have found that different batches of the same brand of wool may yield significantly different survival patterns for most Gram-positive organisms. However, if we substitute serum swabs for the usual plain type then the first factor is automatically removed and the second becomes less critical. As a result, estimates of survival time on serum swabs may be accepted with greater confidence than those applying to untreated swabs.

Assuming a moderately heavy contamination of a serum swab (this is an important variable impossible to control clinically), we suggest that an examination may be expected to yield a valid result when cultured within the following time limits: (1) Organisms viable for less than eight hours: meningococci and gonococci. Downie's method or Aycock and Mueller's method is recommended for the former and Saint-Martin's for the latter. (2) Organisms viable for at least eight hours: *H. pertussis*, *V. cholerae* (moist swab is essential), *C. diphtheriae*. (3) Organisms viable for at least 24 hours: haemolytic streptococci, *Str. viridans*, *Cl. welchii*, pneumococci, *Shigella*, and *Salmonella* (moist swabs are essential for the last two genera). (4) Organisms viable for at least 48 hours: *Staph. aureus*, *Klebsiella*, *Proteus*, *Pseudomonas*, and *Escherichia* (moist swabs are essential for Gram-negative species).

The above estimates are based on laboratory experiments, but since the clinical findings for haemolytic streptococci closely paralleled the laboratory tests we consider that the same relationship will hold for most other organisms. However, in the case of *C. diphtheriae*, although good survival has been obtained in laboratory experiments (Table II), we do not recommend delaying plating longer than eight hours. In some clinical cases which we have examined the organisms failed to survive 24 hours on serum swabs.

Although autoclaved albumin-dipped swabs have not been studied so exhaustively the results were similar to those achieved with serum.

We have attempted to discover how serum prolongs survival, but without success. For instance, it could not be shown that serum inactivated a toxic lipid or water-soluble agent in the wool or that it acted as a substrate for growth. The effect of serum protein is probably a physico-chemical one acting on the bacterial cells and prolonging their survival irrespective of the materials on which they are lodged.

It is felt that these findings may have a broader significance than the somewhat restricted object of this investigation. Two facts are worthy of consideration from an epidemiological point of view. The first is the rapidity with which enteric pathogens die off when dried in air, and the second is that organisms leaving their hosts in serous exudates will live longer than those discharged in secretions of low protein content. These two points may throw some light on factors determining the survival of pathogenic organisms outside their natural hosts.

Summary

A study has been made of the survival patterns of a large number of organisms on plain swabs under standard laboratory conditions. From this study the following conclusions have been drawn: (a) Survival time of Gram-positive organisms is variable, depending on the batch of cotton-wool used and the presence of moisture, the latter tending to accelerate rate of death. (b) Survival time of Gram-negative enteric pathogens is uninfluenced by the type of wool but depends on the degree of moisture on the swab. On moist swabs survival is greatly prolonged.

A new type of swab was developed, termed a serum swab, on which survival times of all organisms tested, except the *Neisseria*, were increased.

Other factors such as temperature of storage, relative humidity, and anaerobiosis were investigated and found to be relatively unimportant.

The mechanism of serum protection is unknown.

We wish to record our thanks to Margaret Gibson, M.Sc., for her assistance in the early stages of this work and to the various laboratories who sent us specimens of their cotton-wools.

