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Blood Pressure of the Normal Rhesus Monkey. (23499)

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This laboratory has been interested in developing procedures for evoking hypertension in subhuman primates such as the rhesus monkey(1). There being essentially no definitive data on variations in blood pressure of the normal rhesus monkey, determination of the limits of such variations was a necessary preliminary to studies on hypertension. This report includes observations on blood pressure variations in normal and splenectomized monkeys acquired with 2 indirect methods as well as comparisons of these indirect readings with measurements of the arterial pressure obtained directly with a strain gauge.

Materials and methods. Animals. Young male and female rhesus monkeys weighing from 3 to 12 kilos were used. Details of the care and feeding of animals in this colony have been described by Schmidt and Genther (2). Three groups of monkeys were employed in these studies. The first group comprised 14 normal monkeys on which blood pressure measurements were made repeatedly over a 2-month period using the 2 indirect blood pressure methods described below. The second group consisted of 27 splenectomized animals on which control blood pressures were meas-

ured for 2 months in the same fashion as the first group. These monkeys had been infected with malaria, their infections cured by various chemotherapeutic agents, and this fact confirmed by splenectomy. The blood pressure studies were begun 2 or more months after splenectomy. After the control period the majority of these animals were used in studies on experimental hypertension. However, 6 were observed as controls for an additional 12 months, observations on these animals providing data on stability of simian blood pressure levels over an extended period. The third group consisting of 46 anesthetized monkeys was used in comparing the direct and indirect blood pressure methods. Of these, 43 had no known cardiovascular or renal disease while the remaining 3 had moderate experimental hypertension. The procedure used in handling the monkeys was an important factor in securing reproducible blood pressure measurements. The monkeys were housed in large cages, each containing 6 to 10 animals. The cages opened individually onto a narrow corridor to which animals were admitted one at a time. The monkey was caught on its first run, then allowed to rest

with minimal manual restraint for 5 minutes prior to beginning blood pressure measurements. During the measurements the animal was held in a sitting position with its legs pinned gently over the edge of the table by the thigh of the assistant. The monkey's head was held in the assistant's right hand and its left arm (if this extremity was to be used for pressure measurement) extended horizontally by the assistant's left hand. Most monkeys could be trained to sit quietly; however, those that showed no evidence of training after a 2- to 3-week period were returned to stock.

Blood pressure measurements. Indirect methods. Indirect measurements of systolic and diastolic blood pressures were made essentially as in man using either a "cloth" or "metal" cuff. The cloth cuff, a modified "newborn" cuff, consisted of an inflatable rubber bag, 1 by 2 inches, enclosed in a cloth cover $1\frac{1}{4}$ by 14 inches. Ties sewed to the end of the cover facilitated rapid application to the animal's arm. The cuff was wrapped snugly around the extended left (or right) arm as close to the body as possible. Care was taken not to occlude venous return; when the cuff was applied loosely, high and variable readings resulted. The "metal" cuff consisted of a short metal or plastic cylinder fitted inside with an airtight rubber sleeve. Air pumped into the space between the cylinder and sleeve through a tubulature forced the rubber sleeve against the arm, compressing the arm equally from all directions. Since the diameter of the arm varies with the size of the monkey, a series of cuffs with internal diameters of 45, 55, 65 and 75 mm and varying in length from 45 to 65 mm were employed. These sizes were adequate for monkeys weighing from 2 to 12 kilos. The Korotkoff pulse sounds were rather faint in some animals; therefore, to obtain the best sound it was important to use a small stethoscope bell (15 mm I.D.) and to place the bell directly over the artery. Pressure readings were made in triplicate, the average to the nearest 5 mm being recorded. In quiet, trained monkeys these readings never varied by more than 10 mm Hg; wider variations indicated that the animal was excited or insufficiently rested.

Since excited animals usually had elevated cardiac and respiratory rates as well, these latter measurements, which were obtained routinely, provided additional checks on the reliability of the blood pressure readings.

