

**On the comparative action of Bertoni's ether (tertiary amyl nitrite), amyl nitrite, and iso-butyl nitrite / by T. Lauder Brunton and T.J. Bokenham.**

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# COMPARATIVE AC

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## AMYL NITRITE.

T. LAUDER

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The simplest alcohol,  
sometimes termed, carbinol,  
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to the radical, hydroxy-  
graphically thus:—

By replacing one atom  
alcohol, primary alcohol  
 $\text{CH}_3\text{CH}_2\text{OH}$ ; propyl alcohol  
 $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ ; amyl  
graphically—

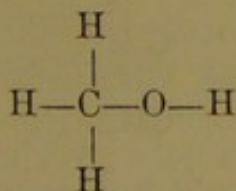


ON THE  
COMPARATIVE ACTION OF BERTONI'S ETHER  
(TERTIARY AMYL NITRITE),  
AMYL NITRITE, AND ISO-BUTYL NITRITE.

BY  
T. LAUDER BRUNTON, M.D., F.R.S.,  
AND  
T. J. BOKENHAM.

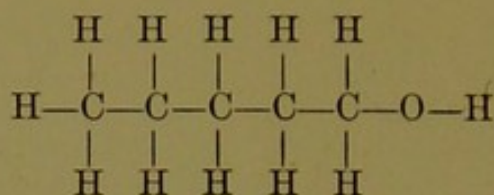
In 1887 Bertoni tried to find a compound having greater stability than ordinary amyl nitrite, while possessing the same utility as a remedy. He accordingly prepared the tertiary amyl nitrite. In order to understand the relationship of this compound to the others mentioned in our title, it may be advisable to give a short account of the chemistry of the alcohols from which they are derived, and of the terminology commonly adopted.

The simplest alcohol, methyl alcohol ( $\text{CH}_3\text{OH}$ ), or, as it is sometimes termed, carbinol, consists of an atom of carbon, of whose four affinities three are united to hydrogen and one to the radical, hydroxyl ( $\text{HO}$ ). Its formula is represented graphically thus:—



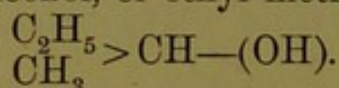
By replacing one atom of hydrogen by alcoholic radicals or alkyls, primary alcohols are formed, *e.g.*:—Ethyl alcohol,  $\text{CH}_3\text{CH}_2\text{OH}$ ; propyl alcohol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ ; butyl alcohol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ ; amyl alcohol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ , or graphically—





When two atoms of hydrogen in the carbinol are replaced by alkyls, secondary alcohols result, *e.g.* :—

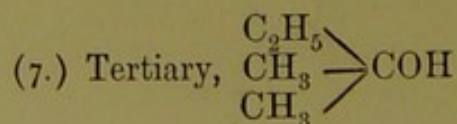
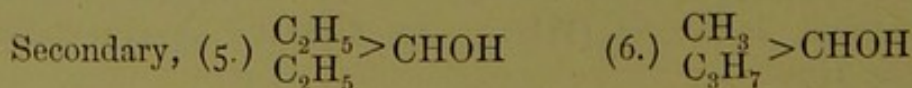
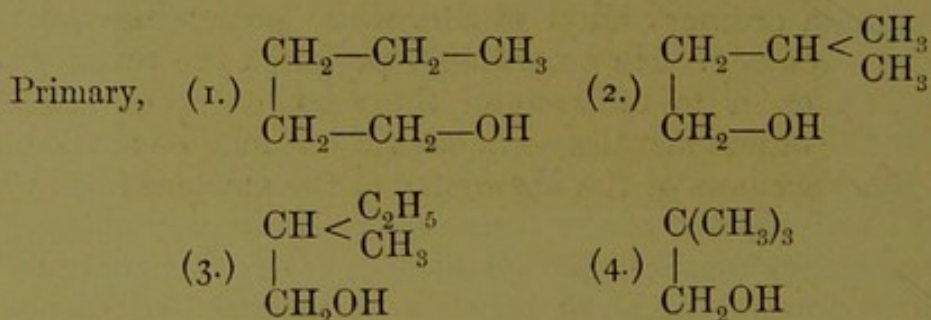
Iso-propyl alcohol or dimethyl carbinol,  $(\text{CH}_3)_2\text{CH}(\text{OH})$  ;  
secondary iso-butyl alcohol, or ethyl-methyl carbinol,



