

Graduation Thesis.

Results of a Series of Experiments  
with Nitrites in cases of Asthmatic  
Dyspnoea: (from nearly 300 trials).

W. Sowers Scott.

M.B. C. M.

Fallowfield  
Manchester

April 1889.

i

Result of a Series of Experiments with  
Nitrites in cases of Asthma.  
From nearly 300 Trials.

In 1885 I had the pleasure of assisting Professor Fraser in trying the effects of various nitrites on cases of Bronchitic Asthma in the wards of the Royal Infirmary. Both at that time & since, during the past four years I have continued to collect cases & now present the results arrived at. No merit of originality either in object or method of investigation can be claimed for myself, both are due to Professor Fraser: I have merely endeavoured to enforce from knowledge gained from an extended number of cases the fact he has already stated, that in Nitrites we have a most invaluable means of relieving the distressing symptoms of the Asthmatic Paroxysm.

First I must be allowed to express my indebtedness & thanks to several friends who have sent or allowed me to see cases for suitable for trying the effect of these drugs. The larger proportion have occurred either in out-door dispensary work or in private practice: comparatively few in hospital. For this reason it has

has been an investigation costing a great deal of indirect trouble: a great amount of care & tact being needed in carrying on, outside the walls of an hospital, a series of clinical experiments requiring frequent & minutely notes of the patient's physical condition. Notes had to be taken anywhere & anyhow on the best available pretence. Where the patient took an intelligent interest in his own case, & could be taken into confidence, the work was quite easy: & in one instance especially that of Mr H. Mackay, whose own case is a most typical one, I have received much assistance & several valuable suggestions.

Working single handed it has been impossible to obtain sphygmographic observations of the alteration in the pulse following the exhibition of acetate, in more than a small proportion of cases.

The main broad conclusion come to is that: In any cases where there is dyspnoea more or less paroxysmal in character, whether accompanied by true bronchitis or not, but resulting, apparently

from some contraction of the bronchioles, much ~~in~~ immediate relief may be obtained from the administration of nitrites in any form. Nitroglycerine: Amyl: Ethyl: or Sodium Nitrite.

Secondly that for purposes of general practice Sodium Nitrite has distinct advantages over the other forms.

In forming these two main conclusions no case has been taken into account, except those in which at least two observations were made.

By an observation is to be understood:

(1) A personal administration of the drug.

(2) Note of result of auscultation before  
after

with note of time of

A. Comparative

B. Complete

disappearance of rhonchi & sibili

3. Note of duration of relief.

These were ~~in~~ invariable points but in the large majority of cases: it was possible to go further into details when notes were taken of. Pulse rate: Respiration: + duration of time of freedom from Rhonchi + Sibili.

Of such observations, <sup>there</sup> have been obtained  $\bar{IV}$

291. in the past four years: from  
98. patients.

It was hoped that from such an extended series of cases very definite results might be obtained & tables drawn up: showing such facts as: -

The time taken in obtaining the effect from each drug.

The modifying influence of age: sex duration of complaint.

The varying effect due to the varying cause of dyspnoea. local or distant.

But a much larger number of cases must be examined: hardly any two cases in this record are alike: they differ so completely that any attempt to draw up tables of results would end in most errant conclusions.

I can only therefore present details as to the number of experiments & state what broad general conclusions I have drawn personally.

# Details of Experiments

V#

Cases. 98      Experiments 291.

In 33 cases 2 observations were made. = 66

44	"	3	"	"	"	132
14	"	4	"	"	"	56
6	"	5	"	"	"	30
<u>1</u>	"	<u>7</u>	"	"	"	<u>7</u>
98						291.

## Table of Ages.

Under. 13	were	3.	(all girls)
From 15 to 25	"	0	
" 25 .. 35	"	11	
" 35 .. 45	"	19	(10 women)
" 45 .. 55	"	27	
" 55 .. 65	"	23	
" 65 .. 75	"	15	

## Sexes

Males	60
Females	<u>38</u>
Total	98.