REFERENCES

- Aycock, W. L., and Mueller, J. H. (1950). *Bact. Rev.*, **14**, 115.
 Brahdry, M. B., Brody, H., Gaffney, C. A., Lenarsky, M., and Smith, L. W. (1934). *Proc. Soc. exp. Biol. N.Y.*, **32**, 548.
 Buchbinder, L., Buck, T. C., Phelps, P. M., Stone, R. V., and Tiedeman, W. D. (1947). *Amer. J. publ. Hlth*, **37**, 373.
 Councilman, W. T. (1893). *Amer. J. med. Sci.*, **106**, 540.
 Downie, A. W. (1940). *Lancet*, **2**, 36.
 Dunklin, E. W., and Puck, T. T. (1948). *J. exp. Med.*, **87**, 87.
 Goldscheider (1893). *Z. klin. Med.*, **22**, 534.
 Hamilton, D. J. (1895). *British Medical Journal*, **1**, 298.
 Hardman, W. (1895). *Ibid.*, **1**, 387.
 Hewlett, R. T., and Nolan, H. (1896). *Ibid.*, **1**, 266.
 Hynes, M. (1942). *J. Path. Bact.*, **54**, 193.
 Kolle, W., and Wassermann, A. (1903). *Handbuch der pathogenen Mikroorganismen*, vol. 3. Fischer, Jena.
 Mackie, T. J., and McCartney, J. E. (1948). *Handbook of Practical Bacteriology*, 8th ed. Livingstone, Edinburgh.
 Mitchell, R. B., Tuttle, E. E., Dingle, L. C., Grams, L. R., Erdman, G. L., Coombs, F. S., and Holbrook, W. P. (1946). *J. infect. Dis.*, **78**, 128.
 Parish, H. J. (1935). *Lancet*, **1**, 400.
 Preston, W. J. D. (1896). *British Medical Journal*, **1**, 1243.
 Roux, E., and Yersin, A. (1890). *Ann. Inst. Pasteur*, **4**, 385.
 Saint-Martin, M. (1949). *Canad. J. publ. Hlth*, **40**, 78.
 Van Reimsdijk, M. (1924). *Z. Hyg. Infektkr.*, **103**, 106.
 Wadsworth, A. B. (1947). *Standard Methods*, 3rd ed. Baillière, London.

INVESTIGATION INTO THE EFFECTS OF AUREOMYCIN AND CHLORAMPHENICOL IN HERPES ZOSTER

BY

A. BARHAM CARTER, M.D., M.R.C.P., D.P.M.
 Physician, Ashford Hospital, Middlesex; Adviser in
 Neurology to the War Office

Recent advances in antibiotic therapy have been sufficiently great to produce an effective remedy against most bacterial infections, and it is therefore natural that the effects of antibiotics on virus infections should be put to the test. Particular success accompanied such an investigation in the case of "aureomycin" and virus pneumonia. Finland *et al.* (1949) have described the effects of aureomycin on the course of 24 cases of herpes zoster; they conclude that this drug increases the rate of healing of the skin lesions, causes a rapid subsidence of herpetic pain, and seems to be followed only rarely by post-herpetic neuralgia. No controls were used in their series, and the total dosage for each case varied from 7.4 to 54 g. From this evidence they conclude that an effective dose might be 4 g. daily for two to four days followed by 2 g. daily for a further three to five days, and that particular benefit results if the treatment is begun early. They claim that in most of the patients there was no evidence of secondary infection, that no new lesions developed after the first day or so of treatment, and that pain was relieved after the first day.

Dawson and Simon (1949) have reported beneficial effects from the use of chloramphenicol in a small controlled series of cases, and Binder and Stubbs (1949) administered aureomycin to four cases of zoster and obtained satisfactory results in three and a fair result in the fourth. One patient, a child of 11, developed poliomyelitis five days after the subsidence of the zoster rash. Their dosage scheme was only 2 g. daily for two days for the adults and half this for the child.

Case (1949) has described good results in one patient, and Brainerd *et al.* (1949) were impressed by the rapid improvement of a case of herpes ophthalmicus similarly treated. In view of these claims and in spite of the difficulties of assessing the effects of treatment on a syndrome of such varying severity as herpes zoster, the following small controlled investigation was carried out.

Material and Method

The material comprised every case of herpes zoster admitted to Ashford Hospital, Middlesex, between June, 1950, and March, 1951. The local doctors were asked to send in all cases except those whose rash had been present for 14 days or more. Mild cases either refused to come in or had been unrecognized. The patients were nursed in the acute medical wards, and no case of zoster or varicella occurred in other patients, although doctors were asked to watch for possible contact cases in the district. This request produced the interesting observation that in 8 out of the total 44 cases chicken-pox occurred in one or more of the patients' children from 8 to 14 days after the patient's admission to hospital.

The investigation was divided into two parts. First, a series of 11 controls (group 1) treated with a placebo (glucose) made up in capsules to resemble aureomycin was compared with a series of 11 cases (group 2) treated with aureomycin 2 g. daily for six days. Secondly, a similar series (group 3) treated with a larger dose of aureomycin for a shorter period (4 g. daily for four days) was compared with a series (group 4) treated with chloramphenicol 2 g. daily for six days.

