he reached 999 years, and that among others the local clergyman might claim the fees he would normally receive for the burial service. Pockrich was a most remarkable rather off-beat character who produced visionary schemes which caused him to be referred to at a recent meeting of the Section of History in the Royal Irish Academy of Medicine in Ireland as a poor man's Leonardo da Vinci. —I am, etc.,

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"Acrosclerosis"

SIR,—The recent article by Drs. A. W. Dellipiani and M. George (11 November, p. 334) on the syndrome of sclerodactyly, calcinosis, Raynaud's phenomenon, and telangiectasia, prompts us to report a further case.

A 75-year-old lady was admitted because of a hemiplegia due to cerebrovascular disease. She was noted to have tight shiny skin on some of her fingers, together with very rigid flexion deformities. Both thumbs showed dislocation of the distal interphalangeal joints. The tissues of the affected fingers were curiously hard and thickened. There were telangiectases on the lips,

face, and the palmar surface of the affected fingers.

Until the onset of the hemiplegia, which has been accompanied by severe dementia, she had been able to look after herself—including cooking, shopping, and doing housework—with some social support. History from friends and relatives gave no evidence of bleeding from the nose or gastrointestinal tract, nor was there any family history of bleeding. The patient had been troubled with Raynaud's phenomenon for as long as anyone could remember.

Later during her admission the skin of one of the affected fingers became inflamed and broke down, resulting in the discharge of a white pultaceous material, which on analysis proved to be composed of calcium and phosphate. The rest of the physical examination was not contributory.

Investigations revealed no definite evidence of involvement elsewhere, but the serum proteins were low at a total of 4.7 g./100 ml., with 3.4 g./100 ml. albumin, and 1.3 g./100 ml. globulin; electrophoresis showed a rather low γ and a high α_2 globulin. The white cell count persisted at a level of 20,000/cu. mm. and she has an iron deficiency anaemia with a haemoglobin of 7.6 g./100 ml. and a mean corpuscular haemoglobin concentration of 27%. However, these findings can be explained by the presence of a large bed-sore. X-ray of the hands showed extensive soft tissue calcification. There being no history or clinical evidence of dysphagia, a barium swallow did not seem justified in our patient. An electrocardiograph revealed nothing compatible with scleroderma.

This patient's history and progress support the contention that this syndrome has a benign course, but the deformities produced in our patient must have been at least to some degree incapacitating.

We are grateful to Dr. Harold Davis for his permission to publish details of this patient.

—We are, etc.,

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Disinfectants and Plastic Mop Heads

SIR,—Prompted by the letters of Dr. D. A. Leigh and Miss Christine Whittaker (12 August, p. 435) and Dr. L. Steingold, Mr. L. J. Dunn, and Mr. S. Henman (2 September, p. 620) we have investigated the effect of polyvinyl acetate, polyurethane, and cellulose sponges on the germicidal activity of various phenolic disinfectants.

One-inch (2.5-cm.) cubes of the plastics were immersed in 50 ml. of the disinfectant solution, allowed to soak for 24 hours; then the solution, with plastic still immersed, was inoculated with 0.5 ml. of a culture of *Pseudomonas aeruginosa*. Reinoculation was made each day over a seven-day period, and 7½, 15, and 30 minutes after each inoculation a 0.1-ml. sample of the disinfectant was withdrawn and examined for surviving bacteria. Not more than 10 survivors from the 0.1-ml. sample at 30 minutes was regarded as a satisfactory result. Controls of disinfectant without plastic were satisfactory over the whole seven-day period even at the seven-and-a-half-minute sample.

Polyvinyl acetate had the greatest effect. At the normal dilutions of use none of the disinfectants retained activity for more than the first inoculation. Polyurethane had only slightly less effect than polyvinyl acetate, none of the disinfectants at their normal dilution of use surviving more than one or two inoculations. Cellulose sponge, however,

did not affect germicidal activity to any great extent, the use-dilutions of all the disinfectants being satisfactory during the complete seven-day inoculation period.

When the disinfectants were tested at one and a half to three times their normal use-dilutions against polyvinyl acetate and polyurethane activity was retained for periods ranging from two to seven days. We found some evidence that the plastics and disinfectants behave in different ways—for example, disinfectant A was less affected by polyvinyl acetate than disinfectant B, while with polyurethane the reverse occurred. We repeated the investigation with polyvinyl acetate and polyurethane, pre-soaking the sponge for 24 hours in disinfectant before transferring it into a fresh solution at the same concentration for testing. While interference with the germicidal activity could still be found it was much less severe than in the earlier investigation, all the disinfectants retaining activity at one to two times their normal use-dilution over the seven-day period.

