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Static electricity is a well-known risk in the operating theatre, where its sudden discharge as a spark may cause an ether explosion. It is a risk also in many industrial processes, wherever paper, plastic, rubber, or other insulating substance is passed at high speed between rollers or some other surface on which there is friction—for example, in both flat-bed and rotary printing presses, and in the rubber-coating of fabrics. A spark may fire an inflammable solvent, but apart from this the static may interfere with the manufacturing process, making sheets of paper fly apart or stick together instead of stacking evenly, and causing powders to clump and stick to surfaces. One of the commonest methods of preventing static is to ionize the neighbouring air so that it becomes electrically conducting and the charge can leak away as it is formed, and radioactive substances are used to do this, most commonly radium itself. This creates a danger to the workers, however, from possible over-exposure to alpha, beta, and gamma radiation and inhalation of radon, the radioactive gas liberated during radium decay. The *Monthly Review* of the New York State Department of Labor for November and December last discusses this as an industrial hygiene and safety problem. It advocates study of each individual instance of the use of a radioactive static eliminator to make sure that it is in the least dangerous position as judged by measuring instruments and by film badges worn by the workers. Gloves should be worn when cleaning the machine, or those parts of it containing the radioactive source. Ordinary ventilation should blow away the radon produced. Periodical medical examination, with a blood count, is also advised, and the skin of the fingers should be examined for flattening of the ridges, which is one of the signs of excessive radiation.

EFFECT OF STREPTOMYCIN ON
VESTIBULAR FUNCTION

BY

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During the early period of the use of streptomycin in pulmonary tuberculosis, when 2 g. was given daily, disturbances of vestibular function were frequent. Indeed, this threatened to limit its usefulness almost as seriously as did the emergence of bacterial drug resistance. After it had been shown that the daily dose could be halved without reducing the therapeutic effect, the importance of this toxic manifestation diminished. But evidence of vestibular dysfunction is still found in about 15% of patients being treated with the usual 1-g. dose daily, and the toxic action of streptomycin on the vestibular apparatus therefore remains of some importance to the clinician.

The following observations are based on a study of 76 patients with pulmonary tuberculosis receiving streptomycin treatment at the Brompton Hospital during the Medical Research Council clinical trials of this antibiotic.

All patients were treated for at least 12 weeks and some for as long as 32 weeks. Sixty-five were given streptomycin alone, 23 receiving 2 g. daily in doses of 0.5 g. six-hourly, 13 receiving 1 g. daily in doses of 0.25 g. six-hourly, and 19 having 1 g. daily in a single injection. Four patients received 2 g. daily in doses of 0.5 g. six-hourly during alternate weeks and 6 were given the same dosage during alternate months. Eleven patients were treated with 1 g. streptomycin daily in a single injection and from 5 to 20 g. of the sodium salt of *para*-aminosalicylic acid (P.A.S.) daily. The patients were examined at weekly intervals and more frequently if toxic symptoms were present. Tests of vestibular function were carried out in 50 patients.

Giddiness

In several patients the earliest symptom of vestibular dysfunction was a complaint of mistiness of vision. This was noticed mainly during the evening when changing quickly from near to distant vision. There might also be difficulty in reading, probably due to incoordination of eye movements. Some patients had no other evidence of toxicity, the disturbance of vision disappearing after a few days. In others it was followed by giddiness. This was only rarely a definite sense of rotation; more commonly there was merely a sense of

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instability of movement, the sensation of movement continuing after the change of posture had been completed.

The incidence of giddiness in the different dosage groups is shown in Table I. Of 23 patients having 2 g.

TABLE I.—Incidence of Giddiness in Patients Treated with Different Doses of Streptomycin for at Least 12 Weeks

Dosage	Total Patients	No. Complaining of Giddiness
2 g. daily in divided doses ..	23	14 (60.8%)
1 g. daily in divided doses ..	13	4 (30.7%)
1 g. daily in a single dose ..	30	3 (10%)
Total 1 g. daily ..	43	7 (16.2%)
2 g. daily during alternate weeks ..	4	1 (25%)
2 g. daily during alternate months ..	6	2 (33.3%)
Total patients ..	76	24

daily 14 (60%) complained of giddiness, compared with only 7 of 43 (16%) having 1 g. daily. It must be admitted that of those on 1 g. a day some were treated for three months only, whereas all those on 2 g. were treated for four months. But of 25 patients on 1 g. a day treated for four months or more only one first complained of giddiness after the end of the third month. It seems unlikely, therefore, that any considerable error has been introduced by including both those treated for three months only and those given longer courses. The numbers of patients having intermittent treatment are too small to allow of comparisons with the continuous-treatment groups.

