

mandible of a large gavial-like crocodile, cranium and skeletal parts of a large mylodont ground sloth, cranium of a leontiniid, ventrally complete cranium of an astrapothere, and a complete cranium and mandible of a juvenile interathere.

*Earlier work in the area.* The nonmarine Miocene beds, Honda formation, in the north-central district of Huila have yielded the most complete fossil vertebrate assemblage yet known in northern South America. Oil geologists had known of bones in these deposits and had made reports of these occurrences to their companies by 1938. Royo y Gomez (1) and Stirton (2) have discussed the reports of these geologists. The first published report on a fossil vertebrate from Huila seems to have been Cabrera's (3) paper on a new species of astrapothere from the Tertiary beds. Mook (4) described a new species of crocodilian from an unspecified locality not far west of Neiva, capital of Huila. Brother Ariste (Mauricio Rollet) collected the crocodilian in 1920; he also collected the astrapothere named by Cabrera. The crocodile was thought to be possibly Cretaceous in age; however, Royo y Gomez (5) points out that the specimen probably came from the Honda formation (Tertiary). Royo y Gomez (5) reported on crocodilian, chelonian, rodent, and notungulate specimens from sandstones of the "Honda superior," which were found north of the village of Villavieja along the trail to San Alfonso. Royo y Gomez (1) has also published a preliminary survey of the Villavieja Miocene badlands, including an introductory list of fossil vertebrates and a generalized section of the Honda sediments. Personnel from the University of California now have additional papers in press on the fossil vertebrates of this area; these papers are indicated in Table 1.

*Honda formation and La Venta fauna.* The fossiliferous beds northeast of Villavieja have been identified as the Honda formation because of lithologic similarity and corresponding stratigraphic, structural, and physiographic position to the Honda in its type locality. The beds here were apparently laid down as flood-plain deposits in a system of streams and include red-colored mudstone members and gray to brown sandstones, mudstones, and conglomerates. In this area more fossils seem to have accumulated in the gray mudstones than in the other types of sediments, although one ferruginous sandstone was notably fossiliferous.

Fossil vertebrates of late Oligocene age have been collected from the Honda formation approximately 50 miles north of the Villavieja district. It becomes apparent, then, that components of the Honda formation in different geographic provinces were not laid down at the same time. In order to distinguish the Honda lithogenetic unit from any concept of geologic time based on the fossil vertebrates, Stirton and Savage (6,7) employ the name "La Venta fauna" for the special late Miocene vertebrate assemblage from the Honda beds at Villavieja. The list given in Table 1 will indicate our present knowledge of the systematics of the assemblage and will also indicate status of our

research program on the fauna. Wann Langston, Jr., has kindly furnished preliminary identifications of the reptiles, amphibians, and fish.

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## Effects of Various Analgesics on Inflammatory Edema Resulting from Silver Nitrate Injection

Annette La Belle and John A. Tornabene

The Wellcome Research Laboratories,  
Tuckahoe, New York

It was noted during analgesia experiments on silver nitrate-irritated rat joint preparations (1) that the ankles of aspirin-treated rats appeared considerably less swollen than ankles of the controls. This action of aspirin has been made the subject of the present investigation. Similar studies have been made on other compounds for the sake of comparison.

The animals used were male CF or RF albino rats weighing approximately 350 g and maintained on Rockland rat diet. Irritation was produced by injecting 0.2 ml 1% AgNO<sub>3</sub> into the ankle joint. The rats were anesthetized with ether to avoid struggling. To inject the left ankle, the rat was placed on its right side and the needle inserted into the posterior aspect of the hind leg approximately 1 cm above the heel and directed down into the joint. Care was taken not to puncture the visible superficial blood vessels. Because of the large volume of solution, the fluid spread through the heel and paw. A ¼-cc tuberculin syringe with a 23-gauge needle was found satisfactory. Silver precipitates of tissue fluids tended to accumulate in the syringe and cause the plunger to stick, but this difficulty was avoided by rinsing out the syringe with distilled water between injections and dissolving out the precipitate with nitric acid when necessary.

Somewhat similar animal preparations have been employed by Winter (2) and Selye (3) to observe the effect of pretreatment with cortisone on the development of inflammatory edema. To produce the swelling, Winter injected 0.1 ml 0.5% AgNO<sub>3</sub> and Selye 0.1 ml of various strengths formaldehyde beneath the plantar aponeurosis of the hind paw of the rat.

Shortly after injection the tissues of the foot and ankle became red and swollen and developed all the signs of acute inflammation. The joint became very sensitive to movement and within 24–48 hr a typical

response consisting of squealing and struggling was elicited from the rat whenever the foot was flexed ventrally with firm pressure. A sterile abscess usually developed at the site of the injection.