Direct measurements. For these measurements the brachial or femoral artery was exposed under pentobarbital anesthesia and cannulated with a short, blunt 18- or 19-gauge needle. The needle was connected to a transducer (Model P23A Statham strain gauge), and pressure changes were recorded photographically (Cambridge Simplitrol electrocardiograph). The indirect blood pressure readings were compared with direct blood pressure measurements in 46 monkeys, a total of 505 comparisons being made of the direct pressure in the brachial or femoral artery with the indirect pressure in the arm measured at the same time with a cloth or metal cuff. The indirect pressure measurements were never biased by knowledge of the direct readings being recorded simultaneously since the direct readings were calculated from photographic records after an experiment was concluded.

Results. Blood pressure range in control monkeys. Mean systolic and diastolic blood pressures of 14 control monkeys determined indirectly with the cloth and metal cuffs are presented in Table I. It is evident that the cloth cuff readings were substantially higher than those obtained with the metal cuff, the cloth cuff technic giving an average systolic and diastolic pressure for the group of 159/127 mm Hg as contrasted with group average of 118/90 mm for the metal cuff. Mean blood pressures in different animals varied widely; with the cloth cuff the mean values for individual monkeys ranged from 137/112 to 188/152, with the metal cuff from 103/78 to 132/101 mm.

Data on splenectomized monkeys, also summarized in Table I, show that mean pressures in this group were slightly but not significantly lower than those of the intact control group. Thus the splenectomized group had average systolic and diastolic pressures of 149/116 and 112/84 mm Hg for the cloth and metal cuffs respectively and exhibited the

TABLE I. Arterial Blood Pressures of Control and Splenectomized Monkeys Measured by Two Indirect Methods.

Type of monkey	No. of		Cuff	Blood pressure in mm Hg	
	Monkeys	Observations		Systolic	Diastolic
				Mean \pm S.D. (range)	
Control	14	315	Cloth	158.8 \pm 12.8 (137-188)	126.7 \pm 11.9 (112-152) (8-15)
	14	315	Metal	117.5 \pm 8.1 (103-132) (6-10)	89.5 \pm 7.4 (78-101) (5-10)
Splenectomized	27	526	Cloth	148.9 \pm 11.9 (123-170) (8-16)	115.9 \pm 10.8 (94-134) (7-16)
	27	526	Metal	111.5 \pm 7.1 (94-131) (4-12)	83.2 \pm 7.1 (70-101) (5-10)

same wide range of mean values in individual monkeys as was observed in the control group. The standard deviations of the metal cuff readings were always smaller than those of the corresponding cloth cuff measurements, *i.e.*, 7 and 12 mm respectively. Thus for an individual monkey systolic and diastolic pressures would vary within a 30 mm range when measured with the metal cuff and within a 50 mm range when the cloth cuff was used. Pressures were more variable in some monkeys than in others, but degree of variation was not related to blood pressure level. There was relatively good correlation between cloth and metal cuff readings in a given monkey; the correlation coefficient (r) of the 2 mean sys-

tolic readings was 0.92 and for the 2 mean diastolic pressures the coefficient was 0.85.

The relative stability of the blood pressure in non-treated monkeys is illustrated by data obtained on the 6 splenectomized but otherwise normal animals studied for 12 months following their initial 2 month observation period. At no time did mean systolic or diastolic pressures of any of these monkeys vary by as much as 10 mm Hg from the mean values obtained for the same animal during the initial observation period.

Comparison of direct and indirect blood pressures. The relationships between the 2 indirect blood pressure readings and the intra-arterial pressure measured directly with a strain gauge were defined by making 8 types of comparisons. The results are shown in Fig. 1 and 2. Each dot represents an associated pair of direct and indirect pressure readings obtained simultaneously in the same monkey. The heavy broken line in each figure represents the regression, calculated by the method of least squares, of the indirect pressure on the direct pressure. The thin solid line in each figure is the line of equal values. In Fig. 3 these 8 regression lines designated A to H have been superimposed to permit easier comparison.

