BILIRUBIN EXCRETION AND BILE FLOW IN FED AND FASTED BRAZILIAN SQUIRREL MONKEYS (SAIMIRI SCIUREUS)

C.E. CORNELIUS, B.A. MYERS*, M.L. BRUSS AND J.W. GEORGE
Department of Physiological Sciences and California Primate Research Center,
School of Veterinary Medicine, University of California, Davis, California 95616,
USA

*Current address: Hazelton Laboratories USA, 1330-B Piccard Drive, Rockville,
MD, USA

ABSTRACT
and fasted Brazilian squirrel monkeys (Saimiri sciureus). Veterinary Research Communications, 13 (5),
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Fasted Brazilian squirrel monkeys (BrSMs) exhibited slightly higher serum bilirubin levels (0.30 ±
0.05 mg/dl) than others in the fed state (0.13 ± 0.01). The mean liver weight was 50% lower following
a 22 h fast. The rate of bile flow was unaffected by fasting and averaged 13.8 μl/min/kg and
475 μl/min/100g liver in six BrSMs. No significant difference in mean bilirubin excretion/min was
observed on a body weight basis following fasting. When the mean rate of bilirubin excretion was
calculated as a function of liver weight, a two-fold higher rate was present in fasted monkeys, but only
at the p = 0.06 level of statistical significance. From data collected in this and earlier studies, it would
appear that BrSMs represent the best animals studied to date to serve as experimental controls in
comparative studies with Bolivian squirrel monkeys which exhibit a Gilbert-like syndrome.

Keywords: bilirubin, bile flow, fasting, squirrel monkey

INTRODUCTION
Little or no information is available concerning endogenous bilirubin excretion
and/or choleresis in ‘new world’ non-human primates (Cornelius, 1982). Bolivian
squirrel monkeys (BoSMs), unlike Brazilian squirrel monkeys (BrSMs), exhibit an
exaggerated and marked unconjugated hyperbilirubinaemia upon fasting (Cornelius et
al., 1985), reduced plasma clearance of bilirubin and lower hepatic uridinediphospho-
glucuronate glucuronosyl transferase (UDPG-T) activity (Portman et al., 1984a,
1984b). BoSMs have been used as experimental animal models for human Gilbert’s
syndrome type I.

Although both BrSMs and BoSMs are classified in the same genus and species
(Saimiri sciureus) and have six acrocentric pairs of chromosomes, other subspecies of
squirrel monkeys of Guyanese and Peruvian origins have five and seven chromosome
pairs, respectively (Ariga et al., 1978). BrSMs and BoSMs can, however, be easily
distinguished phenotypically by their size, coloration, and facial and periocular hair
patterns.

BrSMs have been used as ‘control’ subjects in comparative studies with BoSMs
(which have a Gilbert-like syndrome) since they more closely resemble normal
humans in their physiological responses to fasting. The current study on BrSMs was undertaken to clarify the effects of fasting on various parameters concerning bilirubin excretion, liver size and bile flow. In addition, the rates of incorporation of a labelled precursor, \(^{3}\text{H}\)-aminolevulinic acid (\(^{3}\text{H}\)-ALA), into biliary bilirubin were measured. Since \(^{3}\text{H}\)-ALA is preferentially taken up by hepatocytes and not by the erythroid cells, early labelling of biliary bilirubin during the first few hours after ALA injection is commonly considered a measure of the production rate of bilirubin resulting from the turnover of hepatic haeme-containing proteins, e.g. \(P_{450}\) catalase, tryptophan pyrroline, etc. (Levitt et al., 1968; Robinson, 1969).

**MATERIALS AND METHODS**

**Animals and dietary treatments**

The animals used were obtained from either the Bowman-Gray School of Medicine, Winston-Salem, North Carolina or the Delta Primary Research Center, Covington, Louisiana. All studies were performed on three ‘fed’ and three ‘fasted’ adult BrSMs. Both the fed and fasted groups comprised one male and two female monkeys. Monkeys were housed in standard basket-type cages and maintained under standard laboratory conditions at the California Primate Research Center. Animal care and use was in accordance with the National Institutes of Health ‘Guide for the Care and Use of Laboratory Animals’.

‘Fed’ monkeys were allowed access to food the night before and for 3 h prior to surgery (a combination of eight chow biscuits, Purina High-Protein Monkey Chow 5045, Ralston Purina Co., St Louis, MO and semi-purified diet formulated as banana-flavoured for primates, Bioserve Inc., Frenchtown, NJ). ‘Fasted’ monkeys received the same dietary regime but were fasted for 20 h prior to surgery.

**Materials**

\(^{3}\text{H}\)-D-aminolevulinic acid (\(^{3}\text{H}\)-ALA; specific radioactivity 1.6 Ci/nmol) was obtained from NEN Research Products (Boston, MA); all other chemicals were obtained from Sigma Chemical Co. (St Louis, MO) and were of the highest chemical purity available. Spectrophotometric measurements were made using a Perkin-Elmer (Model 559A) spectrophotometer (Norwalk, CT). Thin-layer chromatography plates were obtained from Whatman Co. (Hillsboro, OR).

**Surgical procedures and sample collection**

Following the feeding or fasting period, the animals were anaesthetized by an intravenous injection of sodium pentobarbital (Fort Dodge Lab. Inc., Fort Dodge, IA) and prepared for surgery. A 22 gauge polyethylene catheter was inserted into the common bile duct. Catheters were also placed in the left saphenous and femoral veins. Approximately 2 h after the initiation of surgery, \(^{3}\text{H}\)-ALA was injected into the saphenous vein at a dose of 100 \(\mu\text{Ci/kg of body weight. Bile samples were}