Graduation Thesis.

Results of a Series of Experiments with Lead in Cases of Asthmatic Dyspnoea, (from nearly 300 Trials).

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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 Bronchial 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 enquire 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 symp.

Toms 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 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 & minute notes of the patient's physical condition. Notes had to be taken anywhere & anyhow on the best available paper. Where the patient took an intelligent interest in his own case, it 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 alternation in the pulse following the exhibition of narcotics 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 bronchial tubes, much immediate relief may be obtained from the administration of nitrites in any form. Nitroglycerine, ashyl, Pithyl, or Soda-hydrate Nitrite.

Secrecy that for purposes of general practice, Soda-hydrate 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 one observation is here understood:
1. A personal administration of the drug.
2. Notes of result of auscultation before and after

with notes of time of:
A. Comparative
B. Complete disappearance of chests shibibi
3. Notes of duration of relief.

These were 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 chests shibibi
Of such observations have been obtained 11

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 and 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 dyspepsia: local or distant.

But a much larger number of cases must be examined: hardly any two cases in this series 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 I have drawn personally.
Details of Experiments

Cases. 98  
Experiments 291.

In 33 cases 2 observations were made = 66

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<tbody>
<tr>
<td>44</td>
<td>3</td>
<td></td>
<td>13.2</td>
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<td>14</td>
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<tr>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>98</td>
<td></td>
<td></td>
<td>291</td>
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</table>

Table of Ages

<table>
<thead>
<tr>
<th>Under</th>
<th>13</th>
<th>were</th>
<th>3. (all girls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>From 15 to 25</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>35</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>45</td>
<td>19</td>
<td>(10 women)</td>
</tr>
<tr>
<td>45</td>
<td>55</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>55</td>
<td>65</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>6.5</td>
<td>7.5</td>
<td>15</td>
<td></td>
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</table>

Sextes

<table>
<thead>
<tr>
<th>Males</th>
<th>60</th>
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<tbody>
<tr>
<td>Females</td>
<td>38</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrite of Ethyl</td>
<td>6</td>
</tr>
<tr>
<td>Amyl</td>
<td>27</td>
</tr>
<tr>
<td>Sodium</td>
<td>193</td>
</tr>
<tr>
<td>Nitroglycerine</td>
<td>86</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>291</strong></td>
</tr>
</tbody>
</table>

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 Leach (Massachusetts Medical Chronicle Dec. 1888) has advocated the use of Ethyl nitrite; he proposed its addition to the official Pharmacopoeia. Following his advice two firms of Chemists have brought out two purely advertising preparations of the Ethyl nitrite solutions in alcohol & glycerine. As these break
down when added to mixtures containing water as pure 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 and the dip noxoa remained in abeyance for nearly as long a time as when Nitroglycerine 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.

Nitroglycerine

In commencing this series of experiments with it was intended to use mainly the 2 % solution of Nitroglycerine. 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 decided less with the latter: a most important point.
from the view of the private practitioner.

Patients who have had both the solution of nitroglycerin and 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 of the Sodium flavoured with a little syrup of oranges has been used for experimental purposes; but the salt can be added to the cough mixture usually given whenever there is any dysphonic tendency.

In using the salt the nitrite should be very clearly indicated, as not being a drug in which request it is unknown at the more common nitrite substituted.

The usual dose given is 1 to 2 grains for an adult. Dr. Atkinson (Jour. Anatomy & Physiology 1889) states that he has himself taken 8 grains without any further disagreeable effect than more painness. So far I have
met with no uncomfortable result following the use, even the prolongation of sodium nitrite. Occasionally a slight feeling of lassitude is complained of but the symptomatics have ever been seen.

Strongly 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 dyspnœoœa but to whom the drop was given with the vague empirical hopes that if the cause of dyspnœoœa were spasm the nitrite might relax the contracting involuntary fibres.

In what cases have nitrites failed to relieve dyspnœoœa?

First it should be again stated that in 3/4 of the cases there has been full or 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 stubborn 
bronchitis complicated with parox 
ysms of dyspnoea, the relief has been 
but slight.

3. There was a sudden failure twice 
in the same case. No. 79. The Sodium 
Hithati was being given to a patient 
suffering from typical bronchitic asthma. 
It kept the medicine by him to 
treat any sudden attacks usually 
with complete success; on the two 
occaasions where it failed a full 
dose 1/2 drachms of Dr. Camphors 
Composition had been taken before 
going to bed. The Solution of Sodium 
Hithati was tested both times but gave 
quite unsatisfactory results. So the failure 
is very plain in except on the theory 
that the opium acted antagonistically 
to the Hithati.