Comparison of systolic and diastolic pressures measured directly in the brachial or femoral artery with the corresponding indirect readings in the arm measured with the metal cuff (Fig. 1; curves A and C, brachial; curves B and D, femoral) indicates that the direct readings were consistently higher than the indirect (metal cuff) readings except for curve

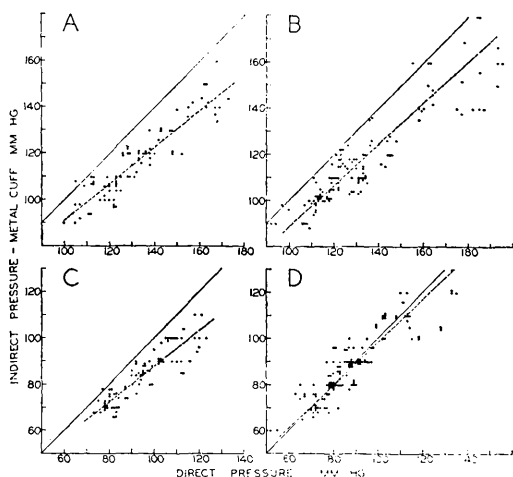


FIG. 1. Comparison of indirect (metal cuff) systolic pressure readings with systolic pressures measured directly in brachial (A) or femoral (B) artery. Indirect diastolic readings compared with direct diastolic pressures in brachial (C) or femoral (D) artery. Solid line is that of equal values on the 2 scales.

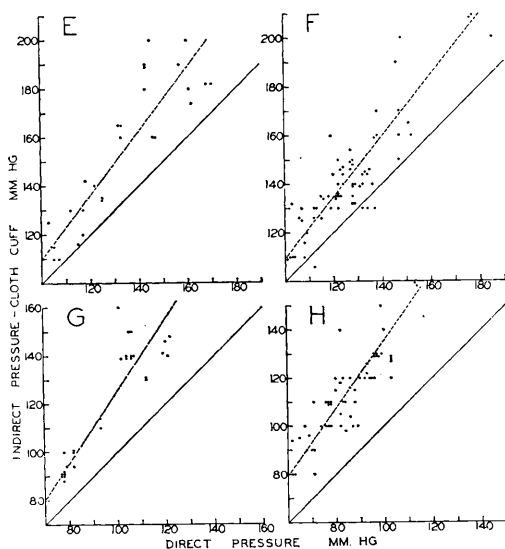


FIG. 2. Comparison of indirect (cloth cuff) systolic pressure readings with systolic pressures measured directly in brachial (E) or femoral (F) artery. Indirect diastolic readings compared with direct diastolic pressures in brachial (G) or femoral (H) artery. Solid line is that of equal values on the 2 scales.

D, in which the indirect diastolic pressure in the arm is compared to the direct diastolic pressure in the femoral artery. The direct readings exceeded the corresponding indirect readings by about 10 mm Hg in the normotensive range. The opposite relationship was found between direct pressure and pressure estimated indirectly using the cloth cuff (Fig. 2). In this case the direct measurements were always lower than the indirect (cloth cuff) readings. As with the metal cuff, the difference became more pronounced at higher blood pressure levels.

These data indicate several noteworthy trends. In the first place, cloth cuff readings were always higher and slightly more variable than the metal cuff readings, the difference between the 2 readings becoming slightly more pronounced at higher blood pressure levels. Secondly, direct blood pressure measurements obtained with a strain gauge fell about midway between the cloth and metal cuff readings. Thus the average blood pressure of normal monkeys, if it could be measured directly without anesthetizing or exciting the animals, would be about 130/100 mm Hg

Discussion. There are very few reports in the literature on blood pressure variations in normal or hypertensive monkeys. Attempts to use the indirect method of McGregor(3) employed by Goldblatt(4) gave extremely variable results even in anesthetized animals. Direct femoral puncture, the procedure employed by Frank and Wakerlin(5) also yielded unsatisfactory results. This method is technically difficult and gives only an undefined average pressure when a mercury manometer is used. Restraint of the monkey on a board, required by either procedure, often excites the animal, causing an abnormal elevation of the blood pressure.