When all three hydrogen atoms in carbinol are replaced by alkyls, tertiary alcohols are produced.

As the number of carbon atoms increases in any alcohol, so does the number of compounds having the same percentage composition, but differing in the arrangement of their component atoms of carbon, hydrogen, and oxygen. Thus only one kind of methyl alcohol or ethyl alcohol is possible, but there are two propyl alcohols, four butyl alcohols, and eight amyl alcohols possible, viz., four primary, two secondary, and one tertiary. Many of these are actually known.

#### FORMULÆ OF THE AMYL ALCOHOLS.

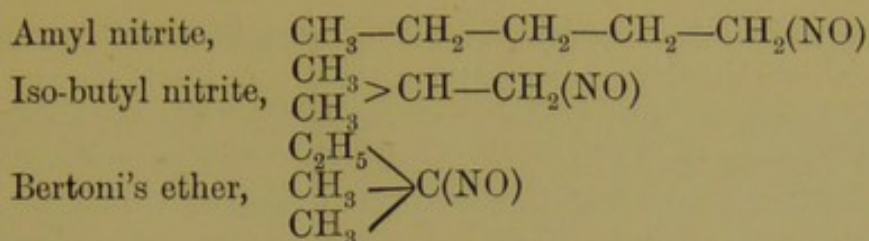


From these formulæ it will be seen that tertiary amyl alcohol is dimethyl ethyl carbinol.

The difference between the alcohols and the nitrites consists in the replacement of hydroxyl (HO) by nitroxyl (NO).

The difference between Bertoni's ether, iso-butyl nitrite, and amyl nitrite will be evident from the following formulæ :—





The action of tertiary amyl nitrite was investigated by Bertoni himself, and also more thoroughly by Balp and Broglio. According to these, it is much more stable and less disagreeable to take than ordinary amyl nitrite. While it can replace the latter in the treatment of other affections, it is said to be especially useful in asthma and in cardiac diseases with imperfect compensation, when digitalis, caffeine, and other cardiac tonics fail. It is said also not to cause the flushing of the face

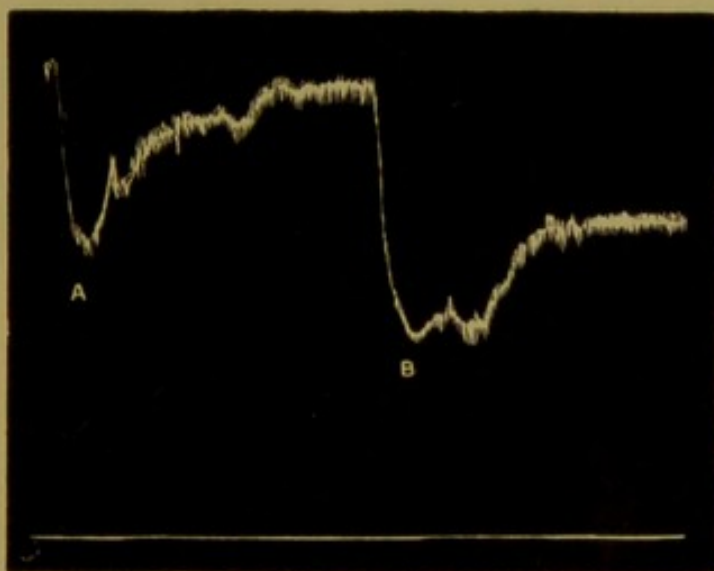


FIG. 1.

and the feeling of heat produced by ordinary amyl nitrite, but to encourage quiet sleep.

