which must be carefully considered in making measurements of swelling.[4] In a preliminary paper (*1*) it was pointed out that untreated chicken erythrocytes, after standing for several hours at 37° C hemolyze more rapidly than they do during the first few hours at this temperature. Fig. 5A–D illustrates that the galvanometer deflection increases as chicken erythrocytes stand at 37° C. At zero time the whole swelling curve can easily be recorded on the 12-cm bromide paper, but several hours later the deflection of the galvanometer becomes so much greater that only the first portion of the curve can be recorded. Figs. 5E and F show that no comparable change is observed when human erythrocytes stand at 37° C.[5]

References

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Comments and Communications

Blood Changes Due to Ammonia Inhalation?

We have read the recent article by Schmidt and Vallencourt entitled "Changes in the Blood Following Exposure to Gaseous Ammonia" (*Science*, November 19, p. 555). There are several serious errors apparent in this work which should be pointed out.

At the meeting of the American Public Health Association in Boston last November, we presented results of a study involving 30-min exposures of 7 human subjects to 500 ppm of anhydrous NH_3 gas. A description of the data was submitted for publication in October 1948 and will soon appear in a scientific journal.

A concentration of 500 ppm was used; therefore our results can be compared to those of Schmidt and Vallencourt. We selected ½-hr exposures since Henderson and Haggard (*Noxious gases*, New York: Reinhold, 1943, p. 126) reported that the maximum allowable concentration for a ½- to 1-hr exposure is 300 to 500 ppm.

All 7 subjects experienced irritation of the nose and throat immediately, and, in some, the irritation persisted for as much as 24 hrs. It is surprising that the subject reported in Schmidt and Vallencourt's paper did not experience marked irritation of the nose and throat after 4 hrs' exposure to a mean concentration of 545 ppm.

The authors failed to report the details of the exposure chamber and the subject's activity during the exposure. It seems unusual to maintain a gas concentration so well in an ordinary room unless the dilution rate is close to the rate of gas evolution. Since only two air analyses were made over a period of 4 hours and these were "grab samples" (L. Silverman, *Industrial air sampling and analysis*, Chem. and Tox. Bull. No. 1, Pittsburgh: Industrial Hygiene Foundation, 1947), it is quite possible that the actual concentration may have varied widely.

The values presented in the authors' Table 1 may be questioned in several respects. The most serious discrepancy appears to be in the blood-NH_3 (mg %) values (column 3). If one assumes a minute volume of 20 l[1] and an ammonia concentration of 545 ppm (mean of two determinations made by the authors) and, finally, that all ammonia is retained in a blood volume of 5 liters, then the values shown below are obtained. These results neglect ammonia conversion to other nitrogenous compounds and are presented below in comparison to the authors' values.

TABLE 1

Time (hrs)	Authors' NH_3 (mg %)	Calculated NH_3 (mg %)
Normal	00.0	00.0
1	12.1	8.7
2	21.9	17.4
3	27.9	26.2
4	36.4	34.9

From this table, it appears that the authors have found more ammonia than could theoretically be retained. Possible explanations might be either greater respiratory minute volume or lower blood volume, but these could hardly vary widely enough to explain the discrepancy. The invalidity of the assumption that all inhaled ammonia is retained is evident from our data, which show that the amount of ammonia retained decreases with time until after 30 min only 20 to 30% of the inhaled concentration is absorbed, as measured by frequent exhaled-air analyses. The data on blood ammonia presented by Schmidt and Vallencourt are rendered even more incredible by reference to Peters and Van Slyke (*Quantitative clinical chemistry* Vol. 1, 2nd ed. Baltimore: Williams and Wilkins, 1946). The method used was apparently not accurate enough to detect normal levels of blood ammonia, which, with proper methods, is of the order of 0.004 to 0.05 mg % (reported by Schmidt and Vallencourt: 00.0 mg %). It is well known that ammonia concentrations multiply rapidly in drawn blood unless rigid precautions are taken. On the other hand, the blood level *in vivo* is kept very near to 0 by the extraordinary efficiency with which ammonia is converted to amide nitrogen in the tissues and to urea in the liver. Ammonium salts are readily absorbed from the gastrointestinal tract; however, even large doses evoke but a slight transitory rise in blood ammonia, the ammonia being rapidly excreted as urea. Administration of 10 to

[1] This represents the mean value of sedentary subjects exposed to 500 ppm in our study and represents the increase produced by NH_3 over normal values of 8–12 liters.

[4] Bacteriologically sterile techniques were observed except during the few minutes when the actual swelling measurements were made.

[5] All records were obtained using a recording camera placed 1 m from a Leeds and Northrop Type R galvanometer with a sensitivity of 0.003 μa/mm at 1 m and a period of 3 sec. A Kipp and Zonen torsion string galvanometer has also been used with satisfactory results. The temperature was 37° C in all cases. Figures 3–5 are tracings of the photographic records.