There is a difference in incidence between those having 1 g. daily in divided doses and those having the same amount in a single daily injection. Of the 30 patients treated with 1 g. daily in a single injection only 6 were under treatment at the same period and with the same batches of streptomycin as those (13) receiving the divided doses. Two of these complained of giddiness, the incidence (33%) thus being almost the same as in the divided-dose group. The remaining 24 patients having a single daily injection were treated later. Only one (4.1%) complained of giddiness. It has been shown that the neurotoxicity of different samples of streptomycin in animals varies, the least pure having the greatest toxicity (Molitor and Kuna, 1949). It may be that the apparent difference between the two groups receiving 1 g. a day is due to increasing purity of the streptomycin batches used, and not to differences in the frequency of administration. On the other hand, it has been claimed that the changes in the vestibular nerve nuclei in cats can be observed when the streptomycin has been given in several daily doses but not when the same total dose has been given in single daily injections (Winston *et al.*, 1948). Differences in batches might also have affected the comparison between the 2-g. and 1-g. groups. As several of the patients received streptomycin from more than one batch we have not been able to allow for this possible source of error.

In those receiving 2 g. daily the mean day of onset was 22.1 (S.D.=7.3). In the patients having 1 g. daily in single or divided doses the mean day of onset was 45.4 (S.D.=24.3). The difference of the means is statistically significant ($t=2.505$, $n=21$, $P=0.02$), and the later onset of giddiness in those receiving 1 g. daily is unlikely to have been due to chance.

The giddiness was severe and disabling in only 2 patients, both of whom were treated with 2 g. daily.

Eighteen had slight giddiness, and in only 5 (27%) did it last longer than four weeks. Six had moderate or severe giddiness, and in 5 it lasted longer than four weeks.

The above observations demonstrate that the incidence of giddiness is diminished by the reduction of the daily dose of streptomycin, and that the time taken for the symptom to appear is lengthened. The length of the latent period may therefore be related to the total dose received. Slight giddiness tends to be transient, but more severe giddiness frequently lasts several weeks when treatment is continued. As no patients in this series were compelled by the severity of the giddiness to stop treatment, no data are available on the duration of giddiness if streptomycin is discontinued as soon as the symptoms appear.

Nystagmus

Nystagmus on lateral deviation of the eyes was observed during treatment in 63% of patients having 2 g. daily but only in 16% of those having 1 g. daily. It did not appear later in the 1-g. group than in the 2-g. group, nor was there any great difference in its duration. Nystagmus was detected in 8 patients (15.4%) who had no complaint of giddiness at any time during treatment. On the other hand, in 6 of the 24 with giddiness there was no nystagmus. Nystagmus therefore tended to be associated with giddiness, being present in 75% of those who complained of giddiness, as compared with about 15% of those who did not. No past pointing was noted at any time in patients complaining of giddiness either with or without nystagmus.

Caloric and Galvanic Tests

As many patients as possible were examined by one of us (J. A. B. T.) before streptomycin was begun or within the first fortnight of therapy. Further examinations were made during the treatment and in some patients after streptomycin had been discontinued. Every patient was given a full routine examination, including caloric vestibular reactions. The galvanic test was carried out when caloric reactions could no longer be elicited.

Caloric tests were performed in the manner described by Fitzgerald and Hallpike (1942), using water at 44°, 30°, and 21° C. The only modification was that the patients sat in a dental chair, which could be tilted to the required angle. The douche-can was placed on a convenient dental arm 18 in. (45 cm.) above the meatus. The galvanic test was performed by placing a flat metal electrode covered with four to six layers of lint soaked in saline over the mastoid region. This was held in place by a bandage around the head. A wooden or metal rod was placed in the bandage over the centre of the forehead and used as an indicator. The indifferent electrode was held in the hand. The current was gradually increased from zero up to 4–8 mA, when the sensitivity of the nerve elements was indicated by a lateral inclination of the head towards the anode or away from the cathode.