Dunstan, Woolley, and Williams showed that ordinary amyl nitrite of commerce is a mixture of nitrites, especially of *a* and *β* amyl nitrites, iso-butyl nitrite, ethyl nitrite, and propyl nitrite. These bodies having been isolated by Professor Dunstan, their physiological action was investigated, in some instances by Professor Cash, and in others by ourselves. We found<sup>1</sup> that the commercial amyl nitrite had distinctly greater power to lower blood-pressure than a mixture of *a* and *β* amyl nitrites (*vide* Fig. 1, in which A represents the action of *a* and *β*, amyl nitrites, and B that of commercial amyl nitrite on the carotid blood-pressure of a rabbit). The specimen of amyl nitrite used

<sup>1</sup> Pharmaceutical Journal, December 22, 1888.

in these experiments was shown by Professor Dunstan to contain a considerable quantity of iso-butyl nitrite, and Cash showed that this body was more active than amyl nitrite. The same fact is shown by Figs. 2 and 3, which are taken from experiments of our own. The greater action of commercial amyl nitrite, as compared with that of pure  $\alpha$  and  $\beta$  amyl nitrites, was therefore in all probability due to the iso-butyl nitrite contained in the former.

Comparative experiments made upon rabbits, anaesthetised by



FIG. 2.

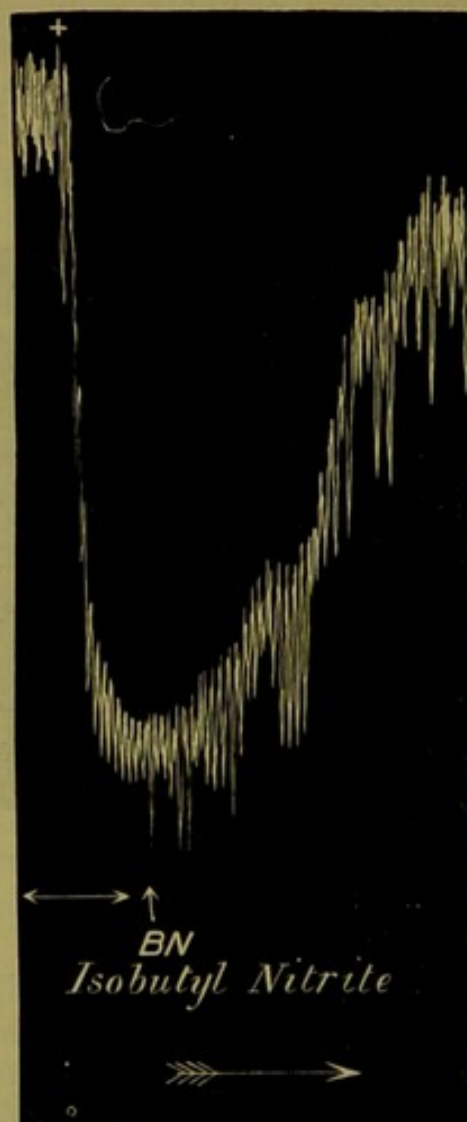


FIG. 3.

ether and then made to inhale the vapours of amyl nitrite or Berton's ether, showed that the fall of pressure with the latter was less rapid, and its recovery was also less rapid, than in the case of ordinary amyl nitrite. This will be seen by comparison of Figs. 4 and 5.

