Plates made from 23 stock strains of *Br. abortus* showed none of these strains to be entirely free of both types, although the ratio of opaque to clear colonies varied over a wide range.

Before the above-mentioned spontaneous changes were noted, the author had been able to produce opaque colonies from typical *Br. abortus* cultures by growing the organisms in glucose-glycerine broth to which had been added 10% of serum from rabbits immunized against *Br. abortus*. The changes which occurred in these cultures were similar to those occurring spontaneously, but were more complete. All colonies appearing on plates made from 2 week old immune broth cultures were of the opaque type in the 6 strains used.

As the 2 types of colonies occurring spontaneously, as well as those obtained by the use of homologous immune serum, agree with *Br. abortus* as to morphology, staining reaction and carbohydrate fermentations, and as, in at least one strain, they both produce *Br. abortus* agglutinins when inoculated into rabbits and guinea pigs, it seems certain that dissociation is responsible for the 2 types. The terms "R" and "S" have been intentionally omitted until the results of virulence tests now in progress have been determined.

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Mechanism of Actions and Toxicity of Nitroprusside.

CHAS. C. JOHNSON. (Introduced by P. J. Hanzlik.)

From the Department of Pharmacology, Stanford University School of Medicine.

The actions and toxicity of sodium nitroprusside ($Na_2Fe(CN)_5NO2H_20$) have been investigated periodically during the past 42 years without, however, definite establishment of the mechanisms on which the actions depend, or indications of its possible usefulness. The original claims of L. Herrmann[1], of his pupil Davidsohn[2], and of Arntz[3] and Cromme[4], that the actions of nitroprusside depended upon liberated hydrocyanic acid suggested the possible use of the compound as a respiratory stimulant. The actions of the compound, therefore, have been re-investigated along different lines with the following results.

[1] Herrmann, *Arch. für Physiol.*, 1886, xxxix, 419.

[2] Davidsohn, *Diss.*, Königsberg, 1888, 34.

[3] Arntz, *Diss.*, Kiel, 1897, 24.

[4] Cromme, *Diss.*, Kiel, 1891, 16.

The marked symptoms claimed by previous investigators, namely sustained, intense respiratory stimulation, followed sometimes by tremors and convulsions in all species, and accompanied by nausea and emesis in mammals and birds, have been confirmed. The odor of cyanogen *post mortem*, following large fatal doses only, has been confirmed, but chemical tests for cyanogen in the blood and tissues have proved inconclusive. Other tests were applied because small and non-fatal doses (2 mgm. per kilo or less hypodermically and about 0.1 to 0.2 mgm. per kilo intravenously), still gave profound effects without demonstrable cyanogen. These effects in narcotized and operated animals consisted of marked respiratory stimulation and a marked and sustained fall of blood pressure accompanied by increases in volume of peripheral organs and diminution in cardiac volume and contractions with increase or without change in rate. The circulatory actions were practically identical with those of sodium nitrite, but opposite to those of cyanide, in the same animals. A nitrite-type of action was further indicated from the facts that the vasomotor center still responded to reflex and asphyxial stimulations, the smooth muscle and sympathetic endings of the blood vessels were responsive in the usual way to epinephrine and the smooth muscle of excised organs was typically depressed. These actions might be expected from the nitroso (NO) group in the nitroprusside, and the respiratory stimulation would result from the depressor action, rather than from the alleged liberation of cyanogen.

Further evidence of a negative character bearing on the cyanogen mechanism was obtained with incubated pigeon corpuscles. The respiration of these cells was promptly inhibited by sodium cyanide (equal to 1:600,000 of (CN), but not by sodium nitroprusside in concentration theoretically capable of liberating 10 times this concentration of cyanogen, or about 16 times the concentration of nitroprusside assumed to be present in blood after definitely effective doses (0.1 mgm. per kilo intravenously). One hundred times the concentration of nitroprusside, however, did cause some depression of respiration in the corpuscles. The fermentation activity of yeast was unaffected by nitroprusside.

Provisionally, it appears that the actions of nitroprusside, in definitely effective but not fatal doses, do not depend upon the liberation of the cyanogen group. Since the circulatory and smooth muscle actions resemble those of the nitrite group, nitroprusside may have some therapeutic usefulness.