In cases showing vestibular disturbances the absence of response to stimulation with hot water was the earliest and most frequent change detected. Directional preponderance occurred less frequently. Occasionally a canal paresis became manifest. The pattern changes are not stressed, owing to the difficulty experienced in many cases in deciding the exact end-point of the nystagmus.

The caloric reactions are recorded as "absent" if there was no response to water at 44° and 30° C. in either ear; as "normal" if there was nystagmus lasting for a measurable period following stimulation with both hot and cold water on both sides; and as "reduced" if the reactions were neither "absent" nor "normal."

The group of patients receiving 2 g. daily was the more fully studied (Table II). Of the 17 with normal

TABLE II.—*Results of Caloric Tests During Treatment with 2 g. of Streptomycin Daily*

Weeks after Start of Treatment	No. Examined	Caloric Reactions		
		Normal	Reduced	Absent
0	17	17 (100%)	0	0
5-8	11	9 (81%)	0	2
9-12	15	7 (46%)	5	3
13-16	13	5 (38%)	4	4

caloric reactions before treatment 13 were examined during the fourth month. Only 5 still had normal reactions, in 4 they were reduced, and in 4 absent. An accurate comparison between the 2-g. and 1-g. groups was not possible owing to the lack of tests before treatment in the latter. In only 5 was it possible to follow the changes in the reactions. During the fourth month 2 of the 5 examined had normal reactions; in 2 they were reduced, and in one absent. In this very limited material there does not appear to have been such a large difference between the groups as was seen in the case of giddiness.

The galvanic test was performed when caloric reactions were absent to water at 21° C. for one minute. The test was found to be positive in all the 13 patients who had no caloric reactions.

Recovery of Vestibular Function

It was possible to re-examine 8 patients twelve or more months after streptomycin therapy had ceased. All of these patients had previously lost the caloric reactions to water at 21° C. for one minute. In 3 there was no evidence of recovery. In 4 it was possible to obtain a reaction with water at 21° C., though the reactions to water at 30° and 44° C. were still absent. No nystagmus was elicited from one patient when tested with water at 21° C. at the end of treatment, though the test caused him to complain of vertigo. When retested three months later there was no response to water at 30° and 44° C. but a normal response to water at 21° C. On testing 17 months later the caloric reactions were found to be entirely normal.

It is clear that in some patients recovery of labyrinthine function is possible even after the caloric test has shown severe depression.

Relationship between Giddiness and the Caloric Reactions

Of the 25 patients in whom caloric tests had been completed 12 had complained of giddiness. In 8 of these the caloric reactions were absent at the end of treatment, in 3 they were reduced, and in only 1 patient did they remain normal. On the other hand, of the 13 who had no giddiness, only 3 lost the caloric reactions, in 4 they were reduced, and in 6 they remained normal. Thus, while alteration of the caloric reaction was commonly associated with giddiness, there were instances in which the caloric responses were abolished although the patient had no symptoms of vestibular damage.

In 22 patients who developed giddiness a caloric test done soon after the symptoms appeared showed responses to be absent in 12, reduced in 5, and normal in 5. Later tests, however, showed that the caloric responses remained normal in only one patient, and in 15 they disappeared entirely. Thus the experience of this group suggests that, when a patient suffers from giddiness during streptomycin treatment and the drug is continued, a single caloric test soon after giddiness has appeared is as likely to show normal or merely reduced responses as it is to show absent responses. Furthermore, unless a caloric test has been done before treatment started it cannot be known with certainty whether the reduction or absence of the reaction is due to the streptomycin. In the 2-g. treatment group 20 patients had caloric tests done before treatment; the reactions were normal in 17, absent in 2, and reduced in one.

It seems that, when giddiness occurs, a single caloric test has a limited value in determining the extent of the vestibular disorder at that time, but that in the majority of cases the caloric reactions disappear when treatment is continued. It is not known what happens to the caloric reactions when treatment is stopped at the first sign of giddiness.