There were therefore four groups of 11 cases each. Group selection for each case was made at random by the sealed-envelope method suggested by Professor Bradford Hill, so that only the hospital dispenser knew which cases were the controls. Daily records were kept on a standardized form regarding pain, paraesthesiae, sleep, extent and severity of rash, including amount of secondary infection and any side-effects noticed by the patients. Cases were divided into two grades, "severe" and "moderate," based on the severity of pain and extent of the rash; and, because of the variations in the description of subjective symptoms, only the simplest terms were used. Local treatment was confined to talc powder to prevent sticking, and only three analgesic drugs were used—codeine, pethidine, and "omnophon."

Because of the cost and the possible side-effects, just enough antibiotic was given to control the infection, and the dosage was standardized for purposes of comparison of effect and for simplicity of administration. Long *et al.* (1950) consider that dosage schedules are well established, and suggest that for moderately ill patients the total daily maintenance dose of aureomycin should be from 20 to 30 mg. per kg. body weight. They suggest that the drug is best given at six-hourly intervals and that there is no need for a loading dose. The length of treatment has not been defined, and an arbitrary figure of six days was used in the present series.

In the first treated group, 0.5 g. of aureomycin at six-hourly intervals was given to each patient for six days—a total of 12 g.—so that a patient weighing, say, 147 lb. (66.7 kg.) would be receiving 30 mg. per kg. as a daily maintenance dose; in the second treated group twice this dose was given for four days, so that these patients were receiving 4 g. daily and 16 g. in all. At first 1 g. was given six-hourly; but this dosage produced severe side-effects, and so 0.5 g. was given three-hourly, the dose being doubled late at night to save waking the patient. In the chloramphenicol group the dosage was the same as in the first aureomycin group.

Table I shows the comparability of the groups in some other respects; although the numbers are small the similarity is great.

TABLE I.—Showing Comparability of Groups Before Treatment

Group	No.	Sex		Average Age of Patients	Average Age of Rash on Admission	Severity		Location	
		M	F			Severe	Mod.	Spinal	Ophth.
1	11	7	4	56 yrs.	4.6 days	6	5	7	4
2	11	5	6	54 "	4.3 "	6	5	8	3
3	11	8	3	50 "	4.1 "	5	6	7	4
4	11	7	4	51 "	4.4 "	4	7	7	4

Course of Untreated Cases

Before the results are analysed the natural history of herpes zoster, shown by the course of the illness in the untreated cases (group 1) and by the history and condition of all the groups before treatment, is worthy of attention.

Prodromal symptoms of malaise and fever were uncommon, and generalized headache occurred in only one of the spinal cases. The first symptom was in many cases irritation with occasional sharp stabs of burning pain, usually in the place where the rash afterwards appeared. The average time between this first symptom and the onset of the rash in all groups was 4.5 days, although in 7 of the 44 cases the rash accompanied the first twinge of pain. The longest interval between pain and rash was 12 days. In three cases the initial pain was located some few segments higher than the subsequent rash, though always on the same side.

In the 15 ophthalmic cases generalized headache was common and at times was accompanied by nausea and vomiting; it was followed by neuralgic pain and irritation over the distribution of the ophthalmic nerve.

The rash itself began as a patchy erythema with oedema of the skin, and, after a short papular stage which was sometimes absent, vesiculation occurred in clusters, usually in the middle of a patch of erythema. When close to each other the vesicles tended readily to coalesce, and if of any size became rapidly haemorrhagic. Fresh vesicles appeared in some cases up to the fifth day of the rash, and these were often seen alongside haemorrhagic and pustular lesions.

On the third or fourth day pustulation occurred, apparently due to a varying degree of secondary infection with staphylococci, and these pustules either ruptured, leaving in some cases a blackish almost gangrenous appearance of encrustation, or began to dry up. This crusting usually began on the fifth to the eighth day of the rash, was complete within thirteen days except in two severely infected cases, and was followed by desquamation, separation of the crust, and eventual fading of the rash.

Pain was, of course, a prominent feature, varying from aching and soreness to pain of great severity variously described as burning, gnawing, drawing, shooting, jumping, or neuralgic. The pain was worse at night, was aggravated by movement or light touching of the skin, was paroxysmal, and could often be relieved by heavy pressure on the skin. It was at its height while vesiculation was occurring and lasted throughout the pustular stage, beginning to fade when crusting started, and leaving an ache or soreness when the crusts had fallen off.

