OCCURRENCE OF DESMOSTEROL IN DEVELOPING RAT BRAIN

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Desmosterol (24-dehydrocholesterol) now is considered to be the penultimate step in the biosynthesis of cholesterol. This compound was first isolated from chick embryo by Stokes, Fish and Hickey (1956), and these authors subsequently showed its presence in rat skin (Stokes, et al., 1958) and liver (Stokes and Fish, 1960). The presence of desmosterol in other rat tissues has been adduced from colorimetric analysis of the tissue sterols (Avigan, et al., 1960a). Interest in the occurrence and metabolism of desmosterol was stimulated further by the demonstration that it accumulated in the serum and tissues of animals treated with triparanol, (1-[p-(β-diethylaminoethoxy)-phenyl]-1-(p-tolyl)-2-(p-chlorophenyl)ethanol) (Avigan, et al., 1960; Mobberley and Frantz, 1959). It now has been demonstrated that desmosterol is only one of several cholesterol precursors which can accumulate in triparanol-treated animals (Frantz, et al., 1960; Holmes, 1961).

Triparanol was fed to pregnant rats for the purpose of determining its effect on the desmosterol concentration of fetal tissues. During the course of this investigation gas chromatographic analysis revealed the presence of appreciable amounts of desmosterol in the brain of newborn rats, from untreated mothers (controls). The amount of brain desmosterol increases during the first two weeks of life, and thereafter, decreases rapidly. Using gas chromatography it has not been possible to demonstrate desmosterol in adult rat brain.

The brains from rats, age 1 to 21 days, were dissolved in 30 per cent KOH in 50 per cent ethanol, and the nonsaponifiable lipid was extracted into

petroleum ether. Gas chromatographic analyses were carried out on the crude extract and, in some cases, on the sterols after purification via the digitonide.

The gas chromatograms of selected samples are shown in Figure 1. It will be noted that the retention times of peaks 1 and 2 are identical with those obtained with an authentic mixture of cholesterol and desmosterol (Fig. 1A). In addition, both components were precipitated by digitonin, as evidenced by the fact that in two-day-old brain the desmosterol-cholesterol ratio was 0.08 when determined on the crude extract, and 0.05 on the purified sterols. For days 13 and 18 the ratios for the crude extract were 2.48 and 0.24, respectively, and for the purified sterols, 2.77 and 0.25.

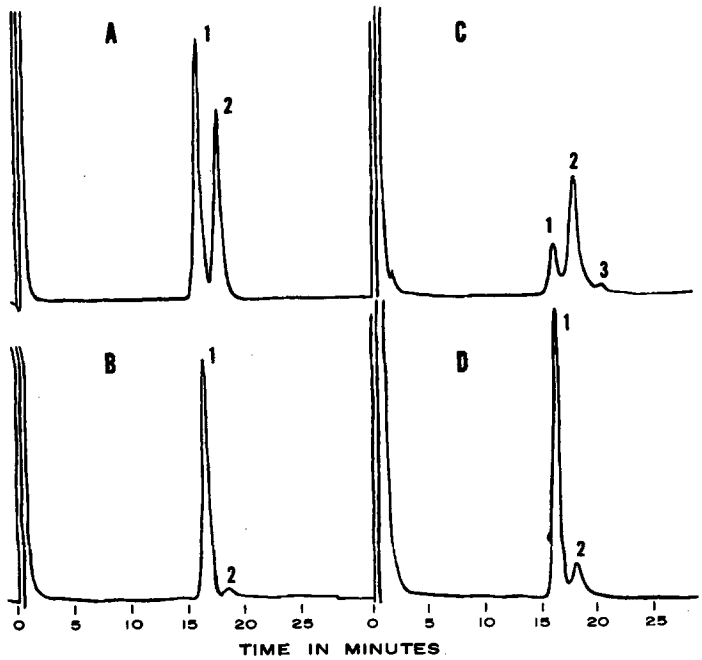

Fig. 1 Gas chromatograms of rat brain nonsaponifiable lipid.

A. standard mixture, peak 1, cholesterol; peak 2, desmosterol.
B. 2-day brain. C. 13-day brain. D. 18-day brain. Column conditions: Liquid phase 0.80% G.E.-SE 52 packed on Gas Chrom 100-140 mesh, 6' column; temperature, 227°C., Argon flow, 20 ml. per min.

The data in Table I show that the desmosterol concentration of brain increased during the first 13 days of life, and then decreased rapidly to a low level by the 21st day. A second series of brains from 1- to 21-day-old rats has been analyzed with similar results, and a third series now is being studied. The rapid increase in the concentration of desmosterol in brain from the 10th to 13th day, as well as the large amount of desmosterol present in the brain of the 13-day-old rat, is worthy of note. This sample (Fig. 1C) also contains a small amount of zymosterol, peak 3. The present findings may help eventually in elucidating the sequence of events involved in the sterol metabolism of developing brain, particularly since the conversion of desmosterol to cholesterol has been demonstrated (Steinberg and Avigan, 1960; Stokes, et al., 1958).

Table I

Desmosterol-Cholesterol Ratio in Rat Brain

Age of Rats Days	Ratio Desmosterol/Cholesterol[a]	Age of Rats Days	Ratio Desmosterol/Cholesterol[a]
1	0.06	12	1.12
2	0.08	13	2.48
3	0.09	14	2.25
4	0.11	15	1.64
5	0.11	16	1.37
6	0.11	17	0.44
7	0.19	18	0.24
8	0.11	19	0.18
9	0.11	20	0.17
10	0.38	21	0.07
11	1.13		

a - Calculated from the area under the chromatographic peaks.

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