The two preparations were also tried on some cases in the wards of the Hospital; but while in one case Berton's ether



seemed to be distinctly preferred, in another there was hardly

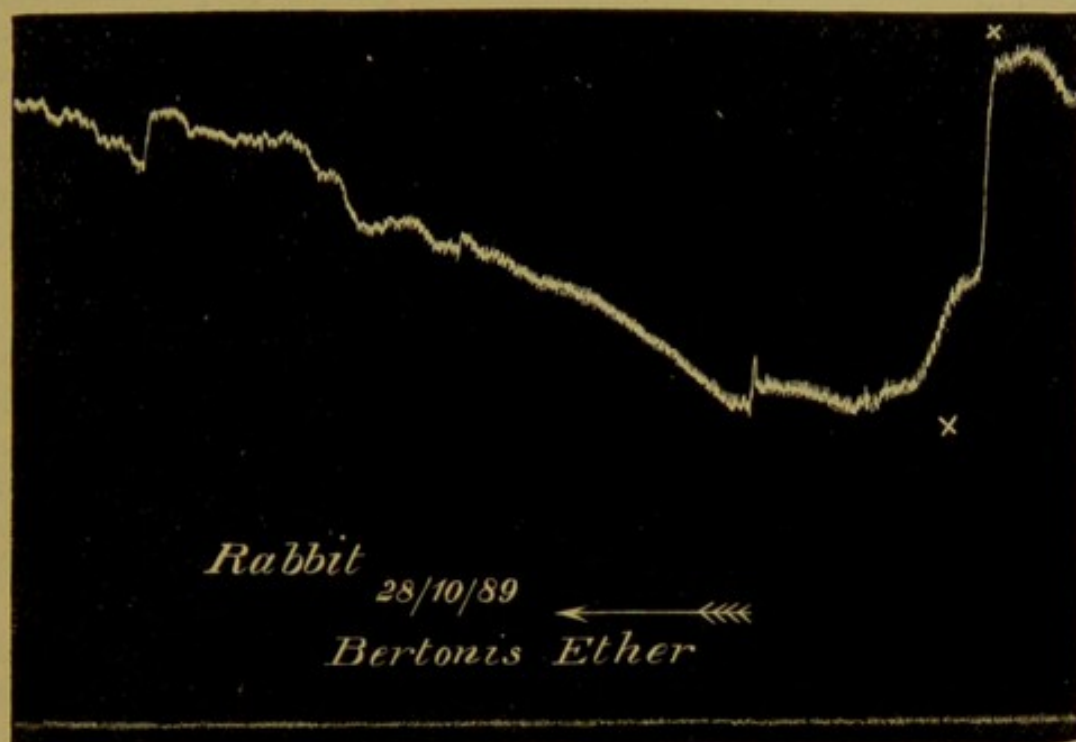


FIG. 4.