Paraesthesiae were always present, and were variously described as irritation, itching, burning, tenderness, tingling, prickling, feelings of stiffness, bruising and heaviness, occasional pins-and-needles, a feeling of rawness, numbness, and thumping. They often persisted longer than the pain and seemed to match in intensity the severity of the rash. In the ophthalmic cases pulling or combing the hair caused "electric shocks" to be felt in the head; these were very distressing.

Objective neurological changes were increased sensitivity to light touch and pinprick in the erythematous and vesicular stage, with decreased sensitivity often amounting to complete loss of feeling in the scars after desquamation.

The cerebrospinal fluid was examined before treatment in every case; if abnormal, examination was repeated, usually at weekly intervals. Of the 44 cases, 14 had abnormal C.S.F.—10 of these were ophthalmic cases, and the other four were very severe spinal cases in which the rash extended over two or three segments.

TABLE II.—Details of Abnormal Cerebrospinal Fluids

Age	Case No.	Group	Type	Days after First Rash	Cerebrospinal Fluid			
					Protein mg./100 ml.	Cells per c.mm.		
						Total	Polys.	Lymphs.
76	16	2	Spinal	8	75	34	18	16
				15	20	27	—	27
				22	20	18	—	18
79	25	2	Ophthal.	7	70	40	24	16
				16	20	2	—	2
				9	210	45	20	25
70	34	2	"	16	50	40	16	24
				24	25	42	—	42
				4	50	16	10	6
69	29	1	"	11	20	12	4	8
				18	20	5	—	5
				5	110	24	16	8
59	23	1	"	12	50	36	12	24
				20	30	12	—	12
				6	90	36	20	16
63	26	1	"	13	40	28	8	20
				21	20	12	—	12
				5	90	44	24	20
70	29	3	"	12	40	30	12	18
				19	20	10	—	—
				4	80	62	40	22
64	30	3	"	11	20	20	8	12
				18	20	8	—	8
				10	70	26	6	20
58	19	2	Spinal	18	30	10	—	10
				4	70	25	15	10
				11	20	12	—	12
54	31	3	Ophthal.	18	20	4	—	4
				4	50	45	30	15
				11	40	20	8	12
53	7	3	Spinal	15	20	10	—	10
				6	75	36	14	22
				13	30	30	—	30
70	41	4	Ophthal.	20	20	8	—	8
				4	90	44	20	24
				11	40	20	—	20
63	22	4	Spinal	18	22	2	—	2
				5	75	28	10	18
				12	40	6	—	6
60	38	4	Ophthal.	19	20	6	—	6

Of the 30 with normal C.S.F., 25 were spinal cases and 5 were mild ophthalmic cases. Thus of the 29 spinal cases in this investigation only 4 had abnormal C.S.F., and of the 15 ophthalmic cases 5 had normal C.S.F. The abnormal fluids are detailed in Table II, in which the high protein in the early stage of illness is to be noted. The average age of the patients with abnormal C.S.F. was 64, whereas that of the whole series was 53.

Analysis of Results

In the first 22 cases an attempt was made to guess whether the patient was having placebo or aureomycin, and the condition of the rash was used as a guide—13 guesses were correct, 2 were incorrect, and in 7 no reasonable guess could be made.

One particular case merits detailed description. A man aged 65 was admitted seven days after he had noticed a neuralgic pain in his right forehead which kept nagging at him particularly at night and made him keep rubbing his forehead. Two days before admission he noticed a red rash on his forehead and his right eyelid began to swell. On admission the whole of the right forehead was swollen and red; chemosis of the lids and conjunctival injection were present, but the cornea was clear. There were two moderate-sized vesicles and one papule on the forehead, and he complained of fairly severe burning and neuralgic pain on the right side of the head. Light touch made the pain worse and heavy pressure relieved it. The right corneal reflex was slightly reduced.

The next day there were five haemorrhagic vesicles, the pain was less, and he noticed "electric shocks" when his hair was combed on the right side. On the third day of treatment there were three more clusters of small vesicles, the pain was moderate, and the paraesthesiae were less marked. Sleep was normal without sedatives, and he was cheerful and ate well. The chemosis of the lid began to go, no further lesions appeared, and the pain changed to a bruised feeling which disappeared on the sixth day of treatment, when drying and crusting of the rash began, being complete on the ninth day. On the thirteenth day separation of the crusts was complete, and he went home feeling well except for a slight sensation of bruising over the right outer canthus. His C.S.F. contained 10 lymphocytes per c.mm. and 60 mg. of protein per 100 ml.