13 gms of ammonium citrate to normal human subjects raised the blood ammonia from 0.02 to 0.04 mg % to only 0.06 mg % (quoted by Peters and Van Slyke). Furthermore, ammonia is a highly toxic material. Bollman and Mann found that liverless dogs developed signs of ammonia intoxication (e.g. convulsions) when the blood level reached 2.0 mg % (*Amer. J. Physiol.*, 1930, 92, 92).

Our studies based on 30-min exposures indicated no significant deviations from normal in blood and urine nitrogen measurements.

Schmidt and Vallencourt state: "It has been known for some time that inhalation of ammonia lowered the blood pressure, but no quantitative data pertaining to this are available." Sollman (*A manual of pharmacology*, 5th ed. Philadelphia: W. B. Saunders, 1936, p. 837) states that the effect of ammonia inhalation is a rise of blood pressure, reflex in origin from stimulation of trigeminal nerve endings. Because of the reflex nature of the blood pressure effect and since our results showed that ammonia retention decreases with time, one would expect the influence of NH_3 on blood pressure to be greatest in the first 30 minutes. We found no consistent change at the concentration used, which agrees with the authors' finding, but it seems very unlikely that a later fall in blood pressure should be attributed to ammonia. Schmidt and Vallencourt are curiously indefinite on their "quantitative" observations of blood pressure. Whether the pressure reported is systolic or diastolic is not stated, and it is impossible to generalize about blood pressure responses from a single experiment on one individual. In view of the steady decrease in pressure shown by the authors for three hrs' exposure, it is curious that further observations were not made, since the decline at 3 hrs was approaching significantly hypotensive levels.

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On New Nicotinolytic Compounds

In previous papers (C. Heymans and G. R. de Vleeschhouwer. *Arch. int. Pharmacodyn. Thér.*, 1948, 75, 307, 413) it has been demonstrated that the diethyl-amino-ethyl ester of phenyl-cyclopentane carbonic acid (parpanit) is a very active nicotinolytic agent. Intravenous injections of 20–30 mg/kg of parpanit indeed suppress all toxic actions of high doses of nicotine.

The present experiments were undertaken with another new synthetic compound: N-diethyl-amino-ethyl phenothiazine (diparcol). Some general pharmacological properties of this substance were already studied by Bovet, Fournel, and Charpentier (*Thérapie*, 1947, 2, 115) and Gordon (*Nature, Lond.*, 1948, 162, 146).

Our experiments (*Commun. Soc. Biol. Montevideo*, November 25, 1948) were performed on chloralosed dogs. Intravenous injections of 15–30 mg/kg of diparcol protect completely against 100–200 lethal doses of nicotine. No cardiac slowing or irregularities, cardiac fibrillation, changes in blood pressure, bronchospasms, hyperperistalsis, convulsions or muscular fibrillations, salivation, or paralysis of the respiratory center occurs after intravenous injections of 100–200 LD of nicotine in dogs pretreated with diparcol. Thus, this new compound is also a very active nicotinolytic agent.

Parpanit and diparcol are not only powerful nicotinolytic substances but also synapticolytic, parasympatholytic and anticonvulsant agents. These compounds also very actively protect against high doses of acetylcholine, pilocarpine, diisopropyl fluorophosphate (DFP), strychnine, and Metrazol.

These experimental observations may have some important practical applications.

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Nazi Persecution of Scientists

In connection with Professor Muller's letter to the Soviet Academy of Sciences (*Science*, October 22, p. 436), I think it would be helpful to call the attention of every American scientist, Army and Navy officer, and congressman, to a few sentences in *Goebbels' diaries* (New York: Doubleday, 1948).

On page 361 Goebbels tells of an occasion on which he, Frick, and Rust were guests of the Fuehrer. He wrote, "Their comments and remarks were so idiotic as to reveal how completely out of the picture they really are. They delivered themselves of stupid phrases . . . ." The important point is that Rust was the Nazi Minister of Education and, as Lochner notes, he had been an inmate of an insane asylum! He was the one chosen to persecute the scientists and university leaders, causing them to flee from Germany for their lives.

This seemed to be a good idea at first, but on May 12, 1943, things were going badly for the Germans in the air and on the sea. The Allies were using new discoveries in physics which were paralyzing the German planes and submarines. And so, on p. 375, one finds Goebbels regretting that Max Planck had been so antagonized. As he said, "It is the fault of Rust and is irremediable . . . . The mediocre talents in the Reich Government are a wall between the Fuehrer and many sectors of public life." In his devotion to his Fuehrer, Goebbels tried to make him out as a would-be patron of science, ignoring the fact that he had appointed a miserable quack as his private physician.

On p. 378, speaking of the critical situation of the submarines in the face of the new detecting devices developed by Allied physicists, Goebbels wrote, "Our technical development both in the realm of submarines and of air war is far inferior to that of the English and the Americans. We are now getting the reward for our poor leadership on the scientific front, which did not show the necessary initiative to stimulate the willingness of scientists to co-operate. You just can't let an absolute nitwit head German science for years and not expect to be punished for such folly."

This paragraph might well be read and re-read now at home and abroad. In times of peace, baiting scientists and great men and putting them in their place is great fun for politicians but Goebbels has told us how disastrously this policy pays off when war comes.

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