The one real failure was in an officer who gets very heavy colds, with symptoms such as blocked nasal passages, together with a sore throat, on waking. Examination revealed a subfebrile temperature, slight faucial inflammation and acute rhinitis. Treatment consisted of 1:10,000 patulin every 4 hours during the day, and 24 hours after beginning treatment the patient reported that he was completely free of symptoms in 24 hours after treatment. As a sufferer from colds he was convinced that his cold would have dragged on for a week or longer had he not been treated.

CASE 3.—A man, who reported with a "streaming cold" of one day's duration. The predominating symptoms were malaise, headache, profuse nasal discharge and sore throat. Treatment consisted of 1:10,000 patulin every 4 hours during the day, and 24 hours after beginning treatment the patient reported that he was completely free of symptoms in 24 hours after treatment. Included among these was a girl motor-transport driver who was given a trial in the treatment of common colds. She woke up on Feb. 4 quite well.

The first bottle of the substance was provided for my office staff and myself to try. The results were so successful that other officers asked to be allowed to use it, and have sent their ratings for treatment. As far as possible we have used it, as instructed, before a cold has lasted more than 24 hours.

The lethal dose for mice is about 0.5 mg. per 20 g. body-weight, whether the substance is given intravenously or subcutaneously. Solutions of the substance were sprayed into the nose or snuffed up from the hand.

The results obtained were encouraging, 57% of the treated cases recovering completely within 48 hours, compared with only 9.4% of the controls.

My thanks are due to Professor Raistrick for supplies of patulin; to the Royal Naval authorities, both executive and medical, at the depot where the trials were carried out for their cooperation; to Surgeon Lieut.-Commander H. W. Clegg for his help in the animal toxicity tests; and to SBPO Geoffrey Smith, who assisted me both in the bacteriological work and clinical trials.

I wish to thank Surgeon Rear-Admiral C. F. O. Sankey for permission to publish this paper.

REFERENCES


V.—Statistical Note

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The purely statistical question which arises in Commander Hopkins's work is a simple one—assuming that the treated and control populations do not differ in any material way, except in regard to the fact of treatment, and that the treatment is equally effective in both the treated and control groups, then the respective percentages of cures would be the same. If two batches of penicillin are tested, the respective percentages of "heads" are likely to differ from 50:50 only because of the particular difference or a greater difference, would occur can be readily calculated. The principle involved in this stock case is fundamentally the same as in our problem, subject to a consideration I shall discuss later on.

The fundamental difference is that Hopkins in his table IV. The three sets—January, February and April—are not in pari materia and must not be aggregated. There is no reason why the proportion of cures
should be the same in different months. Common sense suggests that the chance percentages are unlikely to be "chance" happenings and it will be enough to apply an exact test to the set most favourable to the hypothesis of chance deviation—the third set. Applying such a test (see Fisher, Statistical Methods for Research Workers, pp. 84-85) it is found that in random sampling so wide a divergence in favour of the treated would occur about 3 times in 10,000 trials. It is therefore an improbable happening. In one respect, however, treated and controls are not in pari materia; the former included a larger proportion of patients with symptoms of not more than one week's duration (44.4, against 33.3). But, as the following table shows and common sense suggests, this is not probably material, unless there were a special process of selection, or self selection—viz., only patients with especially "obstinate" colds presenting themselves for treatment.

<table>
<thead>
<tr>
<th>Symptoms of cold</th>
<th>Patients Recovered</th>
<th>% recovered</th>
<th>Patients Recovered</th>
<th>% recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>70</td>
<td>41</td>
<td>53</td>
<td>18</td>
</tr>
<tr>
<td>Symptoms over one week</td>
<td>20</td>
<td>14</td>
<td>140</td>
<td>8</td>
</tr>
</tbody>
</table>

It could, of course, be tested by subtabulation, but, in view of the fact that in the first two series the proportions of treated and controls with symptoms of not more than a week's duration were virtually the same (87.0 and 85.1%), and in these series the divergence is greater, the arithmetic is needless. We may certainly say that, taken as a series, the probabilities of drawing each pair from a common universe are extremely small.

That conclusion is all that purely statistical reasoning can establish. To revert to the illustration, if an expert were made with batches of coins fresh from the mint, and their respective percentages of heads differed in such a way that, tested as these data have been tested, a probability of, say, less than 3 in 10,000 emerged that they came from a common universe, no sensible person would infer that the mint coins were biased.