Effect on Co-ordination

Tests of co-ordination of movement were carried out in 37 patients at the end of the streptomycin treatment. The test consisted in walking along a line, heel to toe, with the eyes open and with the eyes closed. Performance of this manœuvre without unsteadiness demands some delicacy of muscle co-ordination, and a patient who has only recently started to get up after several months in bed cannot be expected to carry it out perfectly even with intact vestibular apparatus. Abnormal co-ordination of movement is therefore defined here as unsteadiness in the walking test greater than would be expected in the particular patient examined. The assessment depends so much on the judgment of the observer that the test cannot be considered an accurate one in the special circumstances of this study.

Twenty patients had abnormal walking tests at the end of treatment. In 6 there was such gross ataxia with the eyes closed that walking became impossible. All but one of these patients had lost the caloric reactions. The importance of minor degrees of ataxia is more difficult to assess. Of 14 with slight incoordination 5 had absent caloric reactions, 5 reduced reactions, in 1 the reactions were normal, and in 3 caloric tests were not done. On the other hand, of 17 patients judged to have normal walking tests 7 had absent caloric reactions, in 4 they were reduced, in 4 normal, and in 2 they were not carried out.

The results of this rough clinical test do not appear accurately to reflect the function of the vestibular apparatus as judged by the caloric reactions. While gross ataxia suggests severe vestibular disturbance, minor degrees of instability in the walking test are unimportant.

Relationship of Giddiness to Nausea

With the larger doses of streptomycin nearly two-thirds of the patients complained at some period of nausea, with or without vomiting. It was found that the nausea could be controlled by the antihistamine drugs and that this was not due merely to their sedative action (Bignall and Crofton, 1949). There seemed to be a possibility that the nausea was a manifestation of

acquired hypersensitivity to the streptomycin preparations. In view of this, it is interesting to examine the relationship of nausea to the giddiness.

In 15 patients both giddiness and nausea were present at some time during treatment. The nausea preceded the giddiness in 2 cases only. In only 3 instances did the nausea begin after the giddiness had disappeared; in 5 it began while giddiness was present, and in 5 the two symptoms started on the same day. Nausea, like giddiness, was considerably less frequent in patients receiving 1 g. (15%) than in those receiving 2 g. daily (60%); but, unlike giddiness, it did not appear earlier in patients receiving the larger daily dose. On the other hand, those with severe giddiness tended to complain of nausea more commonly than those with slight giddiness (Table III). Thus of 6 patients with moderate or severe

TABLE III.—*Relationship of the Severity of Giddiness and Nausea During Streptomycin Treatment*

Giddiness	Nausea			Total
	Nil	Slight	Moderate or Severe	
Nil	36	3	2	41
Slight	8	6	4	18
Moderate or severe	1	2	3	6
Total ..	45	11	9	65

giddiness 5 had nausea and in 3 it was moderate or severe. But of the 18 with slight giddiness only 10 had nausea and in only 4 was it moderate or severe. The observed differences are statistically significant, but the investigation is made less precise by the impossibility of deciding in some cases whether minor symptoms were indeed due to streptomycin.

There does appear to be some relationship between the giddiness and nausea, though this may not, of course, be a causative one. It is interesting that, although antihistamine drugs abolished the nausea, they had no apparent effect on the giddiness once it had occurred.

Giddiness and Blood Eosinophilia

In 52 patients leucocyte counts were carried out at roughly monthly intervals. Before treatment began 6.4% of the counts showed more than 500 eosinophils per c.mm. and none had counts above 1,000 per c.mm. The proportion of eosinophil counts greater than 500 and 1,000 per c.mm. rose during treatment, reaching a peak of 38.5% and 19.2% respectively during the fourth month. The reason for this late appearance of eosinophilia in patients treated with streptomycin is not known.

Of 52 patients 21 had an eosinophil count of more than 500 at some time during treatment. Eight (38%) of these complained of giddiness. Thirty-one patients did not have eosinophilia and 15 (48%) complained of giddiness.

There is thus no evidence that patients who developed eosinophilia during streptomycin treatment were more likely to suffer from giddiness than those who did not.