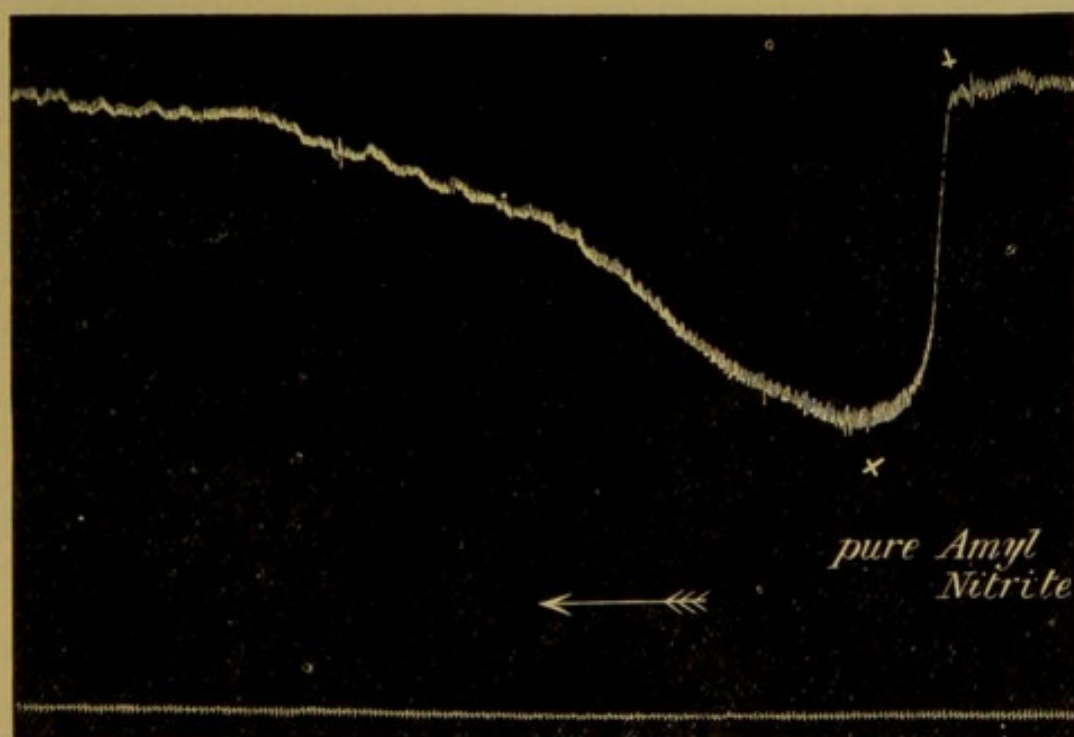


FIG. 5.

an appreciable difference in the action of this substance as compared with that of ordinary amyl nitrite.



CASE I.—C. G., aged 33, had rheumatic fever twenty months ago. Has had shortness of breath since, palpitation, and inability to do any work. Cannot use left arm; any exertion brings on pain in the heart. Orthopnoea at night for one year.

Has attacks of pain accompanied by sweating, chiefly at night. Pain is relieved by pharmacopœial amyl nitrite. The pulse is increased in rapidity during the attacks. Average is 96; during the attacks about 120.

Heart dulness extended to left.

Apex-beat is in sixth interspace,  $1\frac{1}{4}$  inches outside nipple-line.

A double murmur is heard at the right base, and is audible all over the cardiac area. There is a systolic murmur at the apex of a different character from that propagated from the right base. Second sound is accentuated at the left base.

Had amyl nitrite nearly every night for three months, and was uniformly relieved.

On May 12 had a very severe attack, which was not relieved by tertiary amyl nitrite. He was sick very soon after the inhalation.

May 13.—Had a moderately bad attack at 4 A.M., which was relieved by tertiary amyl nitrite; but he says it made him feel sick.

CASE II.—P. O'D., been ill four years or so. In January last lost his voice all at once; has had cough ever since. Difficulty in swallowing for one month, which has disappeared since admission. Never had syphilis. Great impairment of percussion on right side of chest in front; pulsation felt at second and third right interspaces.

Systolic and diastolic murmurs heard all over area of impaired resonance.

Heart's apex-beat not felt. By percussion it is found to be in sixth interspace, half an inch outside nipple. Systolic and diastolic murmurs heard faintly over whole cardiac area, louder at base. Paralysis of left vocal cord, which remains adducted. He snores slightly. Has almost incessant cough and dyspnoea, *which have been relieved by pharmacopœial amyl nitrite.*

June 5.—Cough was relieved by Bertoni's nitrite, and he had no discomfort.

June 10.—Cough ceased after taking Bertoni's nitrite. He says it relieved him more than the capsules of amyl nitrite.

June 11.—Had Bertoni's nitrite; says it relieved him much more than the pharmacopœial nitrite. He says that it made him sweat.



June 12.—Cough ceased again on inhalation of tertiary amyl nitrite.