It would have been expected that the proportion of women would have been greater as for over 14 months I was Resident

at a hospital for Women with a largely attended out-patient department where any asthmatic cases were retained for me.

Table IV.

Number of times each Drug has been used

Nitrite of Ethyl	was used	5 times
" Amyl	" "	27.
" Sodium	" "	173
Nitroglycerin	" "	86
		<hr/>
		291

The Ethyl Nitrite was quickly given up: the solution in Alcohol employed broke down very quickly on addition of water: & the object of the investigation being to decide which Drug was most suitable for general use: such a fault excluded the Ethyl Nitrite at once. Hence it is much to be regretted that Professor Leech. (Manchester Medical Chronicle Dec. 1888) has advocated the use of Ethyl Nitrite & proposed its addition to the official Pharmacopoeia. Following his advice two firms of Chemists have brought out & are perly advertising, preparations of the Ethyl Nitrite: solutions in Alcohol & Glycerine. As these break

down when added to mixtures containing water no surer means could have been taken to discredit the beneficial effects of nitrites.

### Amyl Nitrite

This was used with excellent results, given by the mouth in a little water. The relief was prompt & the ~~oppression~~ dyspnoea remained in abeyance for nearly as long a time as when Nitroglycerin or Sodium Nitrite were given. Owing to its being sometimes the only form of nitrite available it was given more frequently than the ethyl: for with ethyl it shares the fault of not combining well with mixtures. Also the amount of vascular disturbance is greater.

### Nitroglycerin

In commencing this series of experiments in 1885 it was intended to use mainly the 2<sup>o</sup> solution of nitroglycerin. In Professor Fraser's cases it was giving the most favourable results as to quickness, completeness & duration of relief.

Later it has been almost entirely given up in favour of the Sodium Salt. The tendency to produce headache is decidedly less with the latter: a most important point.

from the view of the private practitioner  
Patients who have had both the solution  
of nitroglycerin & the Sodium Nitrite  
can tell in about two minutes that  
nitroglycerin has been given, they  
usually point to the vertex as the  
seat of headache.

Sodium Nitrite

From the preceding table it will have  
been seen that in by far the majority of  
cases this form of administration of  
Nitrite has been preferred. A solution  
in water 1 grain to the drachm flavoured  
with a little Syrup of orange has been  
used for experimental purposes: but  
the salt can be added to the cough  
mixture usually given whenever  
there is any dyspnoic tendency.

In writing the salt the Nitrite should  
be very clearly indicated, as not being  
a drug in which request it is unknown  
& the more common Nitrate substituted.

The usual dose given is 1 to 2 grains  
for an adult. Dr. Atkinson. (Jour. of  
Anatomy & Physiology 1888) states that  
he has himself taken 3 grains without  
any further disagreeable effect than  
mere faintness. So far I have

met with no uncomfortable result following the use, even the prolonged use, of sodium nitrite. Occasionally a slight feeling of nausea is complained of but no syncope has ever been seen.

Strangely enough the only cases in which headache has followed the administration of a two-grain dose of sodium nitrite, have been three patients suffering from dysmenorrhoea to whom the drug was given with the vague empirical hope that if the cause of dysmenorrhoea were spasm the nitrite might relax the contracting involuntary fibres.

In what cases have nitrites failed to relieve dyspnoea?

First it should be again stated that in 3/4 of the cases there has been full & complete relief (for the time being) & in some of the other 1/4 some degree of relief.

1) They have partially failed in 8 or 9 cases where there has been more or less pneumonia.

2). In a few cases of very longstanding  
Bronchitis complicated with parox-  
ysms of dyspnoea, the relief has been  
but slight.

X.