Vestibular Dysfunction and the Antihistamine Drugs

Although established giddiness in man is unaffected by antihistamine drugs it seemed worth while trying to discover whether vestibular damage could be prevented by giving the antihistamine drugs prophylactically. Caloric tests were performed on 22 patients, not included in the M.R.C. trials, before treatment and after they had

received 1 g. of streptomycin daily for two months. Twelve of the patients also had caloric tests done after three months' treatment. This group of patients received streptomycin calcium chloride complex (Glaxo), whereas the patients in the M.R.C. trials were treated with streptomycin hydrochloride (Merck) or streptomycin sulphate (Pfizer). The patients were given 100 mg. of "anthisan" three times daily, the first dose being taken before the initial injection of streptomycin was given. The anthisan was continued in the same dose throughout treatment. A few of the patients received 50 mg. of "phenegan" in the late evening and 100 mg. of anthisan at 4 p.m. No toxic effects of the antihistamine drugs were observed.

The incidence of giddiness and the changes in the caloric responses were compared with the experience of a group of patients in the M.R.C. trials who had received the same daily dose of streptomycin and had had caloric tests done two or three months after beginning treatment. The comparison is shown in Table IV.

TABLE IV.—*Comparison of the Incidence of Giddiness and Changes in Caloric Reactions between a Group of Patients Receiving Streptomycin and Antihistamine Drugs and a Group Receiving Streptomycin Alone*

	After 2 Months		After 3 Months	
	Anti-histamine Group	Control Group	Anti-histamine Group	Control Group
Total patients	22	15	22	15
No. complaining of giddiness	2	5	2	5
Caloric reactions:				
Patients examined ..	22	14	12	13
Normal	13	6	9	4
Reduced	5	4	1	4
Absent	4	4	2	5

Although the antihistamine group appear to have experienced less giddiness and less alteration of the caloric responses than the control group, the differences are not statistically significant. Moreover, allowance must be made for the fact that different batches of streptomycin were used for the two groups. Unfortunately, it also appears that the group of patients who were selected as controls because the results of caloric tests were available has a higher incidence of giddiness than the total group of patients in the M.R.C. trials receiving the same daily dose of streptomycin.

The results of this trial are therefore suggestive rather than conclusive. It can only be claimed that the antihistamine drugs may possibly be of value in reducing the incidence of vestibular damage by streptomycin.

Discussion

The site and nature of the pathological lesions responsible for the disturbance of vestibular function are not known with certainty. The lesions have been considered by some authors to be in the vestibular nerve nuclei, but evidence has also been brought forward that the action of streptomycin is on the labyrinths themselves.

Histological changes in the vestibular nerve nuclei in man have been described (Stevenson, Alvord, and Correll, 1947; Nielsen and Marsh, 1948). Nuclear lesions have also been observed in animals. Rüedi, Furrer, Escher, and Lüthy (1948) described histological changes in the cells of the vestibular nerve nuclei in guinea-pigs; Winston *et al.* (1948), by means of vital

staining, observed lesions in the cerebellar cortex and the vestibular and cochlear nuclei. Decreases in the nucleo-protein content of the ganglion cells of the vestibular nerve nuclei in guinea-pigs were demonstrated by cytochemical methods by Floberg *et al.* (1949). De Kleyn and Van Deinsen (1950) considered that the lesions were in the brain stem. They based their conclusions on the characteristics of the changes in the vestibular function tests in rabbits during the course of streptomycin administration. On the other hand, Mushett and Martland (1946) and Hawkins and Mushett (1947) were unable to find any histological evidence of damage to the vestibular nerve or the nuclei in the brain.

There appears to have been less search for lesions in the labyrinths themselves. Berg (1949) treated 20 cats with streptomycin for long periods and observed histological changes in the labyrinths in 13 of the animals. The appearances were compared with those of the labyrinths in untreated animals. Flattening of the columnar epithelium of the crista ampullaris and swelling and vacuolation of the cells of the basilar membrane of the organ of Corti were observed, and were thought to be due to the action of streptomycin. On the other hand, Glorig and Fowler (1947) failed to find any histological changes in the labyrinths. It should be noted that the dose of streptomycin per kilogram of body weight used in the animal experiments commonly far exceeded that used in man.