Anteroposterior and mediolateral measurements of the ankle were made with calipers 48 hr after injection, and the circumference was calculated, assuming the ankle at this level to be rectangular. An example of the great increase that occurs in the dimensions of the ankle is illustrated in Table 1. The average circumference was 2.49 cm in the controls and 4.51 cm in the injected rats.

TABLE 1  
EFFECT OF  $\text{AgNO}_3$  INJECTION ON SIZE OF ANKLE JOINT OF RAT

Treatment	No. rats	Circumference 48 hr after injection (in cm)
Uninjected	8	2.49 $\pm$ 0.20
Injected with $\text{AgNO}_3$	8	4.51 $\pm$ 0.27

The compounds aspirin, acetophenetidin, and sodium gentisate were administered by stomach tube, 1 mg/g, 40% suspensions in 2% starch solutions, 24 hr after the  $\text{AgNO}_3$  injections. The control rats received 2% starch solution. Measurements were made at 24 hr after the tube feedings. It was evident from the marked reaction of the rats to flexion of the joint that they were obtaining no analgesic effect from these compounds at this time. The results of the measurements are summarized in Table 2. Aspirin and aceto-

TABLE 2  
EFFECTIVENESS OF VARIOUS DRUGS IN REDUCING INFLAMMATORY EDEMA RESULTING FROM INJECTION OF 1%  $\text{AgNO}_3$  INTO ANKLE JOINT OF RAT

Compound	Method of administration	Dose (mg/g)	No. rats in group	Average circumference* and SD (in cm)	Diff (in cm)	P†
Aspirin	Oral	1.0	6	3.45 $\pm$ 0.32	0.71	< 0.01
Starch control	"	—	7	4.16 $\pm$ 0.18		
Acetophenetidin	"	1.0	5	3.64 $\pm$ 0.35	0.52	< 0.01
Starch control	"	—	7	4.16 $\pm$ 0.18		
Sodium gentisate	"	1.0	8	4.40 $\pm$ 0.16	0.11	> 0.05
Starch control	"	—	8	4.51 $\pm$ 0.27		
Morphine	Subcutaneous	0.01	5	4.03 $\pm$ 0.06	0.08	> 0.05
Control	—	—	5	4.11 $\pm$ 0.29		
Demerol	Subcutaneous	0.10	5	3.88 $\pm$ 0.19	0.23	> 0.05
Control	—	—	5	4.11 $\pm$ 0.29		

\* Measurements made 48 hr after  $\text{AgNO}_3$  injection.

† Test of significance was made by calculating statistic *t*.

phenetidin reduced the swelling significantly, but sodium gentisate did not. Sodium gentisate is less toxic

than the other two compounds, and it is possible that better results would have been obtained with higher doses, but on a milligram for milligram basis it was less effective.

Morphine sulfate, 0.01 mg/g as 0.5% solution, and demerol hydrochloride, 0.1 mg/g as 5.0% solution, were each injected twice subcutaneously, once 24 and once 46 hr after  $\text{AgNO}_3$  irritations. Measurements were made 2 hr after the last injection. At this time these narcotics were at the peak of their analgesic activity and no response at all was given by the rat to firm flexion of the swollen joint. The circumferences of the ankles at this time are included in Table 2. Neither compound produced a statistically significant change.

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#### Levels of Nucleotide in the Blood during Shock

George T. Hoffmann, Antonio Rottino, and Harry Albaum

*Hodgkin's Disease Research Laboratory,<sup>1</sup> St. Vincent's Hospital, New York, and Brooklyn College, Brooklyn, New York*

The work of Green (1) and his collaborators is based on the hypothesis that shock is produced by the release of adenine nucleotides from tissue into the blood stream. This idea was suggested by observations that when substances like ATP and related compounds were injected into the intact animal shocklike symptoms occurred. Green was never able to prove his hypothesis because specific methods for the determination of blood ATP and related substances were not available to him.

During the past 18 months we have been studying levels of adenine nucleotides in normal persons and patients with Hodgkin's disease. Blood levels in a number of other pathological conditions were also measured for comparison, and among these were samples from patients suffering from various kinds of shock (Table 1).

The method used in these studies is that of Albaum and Lipshitz (2), a modification of a procedure devised by Kalekar (3, 4), in which ATP, ADP, and AMP are measured spectrophotometrically after successive dephosphorylation and deamination to inosinic acid. In addition to measuring blood levels of these adenine compounds, we also determined the absorption spectrum of the blood filtrates between 2300 Å and 2800 Å.

In the blood samples from patients in shock there were no significant alterations in the levels of ATP,

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