign of toxicity.

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Effects of Hyperbaric Oxygenation on Metabolism III. Succinic Dehydrogenase, Acid Phosphatase, Cathepsin and Soluble Nitrogen.* (31005)

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The concentration of adenosine-triphosphate (ATP)(1) and succinic dehydrogenase activity(2) have been demonstrated to decrease significantly in rat brain, liver and kidney after exposure to 5 atmospheres of 100% O_2 for 1½ hours. These losses could be due to oxygen poisoning of the respective enzyme systems, *i.e.*, oxidation of SH groups, or to a general injury process to cells. Since it has been observed that free acid hydrolytic activity increases during cellular injury(3-9), it was important to determine the extent of release of lysosomal enzymes during oxygen toxicity. Cellular injury to protein structure, as indicated by an increase in soluble nitrogen, has been demonstrated in autolytic liver by Bradley(10). Similar injury to cellular protein would be expected in HPO toxicity if energy stores fall below critical levels. The following study was undertaken to determine the effects of high pressure oxygen (HPO) on succinic dehydrogenase, acid phosphatase and cathepsin activities, and acid soluble nitrogen.

Methods and materials. Male rats of the Sprague-Dawley strain (160-225 g) were fasted for 18-24 hours with water *ad libitum* before any experiment. The control group consisted of animals exposed to air at 1 atmosphere. The animals were subjected to 1 and 3 atmospheres (absolute pressure) of 100% O_2 for 2 hours and 5 atmospheres for 1½ hours using the Bethlehem Steel Hyperbaric Chamber. After slow decompression (5 min) the animals were killed and the cerebral hemisphere, liver and kidney cortex were excised. A 0.25 M sucrose + 0.001 M EDTA homogenate was prepared. The following determinations were made on the homogenate: 1. succinic dehydrogenase by the method of

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