The retention of the reaction to galvanic stimulation after abolition of rotational nystagmus was observed by Vanderhaeghe (1949) in rabbits. In man, Glorig and Fowler (1947) and Hawkins (1950) found that the galvanic reactions were retained although caloric responses had been abolished. Our own observations confirmed this. On the other hand, Norman (1948) stated that he had found depression of the galvanic reactions in patients with reduced caloric responses; and Dix, Hallpike, and Harrison (1949) reported that the galvanic reactions were absent in 10 of 12 patients who had received streptomycin. Variations in individual technique and the absence of a standardized test may possibly account for some of the divergence of opinion. If normal galvanic reactions can be taken to indicate that the vestibular nerve is undamaged, their retention after all caloric responses have disappeared in patients treated with streptomycin strongly suggests that the labyrinth is the site of the toxic action in the relatively small doses used in man. The fact that lesions in the vestibular nerve nuclei are present in animals, even should they be due to a direct toxic effect of streptomycin on the cells, does not conflict with the probability that the earliest lesion is in the labyrinth itself.

The nature of the pathological lesions is even more obscure than their site. The frequency of manifestations of hypersensitivity such as rashes and eosinophilia in patients treated with 2 g. daily during the early period of the use of streptomycin suggested that the vestibular disturbances might also be a hypersensitivity phenomenon. Nausea caused by streptomycin may be due to hypersensitivity, as it can readily be abolished by the antihistamine drugs. There is a definite association between the incidence and the severity of nausea and giddiness, although established giddiness is unaffected by the antihistamine drugs.

Fowler and Feind (1949) investigated the effects of antihistamine drugs on the speed of development of the vestibular dysfunction in cats. They concluded that the antihistamine drugs delayed the appearance of evidence

of vestibular dysfunction. This effect could also be produced by preliminary desensitization with small increasing doses of streptomycin; and desensitized cats could tolerate twice the dose necessary to produce vestibular dysfunction in untreated animals. "Desensitization" has been tried in man (Schwartz, 1948), but the results in the small number of patients observed must be regarded as inconclusive. Eight of 12 patients treated with 2 g. daily for 60 days developed vertigo, whilst only 2 of 8 patients who were "desensitized" complained of this symptom. Our own results with the antihistamine drugs are also suggestive but not conclusive. Meantime, the evidence is insufficient to justify the general use of antihistamine drugs prophylactically; but it is perhaps reasonable to employ them in cases particularly liable to develop vestibular symptoms, such as middle-aged or elderly patients, those whose eyesight is poor, or those receiving more than 1 g. of streptomycin daily for long periods.

The investigation of the toxicity of streptomycin in man is hampered by the differences in the properties of different batches of the drug. Molitor and Kuna (1949) showed that streptomycin samples of varying degrees of purity differed quantitatively in their neurotoxic properties. Samples said to have a high neurotoxicity in man also had a high toxicity in animals. They found that the addition of "streptidine"—a hydrolytic product of streptomycin, and a possible contaminant of commercial samples—to a highly purified streptomycin caused a shortening of the time taken for toxic manifestations to appear. It is suggested that the vestibular damage is caused not only by the pure streptomycin but also by one of the substances closely allied to it or by one of its degradation products.

Now that the daily dose of streptomycin in the treatment of pulmonary tuberculosis has been reduced to 1 g., manifestations of vestibular dysfunction are not so commonly seen. In a recent series of patients only 12% complained of giddiness, and in the majority the symptoms were not severe (M.R.C., 1950). But vestibular dysfunction still remains the most frequent toxic effect of streptomycin therapy and, if one excludes the very rare exfoliative dermatitis, the only serious toxic effect of the drug. There is good evidence that the disorder of function may not be permanent, even though symptoms have been severe and all caloric reactions lost (Chase, 1948; Guilbert, Rothstein, and Wood, 1948). Our own observations are in agreement with these earlier findings. But in many patients the damage does appear to be irreversible. Canada *et al.* (1950) found that 42 of 100 patients who had vertigo at the end of treatment still complained of this symptom three years later, and 41 out of 95 still had impaired or absent caloric reactions.