He would conclude that either (1) the samples were not in pari materia (there had been some "trick in tossing), or (2) a very improbable event had happened—in this case, the probability of drawing each pair from a common universe is extremely small.

In our case there is no such a priori improbability that the antibacterial substance might accelerate a cold; that it does so is a tenable hypothesis. But, and this is the point always to be had in mind, what the statistician has shown is not that the odds are so and so many thousands to one in favour of the hypothesis that the antibacterial substance might accelerate a cold; and so many thousands to one against the chance that such results would emerge without some differentiation between the groups. Whether at other times and in groups differently chosen the same differentiation would be found can only be known when further trials have been made.

I am indebted to my colleague, Dr. W. J. Martin, who carried out the arithmetic tests.

INTERSTITIAL EMPHYSEMA AFTER EXTRACTION OF A LOWER MOLAR

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At 10.10 AM on May 22, 1943, a male postal worker, aged 49, had his lower left second molar extracted under local anaesthesia. The tooth was broken during the first attempt at extraction. A further injection of local anaesthetic was made and the roots successfully extracted, but with difficulty. The patient arrived home at 11 AM, and on looking in a mirror was shocked to find great difficulty in swallowing solid food. At 2 PM he lay down to sleep but had to sit up because of respiratory embarrassment.

He was seen at 6 PM. At this time the upper line of demarcation was at the base of the mouth, and there was a large area of interstitial emphysema below the left molar bone, at which point the swelling stood out for about \(\frac{1}{2}\) inch. From this point the swelling gradually increased as it descended to the mandible, and then decreased towards the base of the neck. The upper part of the swelling was soft and sometimes could be heard throughout the entire swelling to the base of the neck. The supra- sternum fossa was puffed out with a soft swelling in which crepitus was easily heard. There were no signs of emphysema in or around the orbit. The soft palate was pressed against the side of the mandible, and the anterior margin of the masseter muscle could be palpated when the mouth was closed. The swelling to the base of the neck and the entire swelling was soft and tender on the left side of the pharynx could be swelled to a point half way towards the middle line. There was no unusual laceration of tissues at the site of extraction, nor was there any suggestion that bleeding had been more than usual.

There was no increase in the swelling after he was seen, and in his opinion there had been little increase after he reached home. The condition took a full week to subside.

Prof. H. A. Harris suggests that there was probably a break in the soft palate, and that this resulted in air passing into the floor of the mouth or of the buccinator muscle in the vestibule of the mouth. In the former case, air may pass downwards into the loose deep fascia of the neck and upwards over the mandible anterior to the masseteric fascia and is likely to be retained there for a considerable time. In the latter case, air may pass medial to the buccinator and backwards towards the pterygomandibular raphe and the soft palate; also lateral to the buccinator in relation to the space occupied by the corpus adiposum buccae. The passage of air from neck to mouth would result in the swelling extending to the anterior margin of the masseter at the lower border of the mandible, along the loose fascia surrounding the external maxillary (facial) vein and artery.

Two cases of interstitial emphysema after maxillary molar extraction are referred to by Collyer and Sprawson (1942), one reported by Turnbull (1900), and another by Binns (1935). In Turnbull's case a bugler had bugled immediately after the dental extraction, while in Binns' case the patient had been seen at 10 AM, and he had tried to blow through a choked pipe shortly after the extraction. Two cases of emphysema after mandibular molar extraction have been reported in America. In the first, reported by Schaefer and Williams (1933), the condition was attributed to the use of compressed air irritators. In the second, reported by Hopkins (1935), the extraction was of an impacted molar and apparently required a lengthy operation. Hopkins traced the emphysema from the scalp and down to the breasts. Another case, reported in France by Hozneau (1936), followed an easy and complete extraction of a lower right third molar; no explanation was offered. A case of unilateral interstitial emphysema of the face was reported by Kirby in 1919, but this developed as the result of drying the pulp cavity of an incisor root, to which it was intended to fit a crown, with an electric pneumatic hot-air syringe. Extraction was performed after the development of the emphysema. The root was found to have a large apical foramen. Kirby does not state whether it was an upper or lower tooth. 

In the case now reported no suction or compressed air was used. The patient did not say that on the way home he kept the left side of his face covered with his hand because his jaw was aching, and that he kept his mouth closed to prevent cold air getting into his mouth. It is possible that the pressure on the chest persuading the patient to close his mouth was comforting. Thus, with the mouth kept firmly closed, air may have been driven into the vestibule to blow out the cheeks and keep pressure off the painful socket.

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