This case is described in detail because it was thought probable that an attack of ophthalmic zoster had been "aborted" by aureomycin about the fourth or fifth day. Actually he had been receiving the placebo. This sort of case should be borne in mind when remedies are alleged to "cut short" or "abort" an attack of zoster.

Comparison of Rash

Fresh vesicles appeared in all of the controls that were admitted within 72 hours of the onset of the rash. These continued to appear up to the fifth day of observation. In four similar cases of group 2 admitted within 72 hours, fresh vesicles appeared up to the fourth day of observation. One of these cases received aureomycin within 48 hours of the appearance of the rash, and in spite of this fresh lesions occurred. In the cases receiving a higher dosage of aureomycin (group 3) four showed a few fresh lesions up to the third day of observation. These four cases were admitted on the third (two cases), fourth, and fifth days of their rash. Fresh vesicles were seen in two of the chloramphenicol cases up to the fourth day of the rash.

These figures suggest that treatment had a slight but not significant effect on the early cutaneous manifestations. It was hoped that bacteriological control would be possible, and that it could be shown whether the

virus could be grown from the vesicles of the treated cases as it can from the untreated; but Professor Bedson through the Medical Research Council and Dr. Weston Hurst in a personal communication have stated that this procedure is impracticable.

The average time taken for the rash to become crusted and completely dry was 13 days in group 1 (controls), 11 days in group 2, and 10 days in group 3 and group 4. The difference in the first two groups was due mainly to four cases in which aureomycin had been given within three days of the rash appearing: in these the rash was dry in eight days. One case in group 3 is excluded, as it showed no vesiculation at all and progressed most dramatically from papules and erythema to recovery.

The most marked difference between the controls and the treated cases was seen in the occurrence and control of secondary infection. This infection was universal in the controls, and often it was very severe. Staphylococci were grown from the vesicle fluid in all the controls, but not in the treated cases while they were receiving aureomycin or chloramphenicol. One very severe case was of interest in this connexion.

A woman aged 76 was admitted with a very severe zoster of some eight days' duration affecting D12 and L1 on the left side. She was very ill, and the case was complicated by hypertension and diabetes mellitus. The rash was heavily infected with staphylococci. She received aureomycin, 2 g., daily for six days. On the fourth day of treatment vesicular and pustular fluid was sterile. Two days after treatment had been discontinued the rash looked grossly infected again and the fluid once more grew staphylococci in profusion.

Early treatment seemed to prevent any secondary infection and shortened the time from the first sign of the rash to complete desquamation. In the control group this averaged 24 days and in the treated groups 20 days. In those cases (10) treated within 72 hours of the rash appearing, desquamation was complete in an average of 15 days.

Pain

Comparison of a symptom that is wholly subjective is always beset with difficulties. The duration was measured simply by asking whether pain—not paraesthesiae—was present or not, and a note was made of the first pain-free day and the first good night's sleep unaided by drugs. The severity was roughly gauged by the need for analgesics; the drugs allowed were limited to three, and a standard dose used in each case—

TABLE III

Group	First Pain-free Day	First Unaided Normal Night's Sleep	No. of Patients Receiving			
			Omnopon	Pethidine	Codeine	Nil
1	12th	9th	3	6	7	2
2	11th	10th	3	5	8	2
3	12th	6th	1	2	9	2
4	11th	7th	2	3	7	2

omnopon 1/3 gr. (22 mg.), pethidine 100 mg., and tab. codein. co. (two tablets). An analysis is given in Table III. It shows that there was no significant difference between groups 1 and 2, but groups 3 and 4 required less analgesic and slept better.

Paraesthesiae

Perhaps of all the symptoms of herpes zoster the severity and duration of the paraesthesiae give the truest picture of the effects of viral infection on the nervous system. These paraesthesiae are usually clear-cut, easy

to define by the patient, and independent of pain sensitivity, which is always one of the factors which make the assessment of pain so difficult. They were of two kinds—those spontaneously experienced by the patient without stimulus, and those in which stimuli affecting the skin and deeper structures were wrongly interpreted. The former type lasted longer than the latter and occurred more often in the ophthalmic than in the spinal cases.