The indirect procedures described in this report are applicable to either unanesthetized or anesthetized animals. The methods possess certain inherent sources of error characteristic of most indirect procedures(6,7). However, by careful attention to detail it has been possible to define accurately blood pressure levels in untreated animals and to establish the significance of blood pressure changes following several types of treatments (1). Roughly 11,000 determinations on about 90 animals have been made to date; in some

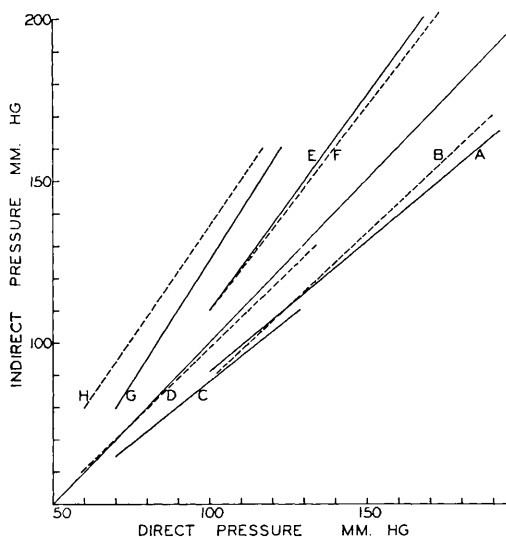


FIG. 3. The 8 regressions of indirect on direct pressure measurements shown in Figs. 1 and 2 are superimposed. A and B, metal cuff systolic; C and D, metal cuff diastolic; E and F, cloth cuff systolic; G and H, cloth cuff diastolic. In A, C, E and G direct pressure was measured in brachial artery and in B, D, F and H, in femoral artery. The thin solid line is that of equal values on the 2 scales.

animals blood pressure levels have been followed for as long as 2 years. The rather unexpected stability of systolic and diastolic blood pressures in rhesus monkeys makes this animal admirably suited for experiments in which blood pressure changes accompanying an experimental procedure are to be investigated.

Summary. Arterial blood pressures have been determined in unanesthetized monkeys by 2 indirect methods. Using a small "new-born" cuff (cloth cuff) on the upper arm and auscultation of the sounds in the brachial artery, mean blood pressure in 14 normal monkeys was found to range from 137/112 to 188/152 mm Hg with a group average of 159/127. With a cuff consisting of a rigid metal shell enclosing a rubber sleeve (metal cuff), mean pressures ranged from 103/78 to 132/101, the group average being 118/90 mm. In 27 splenectomized, but otherwise normal, monkeys the blood pressures were slightly but not significantly lower. Metal cuff pressure readings were found to be consistently less variable than corresponding cloth cuff values, the respective average standard deviations in normotensive animals being 7 and 12 mm. Blood pressures in untreated animals estimated by either indirect

method were relatively stable; in no instance did mean systolic or diastolic pressure during a 12-month period vary by as much as 10 mm Hg from the mean values obtained during an initial 2-month observation period. Simultaneous comparisons of indirect (cloth or metal cuff) and direct (strain gauge) blood pressure measurements in 46 anesthetized animals indicated that the metal cuff readings were lower and the cloth cuff readings higher than measurements obtained directly in the same artery with a strain gauge. The blood pressure as measured directly with a strain gauge fell about midway between the corresponding cloth and metal cuff readings.

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Experimental Hypertension in the Rhesus Monkey. (23500)

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There have been few reported studies on induction of experimental hypertension in the rhesus monkey. The investigation described here deals with attempts to provoke hypertension in this species by procedures which have been successful in rats, dogs, and other experimental animals. These procedures included temporary unilateral renal artery occlusion(1), unilateral or bilateral silk perinephritis(2), unilateral or bilateral constriction of the renal arteries with silk ligatures (3) or clamps(4), and oral administration of excessive amounts of sodium chloride(5).

Materials and methods. Animals. Sixty rhesus monkeys (*Macaca mulatta*), 26 males and 34 females, weighing from 3 to 12 kilos were used in this study. General care and feeding followed the pattern described by Schmidt and Genter(6). All animals had been infected previously with malaria, their infections cured by various chemotherapeutic agents, and this fact proved by absence of parasitemia following splenectomy. These monkeys were indistinguishable from intact control animals insofar as range and variability of systolic and diastolic blood pressures