It would appear that cellulose sponge is the plastic of choice to avoid loss of phenolic germicide from solution. With other sponge materials the problem can be overcome by pre-soaking (preferably in overstrength) disinfectant and/or changing the solutions frequently as a matter of good housekeeping.

—We are, etc.,

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Carcinogenicity of Tobacco and Tobacco Smoke

SIR,—Dr. M. Glass has asked two pertinent questions (5 August, p. 373), reiterated (9 December, p. 621), to which, he says, he has had no answer. I doubt if anyone can answer completely the vexed question of the pathogenesis of lung cancer in cigarette smokers, but the possibility that "some other essential factor, in addition to cigarette smoke," may be involved cannot be excluded. The important point is that in the absence of cigarette smoking, as opposed to smoke, to which non-smokers are often exposed, other possible factors that may be concerned in the evolution of cancer of the lung are less carcinogenic.

The absence of neoplastic reactions in the skin of the often heavily stained fingers of habitual chain-smokers may be related to the paucity, or absence, of pilosebaceous follicles in the lateral aspects of the fingers; assuming that the distillate from the tobacco contains fat-soluble potential carcinogens. There is experimental evidence from several independent sources which would support this explanation, which I reviewed in a different connexion.¹

The more difficult problem of the sequence of events in the pathogenesis of lung cancer in man, though unsolved, is not without clues. The demonstration² of basal cell hyperplasia and squamous metaplasia in the tracheobronchial tree in smokers, with or without lung cancer, as a more frequent finding than in non-smokers, and the observation³ that the increased incidence of primary lung cancer in smokers is practically limited to the epidermoid and undifferentiated

FIG. 1.—Hand showing deformity and discharging area.

FIG. 2.—X-ray of hand.

types suggests that these facts are causally related. Coughing, a regular accompaniment of smoking in many people, may be a contributory factor in the detachment of ciliated epithelium.

These may be some of the "other possible factors" postulated by Dr. Glass to which smokers are more liable than non-smokers.—I am, etc.,

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Antibiotic Combination in Staphylococcal Infections

SIR,—A recent *in vitro* study¹ has shown the advantages of kanamycin and cephalothin or kanamycin and methicillin in combination against methicillin-resistant strains of *Staphylococcus aureus*. It was suggested that combination therapy be initiated against all methicillin-resistant strains while awaiting the outcome of the appropriate *in vitro* tests. Others have recently extended this recommendation and have suggested combination therapy in all serious staphylococcal infections even before it is known whether or not the infecting strain is methicillin-resistant.^{2,3} Before accepting this latter recommendation, especially since infections with methicillin-resistant strains are uncommon, it is important to know whether antagonism occurs when the combination is used against methicillin-sensitive strains of *Staph. aureus*.

Ten strains of methicillin-sensitive coagulase-positive *Staph. aureus* isolated from clinical specimens were used to investigate this possibility. Pure cultures were obtained by transfer of single-colony isolates. Routine disc sensitivity tests were done on all strains according to the method of Bauer and Kirby.⁴

Routine tube dilution minimal inhibitory tests (M.I.C.) were performed simultaneously, comparing kanamycin, cephalothin, and kanamycin/cephalothin. All tests were made of an inoculum of 10^7 organisms per ml. using tryptose-phosphate broth; tubes were read for macroscopic turbidity after 18 hours of incubation. Subcultures of 0.01 ml. of all clear tubes were made on to agar plates; the concentration of antibiotic which yielded no growth was considered to be the minimal bactericidal concentration (M.B.C.), although this test guarantees only that there are less than 10^2 survivors/ml. With two strains, dynamics of growth were studied

in the presence of antibiotics singly and in combination, with counts of colony-forming units made at 0 time, 1, 2, 4, and 24 hours. The rate of killing over the first four hours is thought to be particularly important in evaluating antibiotic combinations.^{5,6}

The patterns of antibiotic resistance and the M.I.C. and M.B.C. are shown for all 10 strains in the Table. On the basis of minimal bactericidal concentrations, the combination was of some advantage in five cases, but in the others was only as effective as cephalothin used alone. Nine of the 10 strains were killed in 0.5 $\mu\text{g./ml.}$ of each of the agents in combination.

Growth curve characteristics of strain 2576 are shown in the Figure and illustrate some synergism. The second strain tested in this fashion showed no difference in the rate of killing between the combination and cephalothin or methicillin used alone.