3. There was a sudden failure twice  
in the same case. No. 79. The Sodium  
Nitrite was being given to a patient  
suffering from typical Bronchitic Asthma.  
He kept the medicine by him to  
treat any sudden attacks usually  
with complete success: on the two  
occasions where it failed a full  
dose  $1\frac{1}{2}$  Drachms of Tr. Camphorae  
Compositae had been taken before  
going to bed. The Solution of Sodium  
Nitrite was tested both times but gave  
quite satisfactory results. So the failure  
is unexplained except on the theory  
that the opium acted antagonistically  
to the Nitrite.

4. The most curious series of  
complete failure has been in the  
cases of three children, all girls, under  
13 who were in my charge at the Clinical  
Hospital Manchester. And here I would  
note that these were the only three cases  
of Asthma occurring in children

that I was able to find in so large a number of children as 4,576 the total number of new cases seen in the out-patient department of the Clinical Hospital during my term of office. 86-87. This number includes 527 cases of bronchitis. Dr. H. Salter states that one tenth of his cases began in early life before the tenth year: possibly his experience lay among a more highly developed, nervous, class of children. possibly difference in locality may have some effect.

All these three cases, to which I wish to call special attention & the experiments on which I propose to state in detail, were typical cases of Bronchitic Asthma by which I wish to understand asthmatic paroxysms starting from local lung irritation. ~~It~~ In two there was a history of asthmatic attacks on the father's side in the third case no history could be obtained. Nitroglycerin, Amyl Nitrite, Sodium Nitrite were tried in turn on each case, & while a certain amount of vascular change was produced the dyspnoea persisted & rhonchi & sibili went on unchanged in extent or pitch.

Case 37. Clinical Hospital

7. aet. 11. girl. (Ward C).

Fairly well developed child.

Family history: Father's brother has suffered from attacks of asthma for many years. Patient has had these "fits of breathlessness" for about 9 months: they began with a cold.

Physical examination Temp. 99.

Chest: slightly pigeon-breasted: no nodes. Percussion note slightly hyper-resonant especially over the first three interspaces. Lower borders of lungs posteriorly, lower than normal. No dullness anywhere. Faint rhonchi & sibili generally audible over the chest: cough slight, no sputum. Heart normal except for a commencing reduplication of the 2<sup>nd</sup> sound.

June 3<sup>rd</sup>

Exp. i. Sodium. Nitrate

10.55. A.M. Called to see patient in an attack: orthopnoea: rhonchi audible at bedside: very loud snoring rhonchi over 3<sup>rd</sup> right intercostal space

11.5'. 1 gm. Sodii Nitriti in 1 Ounce of water

11.6'. Respiration 33 pulse 102

11.7.15". No change: no flushing

11.7.40". Sphygmogram. resp. 34. p. 100

11.8.30". Sound unaltered.

11.10'. Sphygmogram. resp. 33. p. 96.

- 11.11. No relief from dyspnoea: sounds the same.
- 11.13.30. No change. resp. 36. pulse 90(?)
- 11.14. Sphygmogram.
- 11.15. As there was no improvement a second dose of 7 gm. Sodium bitrite was given.
- 11.17.50. No change in sounds.
- 11.18. Sphygmogram resp. 36. pulse 84
- 11.20.10. No relief: patient much distressed
- 11.24.35. Sphygmogram. resp. 34. p. 82.
- 11.26.35. Rhonchi softer: not quite so prolonged
- 11.28. Rhonchi as harsh + prolonged as before
- 11.30. Sphygmogram. resp. 34. p. 80
- 11.34. Sounds unchanged.
- 11.42. No change resp. 33. p. 82.
- 11.45. Sphygmogram " " "
- 11.52. No change " " "
12. 3. p.m. Rhonchi + sibilii appear to have undergone no change: patient is propped up in bed. resp. 36 p. 82.
- 12.13. No marked change.
- 12.30. Sounds unchanged. resp. 36. p. ~~80~~<sup>86</sup>
1. 14. Attack is gradually passing off

Not to go too much into detail it may suffice to state during this patient's (No 37) stay in hospital solutions of bitrite, glycerin + Amyl bitrite were tried with the same absence of relief to dyspnoea, but with more marked vascular disturbance.