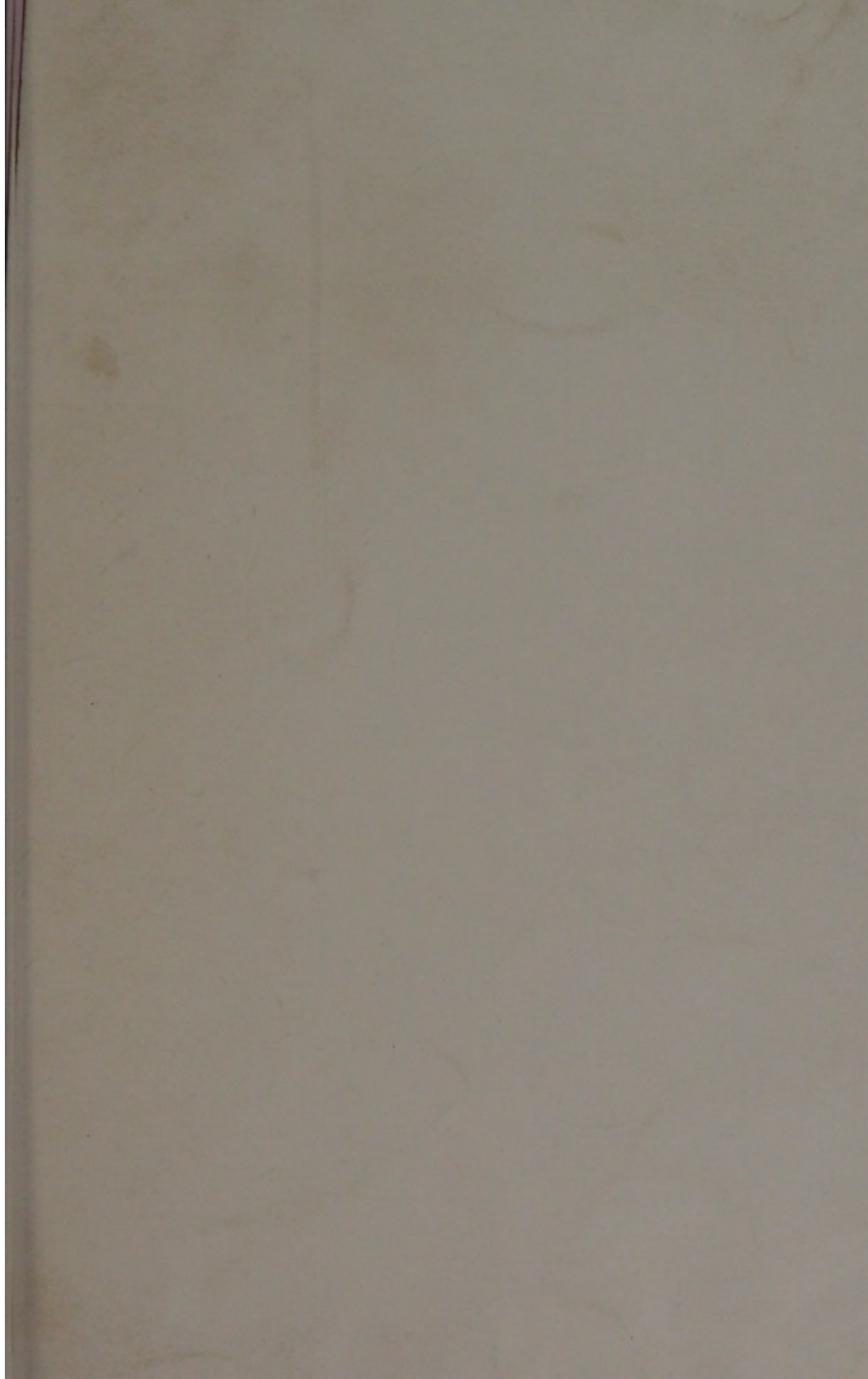
June 17.—Has had Bertoni's nitrite every morning; has had a fair night's sleep after it. It lessens the cough for a time, and so enables him to fall asleep. It has never made him sick, and he has only stated that it made him sweat on one occasion. He says that it makes his head throb more than the pharmacopœial preparation.

This patient died a short time afterwards, and the *post-mortem* examination showed that the trouble had been due to an extensive aneurysm.

