The Procaine Esterase Activity of Serum from Different Mammalian Species[1] (36611)

MARCUS M. REIDENBERG[2]

Departments of Pharmacology and Medicine, Temple University School of Medicine, Philadelphia, Pennsylvania 19140

Several systematic studies of mammalian serum esterase activity have been carried out. Using acetylcholine and butyrylcholine as substrates, Levine and Suran (1) found both the horse and monkey to have greater activity than man. Augustinsson (2) found the mangabey monkey's serum to have a greater cholinesterase activity than man's, the horse's about equal to man's, and the macaque's definitely less than man's.

Kisch, Koster, and Strauss (3, 4) studied the procaine esterase activity of whole blood and found man's activity to be much greater than the horse's. Aven, Light, and Foldes (5) studied the procaine hydrolysis rate in serum and found that the mouse had greater activity than the horse but did not present data for man.

The present study was done to measure the rate of procaine hydrolysis in serum from various species of primates and other mammals.

Materials and Methods. Serum was obtained from individual animals of many species. Sera from individual mice, gerbils, galagos, and squirrel monkeys were pooled. All other species had individual determinations. The unmodified serum was incubated at 37°, procaine HCl was added to produce a concentration of 10 μg/ml, and the reaction was stopped in aliquots of the mixture at 30 sec intervals by adding sodium arsenite. The procaine remaining in the mixture was extracted by the method of Brodie, Lief and Poet (6) and measured fluorimetrically as suggested by Udenfriend *et al.* (7). The maximum duration of incubation was 2 min. Details of the methods have been reported (8). When the amount of procaine metabolized in a serum sample in 2 min was sufficient to have the kinetics analyzed and the disappearance of procaine seemed to be first order, then the half-life of procaine in the serum was determined by calculating the regression line for the logarithm of the serum procaine concentration versus the duration of incubation for each sample with the use of the least squares technique. When the amount of procaine metabolized in 2 min was too small for kinetic analysis, then the total amount metabolized in 2 min by 1 ml of serum was determined.

Results. The rate of metabolism of procaine in sera of various animal species is presented in Table I. The chimpanzee has an esterase activity for procaine similar to healthy man. All of the other primate species studied had less activity than healthy man.

Among the nonprimate species tested, a pool of sera from several gerbils produced a procaine half-life of 3.3 min. Sera pooled from groups of 8–12 mice of several strains produced the following half-life values: ICR, 4.0 min; C57BL, 3.6 min; and S-W, 4.3 min. Ten other species of mammals had little or no detectable procaine esterase activity in their sera under these conditions.

Discussion. The data presented are in general agreement with the relative cholinesterase activities of sera from various nonprimate mammalian species presented by others. The initial procaine concentration of 10 μg/ml was chosen to approximate that which occurs clinically in man and so that this

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TABLE I. Disappearance Rate of Procaine in Unmodified Serum of Various Species Incubated at 37°.[a]

Species	N	Half-life	Amount metabolized
Human, healthy adult	12	0.66 ± 0.14	
Apes			
Pan troglodytes (chimpanzee)	4	0.45 ± 0.29	
Hylobates (gibbon)	6		0.63 ± 0.35
Old World monkeys			
Papio anubis[b] (baboon)	5	3.3 ± 0.8	
Papio dogeura[b] (baboon)	3	3.1 ± 1.2	
Papio cynocephalus (baboon)	1		1.5
Macaca mulatta (rhesus)	5	3.0 ± 0.4	
Macaca nemestrina (pig-tailed)	2	3.4, 1.1	
Macaca radiata (bonnet)	3		1.1 ± 0.4
Cercopithecus aethops (green)	7		0.49 ± 0.51
Erythrocebus patas patas (patas)	2		0, 1.9
New World monkey			
Saimiri sciureus (squirrel)	4		1.5 ± 0.8
Prosimian			
Galago (galago)	4		0
Rodents			
Hamster	3		0
White rat	3		0
Mice ICR	1	4.0	
Mice C57BL	1	3.6	
Mice SW	1	4.3	
Gerbil	1	3.3	
Guinea pig	4		0 (3), 0.5 (1)
Miscellaneous			
Rabbit	4		0
Pig	3		0
Ferret	2		0
Opossum	1		0
Horse	4		0 (3), 1.0 (1)
Goat	3		0
Dog	4		0.4 ± 0.3

study of animal sera could be directly compared to a study of man (8).

The present study of various primate species extends the information available about this group of mammals. Man and the chimpanzee both have rapid hydrolysis of procaine in their sera. The gibbon, classified as an ape but different from the chimpanzee, gorilla, and orangutan, has distinctly less procaine esterase activity in its serum than either man or the chimpanzee. Rapid hydrolysis of procaine occurred in sera from several species of Old World monkeys but not in the one species of New World monkeys (Saimiri) or prosimian (galago) tested. The half-life of procaine in sera from *Papio anubis* baboons was identical to that measured in sera of *Papio dogeura* baboons obtained from another source. This is compatible with the idea that these are two names for the same species of baboon (9). While the simplest explanation for the differences between sera of different species to hydrolyze procaine is that different amounts of enzyme are present, other explanations are possible. Some species may have had circulating competitive inhibitors of procaine esterases. The K_m of the enzymes of different species may have been significantly different. The present study does not differentiate from among these possible explanations.

Of all the species tested, the chimpanzee has serum procaine esterase values most similar to those of healthy adult man. Newborn humans or adult humans with chronic liver or kidney disease have much slower rates of procaine hydrolysis in their sera with half-life values up to 3 min (8). Therefore, while the chimpanzee appears to be the species most similar to healthy adult man with respect to

[a] Half-life of procaine is expressed in minutes. When disappearance rate was slow, amount (μg) metabolized per milliliter of serum in 2 min is presented. Values less than 0.5 μg are indistinguishable from zero and are presented as zero. Values presented are mean ± SD or are values of individual animals. *N* represents number of individual animals or number of serum pools.

[b] *P. anubis* and *P. dogeura* may be different names for same species (Napier and Napier, 1967).

procaine hydrolysis in serum, other primate species such as *M. nemestrina* appear to be more similar to sick man. And the gibbon, another species of ape, appears to be quite different from man, healthy or sick.

There are several pathways of drug metabolism that appear to occur in primates but not common laboratory animals. These include the N^1-glucuronide conjugation of sulfadimethoxine (10), the aromatization of quinic acid (11), the conjugation of arylacetic acids with glutamine (11, 12), and possibly the conjugation of diphenylmethoxyacetic acid (a metabolite of diphenhydramine) with glutamine (13). Among all of the nonprimate mammals tested in this study, only the mouse and gerbil had rapid procaine hydrolysis in their sera. Thus rapid hydrolysis of procaine in serum is another pathway of drug metabolism that occurs primarily in higher primates.

Summary. The rate of procaine hydrolysis was studied in unmodified serum at 37°. It was rapid in man, chimpanzee, *Papio anubis, Macaca mulatta,* and *Macaca nemestrina.* It was slow or absent in gibbon, *M. radiata, P. cynocephalus, C. aethops,* Erythrocebus, Saimiri, and galago. Procaine hydrolysis was rapid in sera from mice and gerbils and was slow or absent in sera from hamsters, rats, rabbits, pigs, ferrets, opossum, guinea pigs, horses, goats, and dogs. Thus rapid hydrolysis of procaine in serum is another pathway of drug metabolism that occurs largely in higher primates.

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