Comparison of the groups showed no difference between the treated and the untreated cases in the whole series, nor was there any significant lessening of severity or duration in the four cases in group 2 treated within 48 hours of the appearance of the rash.

This result suggests either that this treatment has no control over the virus in its effects on the nervous system or that the damage has already been done when the skin manifestations appear.

Side-effects

The side-effects of these antibiotics have been described by Harris (1950) and Tomaszewski (1951) among others, although in most of their cases the dosage was greater and was spread over a longer period than in this series. Probably because of this the side-effects have been less noticeable in our cases.

Toxic Effects

Nausea and vomiting occurred with approximately equal frequency in the controls, chloramphenicol cases, and lower-dosage aureomycin cases. In the higher-dosage cases, nausea and vomiting were very troublesome at first with 1 g. six-hourly, but became less severe when 0.5 g. was given three-hourly.

Loose stools occurred in four aureomycin and two chloramphenicol cases within the first two days of treatment but did not persist beyond the fourth day. True diarrhoea did not occur; no granulocytopenia was encountered, although white-cell counts were done on all patients; and depression was no more than could be expected from the underlying illness. Hypersensitive reactions did not develop in any case, and no rash occurred that could be attributed to the drug.

Effects Due to Bacterial Sterilization

Aureomycin and chloramphenicol effectively sterilize the alimentary tract from mouth to anus, and it is suggested that some of the effects mentioned below may be due to the unrestricted growth of fungus in the absence of bacterial competition, rather than to vitamin-B deficiency as has been suggested. It is of course essential to support antibiotic therapy of long duration with vitamin-B complex owing to interference with the normal synthesis of this vitamin if the upper intestine is sterilized, but it seems unlikely that there would be clinical evidence of avitaminosis within a few days. Similar effects have been described in penicillin treatment (Geiger *et al.*, 1946), and evidence of fungus infection was obtained in those cases in the present series which showed this type of side-effect.

In four cases (three women, one man) redness of the oral mucous membrane and tongue appeared on the third and fourth days, and the patients complained of a metallic taste. Two were treated with aureomycin and two with chloramphenicol.

One man and one woman had black tongues after 8 g. and 10 g. of chloramphenicol respectively; in the former

the condition was more severe, with well-marked hairiness of the tongue, and in both patients the dark-brown pigmentation could be seen spreading forward like two fingers over the surface of the tongue on both sides of the median fissure. Tongue scrapings showed a dark monilia in the man and *Candida albicans* in the woman, with no bacterial flora. Angular fissuring of the mouth with buccal ulceration occurred in one case, and anal irritation and soreness in three cases, including the two with black tongues, and one in which anal scrapings showed the presence of *Candida albicans*.

Discussion

The general results of this controlled series show little difference between treated and untreated cases with regard to the appearance of fresh herpetic lesions, the amount and duration of herpetic pain, or the type, duration, and frequency of paraesthesiae.

Further analysis shows that treatment with either aureomycin or chloramphenicol within the first week of the rash modifies the duration of the pustular stage and is associated with earlier drying and earlier desquamation. This effect can reasonably be attributed to the action of these antibiotics on the secondary infection, particularly if it is very severe. This action was remarkably consistent, as, in all cases in the aureomycin groups and all but two of the chloramphenicol group, cultivation of the vesicle or pustular fluid was sterile. In the two chloramphenicol exceptions, only a scanty growth of *Staphylococcus albus* was obtained.

In view of these results it seems unjustifiable to use such expensive drugs in the routine treatment of herpes zoster. It is suggested that their use be confined to two types of patient—one the severe case of ophthalmic zoster, particularly in the elderly, where it is possible that secondary infection plays some part in the severity of the scarring and even of the post-herpetic pain which so commonly follows; the other the severe case of spinal zoster involving two or more segments, where the patient's life may be endangered by the toxic effects of severe secondary cutaneous infection. Diabetic and nephritic patients particularly come into this category.