It has been widely claimed that dihydrostreptomycin is less toxic to the vestibular apparatus than is streptomycin. But dihydrostreptomycin appears to be definitely more toxic to the auditory apparatus, and a number of cases of deafness have been reported (Shane and Laurie, 1950; Van Goidsenhoven and Stevens, 1950; Bernard *et al.*, 1950; Streptomycin Committee of the Veterans Administration, 1950). Therapeutically, it is thought to be less effective than streptomycin weight for weight (Streptomycin Committee of the Veterans Administration, 1950). It therefore seems unlikely that dihydrostreptomycin will be adopted for general use.

As the restraint imposed by bacterial resistance is removed by combinations of drugs and variations in

dosage streptomycin will probably be widely used in the less severe types of tuberculosis. Even slight giddiness occurring in less than 10% of patients might make one hesitate to use chemotherapy in relatively mild cases. It is therefore important that there should be further investigation of the vestibular effects of streptomycin.

Summary

The effects of streptomycin on the vestibular apparatus were investigated in 76 cases under treatment for pulmonary tuberculosis.

Patients receiving 2 g. of streptomycin a day complained of giddiness almost four times as often as those receiving 1 g., and the giddiness was first noted significantly earlier.

Nystagmus and abnormalities in the caloric tests were often associated with a complaint of giddiness. Clinical tests for co-ordination of movement, such as walking along a line with the eyes shut, were useful only when there was gross ataxia; minor degrees of ataxia were difficult to interpret in patients who had been confined to bed, and some cases with absent caloric responses had normal walking tests.

Giddiness and nausea tended to occur in the same patients and at about the same time.

An attempt was made to prevent vestibular damage by giving antihistamine drugs prophylactically to patients receiving streptomycin. The results suggest that some success was achieved, but the evidence is not conclusive.

We are most grateful to the physicians of the Brompton Hospital under whom these patients were admitted; to Professor F. C. Ormerod, Dr. Geoffrey Marshall, and Dr. J. G. Scadding for help and advice; and, not least, to the nursing staff of the hospital for their cheerful co-operation.

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VARIABILITY OF THE SPERM COUNT

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It is not uncommonly assumed that one sperm count is adequate in the investigation of male fertility, and claims have been made for the beneficial effects of various forms of treatment of defective spermatogenesis if a single sperm count following the therapeutic course is substantially higher than a single count performed before treatment.

Our clinical impression being contrary to these views, we decided to ask each husband attending the Fertility Clinic to provide us, at his convenience, with three specimens for examination.

Material

Three seminal specimens have been examined from each of 226 husbands of couples attending the Fertility Clinic. The specimens were collected direct into a dry, clean, though not sterile jar with a screw top and brought to the clinic for examination with as little delay as possible. The husband was instructed to produce the specimen, so far as was conveniently possible, after three days' continence. There was no selection of cases, and all husbands of whom we have records of at least three sperm counts up to the time of the conclusion of the inquiry are included in the series. The counts in the series were not performed by a single technician, nor did the same person necessarily count all three specimens from any one individual patient. The technicians who, apart from ourselves, have carried out many of the counts have done so under our supervision until we were satisfied that their counting was reliable.

Sperm counting was done as follows: (1) Semen was thoroughly mixed and then drawn to the 0.5 mark in a white-cell pipette; (2) diluting fluid was drawn to the 11 mark; (3) the pipette was shaken gently until the fluid in the bulb was well mixed, then the diluting fluid in the fine part of the tube was shaken out; (4) one drop of the mixed fluid was placed on a Neubauer counting chamber; (5) the sperms were counted under a 4-mm. objective and with $\times 10$ eyepiece; (6) the number of sperms in 2 mm.² were counted and five ciphers added to give the count per ml. In cases of marked oligospermia a proportionately larger number of squares were counted and an attempt was made to count at least 100 sperms.

Objects of the Study

The objects of this investigation were to determine in how many instances the three sperm counts varied from one another sufficiently to be misleading if one had had only one or two, but not three, counts available for consideration, and how often the initial count varied materially from one or both of the other two.

For this purpose we have divided the sperm density into three categories. The first is the "fertile" group. It is generally believed, and sometimes stated in treatises on infertility, that if the count is more than 60 millions per ml. there is considerable likelihood, in the absence