Against a large inoculum of a methicillin-sensitive strain of *Staphylococcus aureus*, the kanamycin/cephalothin combination, in concentrations easily attainable in the blood stream, shows greater bactericidal activity than either agent used alone.

In these studies of 10 methicillin-sensitive strains of *Staph. aureus* there were no evidences of antagonism. Since cephalothin and kanamycin are bactericidal in different ways, it would be predicted that there would be no antagonism and that synergism might occur.^{5,6}

On the basis of these tests, it seems reasonable to consider using the kanamycin/cephalothin or kanamycin/methicillin combinations when confronted with a life-threatening staphylococcal infection. If disc tests show sensitivity to methicillin, the kanamycin may be stopped, although some experts prefer the combination in endocarditis, regardless of sensitivity to methicillin. If

the infecting strain is methicillin-resistant, the combination could be used until appropriate *in vitro* tests confirm its efficacy.—I am, etc.,

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Dysmenorrhoea

SIR,—Mr. A. Davis (11 November, p. 357) supports Muir's hypothesis that dysmenorrhoea results from myometrial ischaemia due to hypercontraction of the uterus, but this view is not supported by the studies of Wilson and Kurzrok.¹ Severe ischaemia of the uterus often occurs during the early hours of the puerperium and is not associated with pain.^{2,3} Pain indistinguishable from dysmenorrhoea can be provoked in all women by means of chemical, mechanical, and electrical stimulation of the cervix uteri. A simple and precise method for measuring the critical electrical stimulus which when applied to the cervix causes pain was described in your columns.⁴ If these results are confirmed a foundation for dysmenorrhoea will be established.

A lowered threshold to pain arising in the uterus does not mean, as Mr. Davis suggests, that "it's all up here." He is well aware that but a small proportion of signals arising in the periphery reaches consciousness, for there are many "censors" in the nerve pathways concerned. The operation of these censors can be affected either way by impulses both from the higher centres and from the periphery. Further, the actual cells in the apperception area can similarly be affected. There is no need to stress the point that it is the destination of the signals which determines their message. Experimental studies^{5,6} show that the effects caused by stimulating the hypogastric nerve vary with the hormonal state of the subject.

Such a concept would explain why the same individual can have both painful and painless periods, the degrees of intensity of the pain, why women complaining of severe dysmenorrhoea may have painless periods when admitted to hospital for investigation, as well as the undoubted benefit derived from the varied and multitudinous methods of treatment, ranging from exercise, hygiene, and spinal manipulation to presacral neurectomy. It would also explain why any and all of these treatments may prove unavailing.—I am, etc.,

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Minimal Inhibitory (M.I.C.) and Minimal Bactericidal Concentrations (M.B.C.) Obtained with Ten Methicillin-sensitive Strains of *Staphylococcus Aureus* against Kanamycin, Cephalothin, and the Kanamycin/Cephalothin Combination

Strain	Antibiogram*	Kanamycin		Cephalothin		Kana/Ceph	
		M.I.C. $\mu\text{g./ml.}$	M.B.C. $\mu\text{g./ml.}$	M.I.C. $\mu\text{g./ml.}$	M.B.C. $\mu\text{g./ml.}$	M.I.C. $\mu\text{g./ml.}$	M.B.C. $\mu\text{g./ml.}$
2994	P	32	32	<0.25	0.5	<0.25/0.25	0.5/0.5
3024B	Ch, T	64	128	<0.25	0.5	<0.25/0.25	0.5/0.5
3076	P, E, S, Ch, T	64	64	<0.25	4	<0.25/0.25	4/4
2572	P, Ch, T, K	>128	>128	<0.25	0.5	<0.25/0.25	0.5/0.5
1893	P	32	32	0.5	1.0	<0.25/0.25	0.5/0.5
2529B	P, S, T	16	16	<0.25	0.5	<0.25/0.25	<0.25/0.25
2024	P, T	128	128	<0.25	0.5	<0.25/0.25	0.5/0.5
2560	Sensitive to all	32	64	<0.25	0.5	<0.25/0.25	<0.25/0.25
2562	P	32	32	<0.25	1.0	<0.25/0.25	0.5/0.5
2576	P	16	64	<0.25	1.0	<0.25/0.25	0.5/0.5

* Refers to antibiotics to which the strain is resistant on testing with high concentration discs according to the method of Bauer et al.⁴. Antibiotics tested were: Penicillin G (P), Erythromycin (E), Streptomycin (S), Chloramphenicol (Ch), Tetracycline (T), Kanamycin (K), Cephalothin (C), and Methicillin (M).