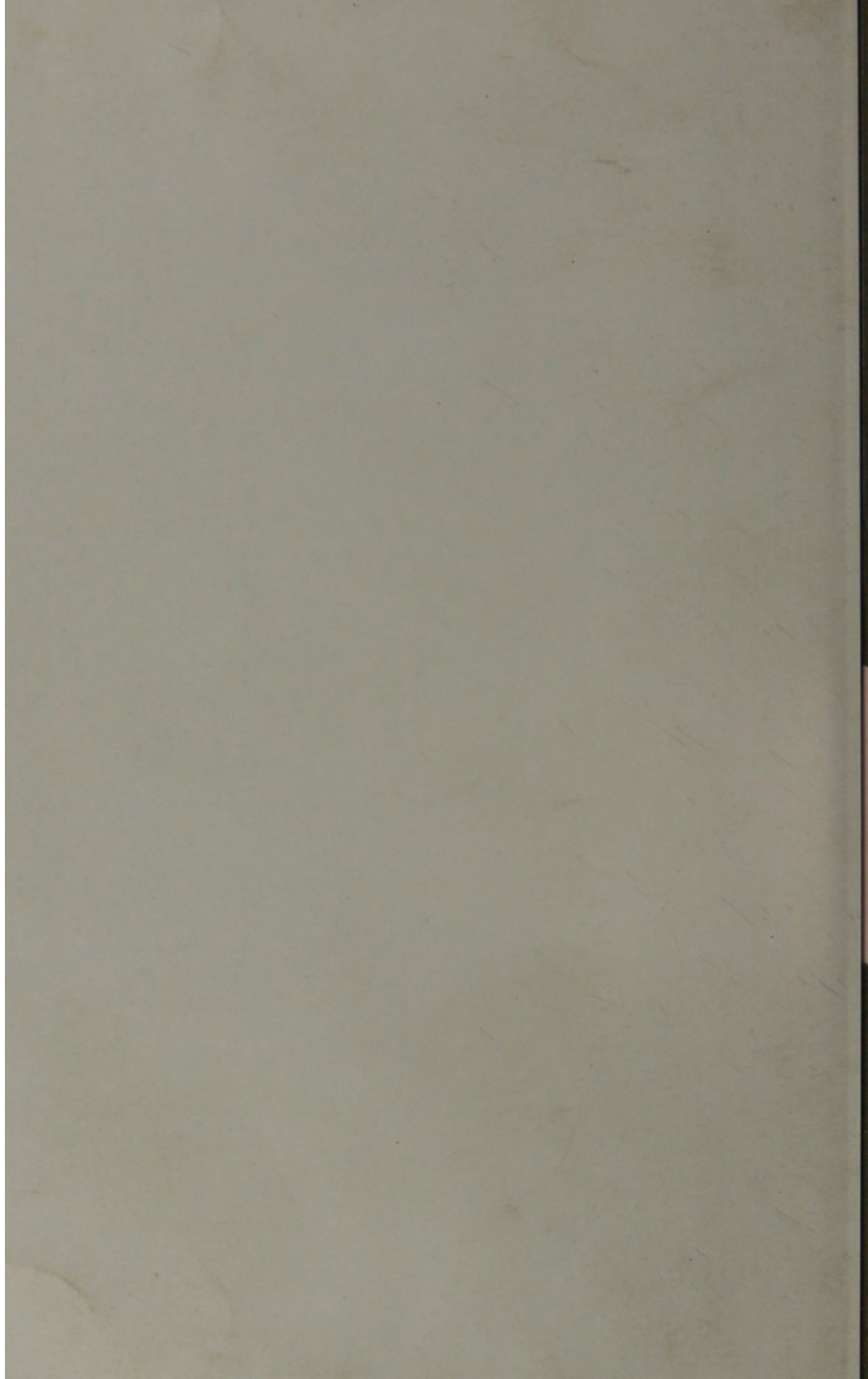
The high price of Bertoni's ether tends greatly to interfere with its general application. As regards its stability, also, Dunstan finds that it does not possess any advantage over ordinary amyl nitrite, but, on the contrary, is less stable.











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