

sepsis.<sup>2,3</sup> Previous reports suggest that impaired triglyceride (TG) clearance, due to suppression of lipoprotein lipase is primarily responsible for hypertriglyceridemia associated with sepsis,<sup>3,4</sup> and fatty infiltration of the liver is attributed to the increment of TG synthesis enzymes, glycerol-3-phosphate acyltransferase and phosphatidate phosphohydrolase, with no concomitant rise in TG secretion rate in the liver.<sup>5</sup> The mechanism leading to the alteration of these enzyme activities is not clear, but it has been proposed that oversecretion of cytokines may play an important role during sepsis.<sup>6,7</sup>

Numerous studies have shown that fish oil has favorable effects in the treatment of coronary heart disease<sup>8</sup> and inflammatory diseases.<sup>9,10</sup> Evidence indicates that the serum TG-lowering effect of fish oil is mainly due to a decrease in very low density lipoprotein (VLDL)-TG synthesis and secretion.<sup>8</sup> Rustan *et al.*<sup>11</sup> reported that liver TG is significantly lower in rats receiving a high fish oil diet than in those fed a safflower oil diet. Previous reports in our laboratory also demonstrated that, compared with safflower oil emulsion, rats infused with fat emulsion prepared with fish oil have lower liver fat accumulation when total parenteral nutrition is administered.<sup>12,13</sup> Results from other studies also indicate that dietary n-3 fatty acid supplementation reduces leukotriene B<sub>4</sub> production and consequently attenuates inflammatory reactions.<sup>9,10</sup>

Recently, Lanza-Jacoby *et al.*<sup>14,15</sup> demonstrated that feeding rats a fish oil diet or intragastrically feeding a structured lipid emulsion containing fish oil before inducing sepsis prevents fatty infiltration of the liver in septic rats. Considering that the fat percentage of the experimental diet in those studies was not high (10%, w/w), and the feeding duration was not long enough to induce fatty liver prior to sepsis, we decided to use a high fat cholesterol-supplemented diet in this study to induce hyperlipidemia and fatty liver prior to sepsis. This was in order to understand whether, with a condition of diet-induced fatty liver, fish oil feeding before sepsis still has a beneficial effect on plasma and liver lipids in sepsis. If n-3 fatty acid administration reduces the production of inflammatory mediators, the abnormalities of lipid metabolism in sepsis might be attenuated by fish oil fed before sepsis. Because sepsis is an inflammatory condition with high oxidative

stress,<sup>1</sup> erythrocyte antioxidant enzyme activities of the septic rats were also analyzed in this study to examine the possible adverse effects of polyunsaturated fatty acids existing in fish oil.

## MATERIALS AND METHODS

Thirty-six male Wistar rats (Charles River, Wilmington, MA) weighing 70-90 g were used in this study. Rats were housed in a temperature and humidity-controlled room with a light cycle from 6 AM to 6 PM and were allowed free access to diet (Purina No. 5001) for 1 week prior to the experiment. After that, the animals were divided into 2 experimental groups and fed a high fat (15%, w/w) semipurified diet containing 0.1% (w/w) cholesterol. The basal composition of the experimental diets was identical except for the sources of the fat (Table 1). One group of rats was

**Table 1. Composition of the Experimental Diet**

Ingredient	% (w/w)	
	FO <sup>a</sup>	SO <sup>a</sup>
Fish oil	15	-
Soybean oil	-	15
Corn starch	57	57
Protein (casein)	20	20
Cholesterol	0.1	0.1
Salt mixture <sup>b</sup>	3.5	3.5
Vitamin mixture <sup>c</sup>	1	1
Methyl cellulose	3	3
Choline chloride	0.1	0.1
DL-methionine	0.3	0.3

<sup>a</sup> FO: Fish oil group, SO: Soybean oil group.

<sup>b</sup> Salt mixture contains the following (mg/g): calcium phosphate dibasic 500 mg, sodium chloride 74 mg, potassium sulphate 52 mg, potassium citrate monohydrate 220 mg, magnesium oxide 24 mg, manganese carbonate 3.5 mg, ferric citrate 6 mg, zinc carbonate 1.6 mg, cupric carbonate 0.3 mg, potassium iodate 0.01 mg, sodium selenite 0.01 mg, and chromium potassium sulphate 0.55 mg.

<sup>c</sup> Vitamin mixture contains the following ingredients (mg/g): thiamin hydrochloride 0.6 mg, riboflavin 0.6 mg, pyridoxine hydrochloride 0.7 mg, nicotinic acid 3 mg, calcium pantothenate 1.6 mg, D-biotin 0.02 mg, cyanocobalamin 0.001 mg, retinyl palmitate 1.6 mg, DL- $\alpha$ -tocopherol acetate 20 mg, cholecalciferol 0.25 mg, and menaquinone 0.005 mg.