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Lester C. Shell
Millikin University

Judith A. Burdick
Millikin University

Kenneth Wilson
Millikin University

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Effects of Medication on Respiration Pattern of Tranquilized White Mice[1]

LESTER C. SHELL [2], JUDITH A. BURDICK,[3] KENNETH WILSON [3].

Abstract. White mice of varying ages were given a definite amount of the tranquilizer, reserpine, over a three-week period. At the end of this period, respiration rates were determined by use of a physiograph with impedance pneumograph and small animal attachments. Mice were given, in addition to the tranquilizer, varying dosages of different medicinals, and their respiratory pattern was recorded.

Such medicinals as thyroxin, streptomycin, vitamins E and C were given and in combination with sulfanilamide, nicotinamide, neonal, kayquinone, hykenone. Effects of multiple medications were noted and recorded.

Reserpine, when given in all combinations, lowered the respiratory rate from that recorded when each drug was given alone. Vitamin C gave a stabilizing effect to the respiratory pattern when given in combination with other medications.

In a series of papers Shell et al. (1961, 1964, 1966) have published the results of reserpine and thyroxine medication on various physiological activities of white mice. Since surprisingly little information is available on the respiratory rate, oxygen consumption and basal metabolism of mice, the authors were interested in the effect of multiple medication as well as single medication on respiratory pattern of Swiss strain white mice. Normal respiration had previously been determined by Guyton (1947), but type of mouse was not specified as recorded by Green (1966).

MATERIALS AND METHODS

Swiss strain white mice of varying ages were given different amounts of the tranquilizer, reserpine, in water solution over a three-week period. Initially, half dosage was given in order for the animals to build up a tolerance to the drug and at the same time to permit checking for toxic effects. After two weeks of half dosage, full medication was given.

After two-week period, 0.25 mg of reserpine was given daily to a group of fifteen animals. At the end of this time their respiration rate was determined by use of an impedance pneumograph connected with a physiograph equipped with small-animal attachments. In addition to the reserpine, ten other drugs were given to groups of fifteen animals with varying dosages of medicines as recorded in Table 1.

As in the medication with reserpine ,initially half dosages of the different drugs were given. In addition to permitting a check

[1] Work supported by a grant from Lilly Research Laboratories.

[2] Professor and Chairman, Department of Biology, Millikin University, Decatur, Illinois.

[3] Department of Biology, Millikin University, Decatur, Illinois.

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Table 1.

Medication	*Daily Dosage*
Reserpine	0.25 mg
Streptomycin	0.10 mg
Thyroxin	0.18 mg
Vitamin C	2.40 mg
Vitamin E	1.20 mg
Neonal	0.10 mg
Hykenone	0.50 mg
Riboflavin	0.25 mg
Sulfanilamide	0.80 mg
Nicotinamide	0.80 mg
Thiamine	0.25 mg

for toxic effects, this gave opportunity for a tolerance to be established.

A combination of reserpine for two days, thyroxine for one day with sequence repeated and another sequence of thyroxine for two days, and reserpine one day was given and observed. Counts per minute for an average of fifteen animals were made.

A similar series of experiments, using reserpine in combination with each of the medications listed, were run and counts per minute as recorded on the physiograph for an average of fifteen animals were recorded. Because of the stabilizing effect of respiratory pattern as recorded on the physiograph, whenever vitamin C in massive dosage was given, counts per minute with the vitamin in combination with other medication were made and recorded.

Results and Discussion

Initial results showed that with the exception of neonal, reserpine and streptomycin all other medications when given alone increased respiration rate per minute over that recorded when no medication was given. With the exception of neonal and streptomycin all medications increased respiration rate over that obtained when the tranquilizer was given alone. This information is recorded in Table 2.

Table 2.

Medication	*Counts/Minute*
No medication	244
Reserpine	240
Thyroxin	260
Streptomycin	235
Vitamin C	247
Riboflavin	252
Vitamin E	300
Sulfanilamide	296
Neonal	192
Thiamine	276
Hykenone	310
Nicotinamide	328

The greatest elevation in respiratory rate was with nicotinamide which seemed to cause an increase in the entire respiration

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and metabolic pattern. Hykenone, a respiratory irritant, gave next highest respiratory rate but low intensity in depth of breathing by the animal. Vitamin E increased respiration rate when given alone; perhaps this was because it elevated the number of red blood cells as found in subsequent experimentation.

Because of the high excretion rate of streptomycin, it was not surprising that the respiration count here was low. Vitamin C, which maintains the optimum oxidation-reduction potential of the cell, would be expected to cause an overall increase in metabolism, but only a slight increase in respiration rate was noted.

Neonal, a barbituate, was not expected to increase respiration rate; in fact, it lowered the rate. Thiamine ,because of its use in coenzyme structures, should be expected to cause an increase in metabolic functions, but our data did not show a great increase.

Riboflavin, a prosthetic group of the flavoprotein enzymes, might be expected to cause an over all increase, but our data did not show significant increases. Sulfanilamide and streptomycin are anti-bacterials and were not expected to cause particular metabolic changes; however, sulfanilamide increased the respiration rate perceptibly and streptomycin decreased respiration rate markedly.

Vitamin E, whose metabolic functions are relatively unknown, gave an increase of respiration considerably above that obtained with no medication. With this was noted a high elevation in red count which could have accounted for this result.

It would appear that the tranquilizer, reserpine, when given alone should lower the respiration rate much below that where no medication was given because of its depressant effect, but this was not noted until combined with other medications. All of these results are recorded in Table 2 above.

When the tranquilizer was given in combination with other medications, in every instance it decreased the rate below that recorded when the medication was given alone. Greatest effects of lowering respiration rate were the streptomycin, nicotinamide, and sulfanilamide and vitamin E where the values were from 60 to 100 counts per minute lower. Results obtained from a combination of neonal and reserpine were slightly higher than those obtained from neonal alone.

Quite by accident, it was noted that vitamin C stabilized depth and respiratory pattern as recorded on the physiograph, when given with various medications. However, the combination of vitamin C with other medications did not lower the respiration rate more than 25 to 30 counts per minute. This information is recorded in Table 3.

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Table 3.

Medication	*Counts/Minute*
Reserpine + Vitamin C	210
Reserpine + Hykenone	256
Reserpine + Sulfanilamide	230
Reserpine + Streptomycin	135
Reserpine + Riboflavin	208
Reserpine + Vitamin E	240
Reserpine + Thiamine	248
Reserpine + Neonal	207
Reserpine + Nicotinamide	238
Reserpine (2) + Thyroxin (1)	252
Reserpine (1) + Thyroxin (2)	247
Vitamin C + Thyroxin	228
Vitamin C + Vitamin E	275
Vitamin C + Streptomycin	204

When reserpine was given with thyroxin in sequence of reserpine two days, thyroxin one day, and reserpine one day, thyroxin two days with sequence repeated, very little change was noted in respiration rate. However these combinations allowed the tranquilizer to be given over a longer period of time without serious dehydration to the animal, and the thyroxin could be given over a longer period without showing toxic effects.

Conclusions

1. Our experimentation and recorded data gave evidence that all medications used affected respiration when given alone or in combination.

2. The tranquilizer, reserpine, when given in combination with all drugs studied lowered the respiration rate with every combination used.

3. Vitamin C, when given in massive dosages in combination with other medications, although not changing respiration rate appreciably, gave a more noticeable effect by stabilizing the respiration pattern as traced on the physiograph.

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