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 
not 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 at 11, 676 the total number of new cases seen in the outpatient department of the Clinical Hospital during my term of office 86-87 this number includes 6-27 cases of bronchitis. Dr. H. Salter states that one tenth of his cases began in early life before the fifth year possibly his experience has 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 especial 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. In two there was a history of asthmatic attacks on the fathers side in the third case no history could be obtained. Hydrocyanic Acid, Nitric Acid, Sodium Bichlorate were tried in turn on each case, while a certain amount of vascular change was produced the dyspnoea persisted & cough & sibilis went on unchanged.
Case 37.  
7. act. 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. Inverted as usual. percussion note slightly hyper-resonant especially over the first three intercostales. Lower borders of lungs posteriorly, lower than normal. No dulness anywhere.
Posteriorly generally audible over the chest: cough slight, no expectoration.
Heart normal except for a commencing diapophysis of the 2nd sound.

June 25
2p.m. 1p.m. Sodium. bitartrate
10.57 a.m. Called to see patient in an attack: orthopnea; shorchi audible at 2nd rib: very loud sunning sound over 2nd right intercostal space.

11.5. 1p.m. Sodium bitartrate in 1 dash of water.
11.51. Respiration 38 Pulses 102
11.7.40. Sphygmomanometer resp. 34 p. 100
11.8. 30. Sound unaltered.
11.10. Sphygmomanometer resp. 33 p. 90.
11.11. No relief from dyspnoea. Sound the same.

11.30. No change. Resp. 36. Pulse 90. (2)

11.45. Sphygmoscopic.

11.15. As there was no improvement a second dose of 7 gm. sodii bicarbonatus was given.

11.50. No change in sound.

11.50. Sphygmoscopic resp. 36. Pulse 84.


11.40. Resp. 34. P. 82.

11.35. Rhonchi softer. Not quite as prolonged.

11.28. Rhonchi as harsh + prolonged as tym.


11.34. Sound unchanged.

11.42. No change. Resp. 33. P. 82.

11.45. Sphygmoscopic.

11.52. No change.


12.13. No marked change.


Not to go too much into detail it was
suffice to state during this patients' stay in hospital solutions of nitro glycerine & arsenic bitartrate were tried with the same absence of relief to dyspnoea, but with more marked nervous disturbance.
Case 39. Clinical Hospital

23. Girl aged 10½.
No family history could be obtained.
Physical examination. Child is thin, has a frightened nervous look, states her "frightness of health" from a right but
in questioning there was an undoubted
attack of whooping-cough at the same time (8 months since).
Chest: Chest walls are thin, intercostal spaces wide
not more resonance than would be accounted
able for by thinness of walls. No distinct shooch,
but expiration is harsh, prolonged, low sound.

Child was several days in hospital before
I was able to see her in a paroxysm. She
had slight attacks of breathlessness when
sibils were found. Unfortunately, I was
unable to leave routine work to test the
effect of drugs
Aug 23.
10 A.M. while making night round found
23, sitting up in bed, coughing with a fit of coughing
constantly. Breathing rapid 24. Temperature
found sibilant. Sibilant sibilis 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
sodium cyanide & watch effects.
Case 39 (Cont.). Exp. 7. Mephytane my 11 20% sol.

1.10. A.M. administered Supp. p. 104. exp. 28
1.11.10. Sounds: loud, short, indistinct
1.14.10. No change in sibilis or occasional
sounds is heard with expiration on
left side.
1.14.10. Patient complains of sense of fulness
of head: places hand on vertex.
1.17.0. Sphygmogram, p. 98. exp. 38
pulsa inconsonant improved in character.
1.19.30. Sibilis not quite so harsh: sounds
lost.
1.23. Sphygmogram, p. 96. exp. 36.
1.24.30. Sounds unchanged from first
state: sounds again audible.
1.27. No change, p. 96. exp. 38.
1.30. Patient quite unable to lie down.
Lips are distinctly ni lent but
not pale; more flushed than
at 1.00 a.m.
1.33. No change in sound.
1.33.30. Sphygmogram, p. 97, exp. 38
1.40. No alteration in character of
sound.
1.50. Sound unchanged. Supp 2, exp. 36-38
2.0. A.M. No change.
Case 39.
10.30 A.m.
Patient not much the same.
2.35 Pm. Sibilant sibilis not as sharp.
4.00 A.M. Patient was decidedly better. Went to sleep.
8.30 A.M. Still fairly abundant sibilant sibilis.

Sodium nitrite: Amyl nitrite also tried.

Case 40
Clinical Hospital.

Mrs. age 13, girl.

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

Child is well nourished; chest barrel-shaped, intercurrences well marked, has always suffered more or less frequently from bronchitis. Never had any chest trouble till last winter since then they have been growing worse.

During attacks this patient also was treated with Soda nitrites 1/2 grns. Amyl nitrite, 2 to 20% sol. & Amyl nitrite 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 various causes 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 and complete; the dyspnoea vanishes at once and 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 ahunching sibilis were infrequent or absent.

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