There is less evidence to support the use of these drugs in the very early stages of this illness, before the rash is established, in the hope that the virus may not yet be completely fixed and may therefore be more vulnerable. A much larger series would be required before enough of these early cases could be found for statistical investigation, and, although no such evidence has appeared here, the following case merits description:

A man aged 54 (Case 31) was admitted on November 3, 1950, with a history of five days' pain behind the right ear and extending to the forehead; it was paroxysmal in character and was relieved by rubbing. This was followed by irritation, redness, and swelling of the right side of the forehead two days before admission. On examination there was a red swollen area over the right forehead extending a little way over the midline with one or two papular collections and three pinpoint vesicles. The right eye was normal and the corneal reflex unimpaired. Aureomycin, 0.5 g. three-hourly for four days, was begun. He described his pain as moderate and said that his forehead felt tender and heavy. He was given pethidine and codeine the first night. The next day his condition was unchanged and he slept well unaided. The third day the swelling was gone and the erythema fading. The fourth day he had no pain, no tenderness, only a moderate feeling of heaviness, and the edges of

the rash were no longer recognizable. On the fifth day the three pinpoint vesicles were crusted, and by the seventh day the rash and paraesthesiae had disappeared, leaving only a slight hypoaesthesia where the rash had been. There was naturally some question whether this was a case of ophthalmic zoster, but the cerebrospinal fluid was typical, as can be seen from Table II.

Summary

Forty-four consecutive patients suffering from herpes zoster have been investigated to determine the effects of aureomycin and chloramphenicol on the course of this condition.

These patients were divided into four groups of 11 each: group 1, the controls, receiving glucose; group 2, aureomycin orally 2 g. daily for six days; group 3, aureomycin 4 g. daily for four days; and group 4, chloramphenicol 2 g. daily for six days. The controls were selected at random and the observers did not know which patients were in this group.

The results showed that there was no significant difference between the groups in respect of pain, paraesthesiae, or the appearance of fresh herpetic lesions. The treated groups were free from secondary infection, which was present in every one of the controls, and this freedom may have modified the pustular stage of the rash so that desquamation was earlier and scarring less.

Two cases in which treatment seemed to bring about a dramatic amelioration of symptoms are described in detail: one was a treated case and the other a control.

It is suggested that in view of these results there is no justification for the routine use of such expensive drugs in herpes zoster, and that they should be employed only in very severe cases, particularly ophthalmic zoster, occurring in elderly or debilitated patients.

I should like to thank my colleagues on my medical firm for their help in observing and treating these patients; Professor Bradford Hill and Dr. J. Knowelden for suggesting the sampling method of selection of controls; the Antibiotics (Non-Tuberculous) Trials Committee of the Medical Research Council for supplies of aureomycin; and the general practitioners of this area for sending me the patients.

REFERENCES

- Binder, M. L., and Stubbs, L. E. (1949). *J. Amer. med. Ass.*, **141**, 1050.
 Brainerd, H., Lennette, E. H., Meiklejohn, G., Bruyn, H. B., and Clark, W. H. (1949). *J. clin. Invest.*, **28**, 992.
 Case, R. B. (1949). *Calif. Med.*, **71**, 214.
 Dawson, L. M., and Simon, H. E. (1949). *Sth. med. J.*, **42**, 696.
 Finland, F., Finnerty, E. F., Collins, H. S., Baird, J. W., Gocke, T. M., and Kass, E. H. (1949). *New Engl. J. Med.*, **241**, 1037.
 Geiger, A. J., Wenner, H. A., Axilrod, H. D., and Durlacher, S. H. (1946). *Yale J. Biol. Med.*, **18**, 259.
 Harris, H. J. (1950). *J. Amer. med. Ass.*, **142**, 161.
 Long, P. H., Bliss, E. A., Schoenbach, E. B., Chandler, C. A., and Bryer, M. S. (1950). *Lancet*, **1**, 1139.
 Tomaszewski, T. (1951). *British Medical Journal*, **1**, 388.

Special ceremonies at the University of Copenhagen on April 27 marked the successful conclusion of the first course at the W.H.O. International Training Centre for Anaesthesiology. The Centre, founded just a year ago, is the first major training project established by the World Health Organization to aid medical science in Europe. Thirty medical Fellows from seven European nations made up the graduating class. They are all doctors or surgeons who are now returning to their own countries to teach the new techniques of modern anaesthesiology. A second group of 30 Fellows, like the first group supported for the most part by W.H.O. fellowships, arrived in Copenhagen on May 3 for the next year's course.