A.S. Girl aet. 10 $\frac{1}{2}$ .

No family history could be obtained.

Physical examination. Child is thin, has a frightened nervous look: dates her "tightness of breath" from a fright but on questioning there was an undoubted attack of bronchitis at the same time. (8 months since)

Chest: Chest walls are thin, interspaces wide not more resonance than would be accountable for by thinness of walls. No distinct rhonchi but expiration is harsh & prolonged. No moist sounds.

Child was several days in hospital before I was able to see her in a paroxysm: she had slight attacks of breathlessness when sibilic were found unfortunately I was unable to leave routine work to test the effect of drugs.

Aug 23.

1.0. A.M. while making night round found A.S. sitting up in bed: woke with a fit of coughing no apertures. Breathing rapid 40. On auscultation found student sibilic all over the chest from apex to base. From previous failure with case 37. I decided to give a full dose 2 minims 2% sol. of nitroglycerin & watch effects.

Case 39 (c<sup>trud</sup>). Exp. I. Whoopycarin  $\text{mg} \frac{1}{11}$  2% Sol.

- 1.10. A.M. administered Drug. Sp. 104. resp. 38
- 1.11.40. Sounds: loud strident sibili
- 1.12. Sphygmogram Sp. 104. resp. 40.
- 1.14.10. No change in sibili an occasional  
shouchus is heard with expiration over  
left side.
- 1.14.50. Patient complains of sense of fulness  
of head: places hand on vertex.
- 1.17.0. Sphygmogram. Sp. 98. resp. 38-40  
pulse is somewhat improved in character.
- 1.19.30. Sibili not quite so harsh: shouchus  
lost.
- 1.23. Sphygmogram. Sp. 96. resp. 36.
- 1.24.30. Sounds unchanged from first  
state: shouchus again audible.
- 1.27. No change. Sp. 96. resp. 38.
- 1.30. Patient quite unable to lie down.  
lips are dusky in tint, but  
not pale: more flushed than  
at 1.0. A.M.
- 1.33. No change in sounds.
- 1.33.50. Sphygmogram. Sp. ~~9~~ 92: 2.38
- 1.40. No alteration in character of  
sounds.
- 1.50. Sounds unchanged. Sp. 92. resp. 36-38
- 2.0. A.M. No change.

Case 39. contd

- 2.20. A.M. state much the same patient appears a little easier.
- 2.35. No rhonchus: sibili not so sharp.
- 4.0. A.M. patient was decidedly better. went to sleep.
- 8.30. A.M. Still fairly abundant ~~rhonch~~ sibili.

Sodium bitartrate: Amyl bitartrate also tried.

Case 40 Clinical Hospital.

M.D. Oct. 13. girl.

Family history: Father (dead) is said to have had asthma.

Child is well-nourished: chest barrel-shaped. interspaces well marked: has always suffered more or less frequently from bronchitis & never had any dyspnoea till last winter since then they have been growing worse.

During attacks this patient also was treated with Sodii bitartris. 1 + 2 grms. Nitroglycerin. 2 mg 2% sol. + Amyl bitartris by the mouth & by inhalation. with the same results as in the former two cases.

I do not wish to draw any conclusions from these three cases: they may be merely coincidences. Indeed the whole thesis must be regarded as an interim report: the investigation is merely beginning. The varieties of cause of asthma have not been touched upon & there are many side issues which require many more observations to render at all complete or fit for any scientific report.

I would just notice that some of the most successful results have been obtained in cases of asthmatic dyspnoea coming on during the menopause. Here the relief is very quick & complete: the dyspnoea vanishes at once & completely. In these cases I think one must conclude that the cause of dyspnoea, is not local, not seated in the respiratory system but due to certain uterine conditions.

In these cases rhonchi or sibili were infrequent or absent.

W. Sawers Scott.

Fallowfield  
Manchester.