or to erythromycin emerged during or after that trial, though lincomycin-resistant *Staphylococcus aureus* appeared and became fairly common in the unit during the trial. Later, when lincomycin was no longer used, lincomycin-resistant staphylococci became scarce and soon disappeared.

On 18 December 1967 erythromycin-resistant *Str. pyogenes* was isolated from the burns of a patient who had been treated with erythromycin. This organism was sensitive to lincomycin, but *Str. pyogenes* resistant to lincomycin as well as to erythromycin was soon isolated from the burns of this patient and of other patients in the ward. Between 18 December 1967 and 22 February 1968 seven patients showed infection of burns with *Str. pyogenes* resistant to erythromycin (9 isolates), or to lincomycin (2 isolates), or to both lincomycin and erythromycin (22 isolates). All but one of these strains were also resistant to tetracycline. A selection of 13 of these strains tested for serotype proved to be of type 12 (the strains reported by us in 1959 were of types 3 and 14). From the same patients 23 strains of *Str. pyogenes* were isolated which were also resistant to tetracycline but sensitive to both erythromycin and lincomycin; two of these strains which were tested for serotype were of type 12. Tests showed considerable variation in the degree of resistance of the streptococci to erythromycin and lincomycin, but some were highly resistant to both antibiotics (minimal inhibitory concentration over 100 µg./ml.). The resistant strains were resistant also to oleandomycin and to spiramycin. On storage of culture these strains, like those isolated in 1959, reverted to sensitivity. All these infections responded well to a course of oral cloxacillin.

It is hard to explain the emergence of lincomycin-macrolide-resistant variants of *Str. pyogenes* after a very long period when they were not found in spite of continuous opportunities for their selection. Something like it happened with the widespread emergence of neomycin-resistant staphylococci of one type several years after the introduction of neomycin.^{2,3} Unlike the outbreak described at Roehampton, the one in Birmingham could not be attributed to the use of lincomycin, since lincomycin had not been used for several years; nor has lincomycin-resistant *Staph. aureus* been isolated in this unit for a long time, though erythromycin-resistant strains are very common. As the outbreaks in Roehampton and in Birmingham were due to streptococci of different types, it would seem that this rare mutation appeared independently and almost simultaneously in two places, which must be considered a remarkable coincidence. The coincidence may be associated with a simultaneous increase in the use of these antibiotics in both units; in Birmingham erythromycin was introduced during the past year for prophylaxis against tetanus in the non-immunized. An alternative hypothesis is that transferable resistance has appeared in these streptococci through contact with a lincomycin-resistant or macrolide-resistant organism of different species that was not previously present but is now becoming widespread. The hypothesis is attractive, too, because the observed instability of lincomycin resistance and macrolide resistance of the streptococci resembles that which is known to occur in certain forms of transferable resistance.⁴ So far, however, we have had no success in attempts to transfer resistance to a sensitive *Str. pyogenes* of type 12 by growing it in culture together with an erythromycin-resistant *Staph. aureus* originally isolated from the same burn as the streptococcus—a burn

from which macrolide-resistant *Str. pyogenes* had also been isolated. A possibly parallel phenomenon occurred some years ago, when resistance to the newly introduced erythromycin did not emerge until eight months after the start of a controlled trial of the antibiotic in burns. Within a few days of this emergence, however, staphylococci in the ward of several different phage types were found to be resistant to erythromycin.^{5,6}

Like Drs. Kohn, Hewitt, and Fraser, we are worried about the possible risks of macrolide-resistant *Str. pyogenes* infection in patients sensitive to penicillin, should such strains become common (which seems improbable in view of the lability of resistance). It is important to test the sensitivity of *Str. pyogenes* isolated from burns and to avoid the use of macrolides or lincomycin if the strain is resistant to these agents. If the macrolide-resistant strain is sensitive to tetracycline this is the antibiotic of choice for a penicillin-sensitive patient, since it is highly effective in removal of streptococci, and there is only a very small risk of resistance emerging in the strain for which treatment is being given.^{5,7} If the streptococcus is resistant to tetracycline too, cephaloridine may prove to be the most suitable antibiotic for a penicillin-sensitive patient.

We wish to thank Dr. M. T. Parker and the Central Public Health Laboratory for typing these strains of *Str. pyogenes*.

—We are, etc.,

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Extended Family

SIR,—As a doctor who for the last four years has spent the better part of two weeks each month on medical safaris in Kenya, I was interested in the remarks made in your leading article "Extended Family" (4 May, p. 253).

As you point out, the shortage of doctors in Africa is accentuated by the tendency for doctors to congregate in the larger towns, whereas by far the greater part of the population of tropical Africa lives in the rural areas. Perhaps it is not realized in Britain that one of the reasons for this state of affairs is that a university education creates a far wider cultural gap between the graduate and the countryman in Africa than it does in Europe. This cultural estrangement tends to be further increased by the contents of the medical curriculum, which directs the student's gaze, not to the medical circumstances and situations of rural Africa, but to the highly specialized conditions existing in the hospitals of the Western world. African Governments tend further unwittingly to develop this estrangement by devoting an undue proportion of their limited resources to one central

hospital, to the detriment of the many district hospitals. Consequently these hospitals, serving as they do the majority of the people, become less and less attractive to the young men who have been trained at such great expense for the specific purpose of raising the standards of health of the people.

It would seem, therefore, that if African countries are to learn to stand on their own feet medically, rather than to be the recipients of charity for an indefinite period, a considerable change of outlook all round is required. From his final year at school, and onwards, the embryo doctor needs constantly to be reminded by the substance and emphasis of his curriculum that the object of medical training is not to produce a variety of specialists, but to produce general practitioners with public health and administrative experience who will work in district hospitals and give an active lead to the medical assistants in the health centres of their districts. African Governments need to give far more attention to their district hospitals than they do at present, both in regard to staffing and equipment.

African Governments need to give as much attention to the training and use of the medical assistant category as they do to the production of the qualified doctor. These men have proved their worth over many decades all over Africa, and it will be very many decades before they can be dispensed with. The cost of their training and their salaries is within the budget of every African country, while their relatively limited education enables them to work in the rural areas over long periods with far less strain than their graduate colleagues.—I am, etc.,

London E.C.4.

W. R. BURKITT.

Changing Clinical Picture of Neurosyphilis

SIR,—The paper by Dr. R. Joffe and others (27 January, p. 211) reporting seven unusual cases of neurosyphilis does well to remind us that syphilis is a great imitator of disease, not only involving the central nervous system but all systems and in all its stages. Nevertheless, it is important to ensure that the condition producing an atypical clinical presentation is in fact due to syphilitic infection and not to some unrelated medical cause occurring in a late or latent syphilitic, or in a patient whose serological tests remain positive after treatment for syphilis.

I was asked recently to see a patient admitted with polyneuropathy. She gave a history of backache of three months' duration, with gradual increasing loss of power of legs and arms. The results of relevant tests were: Blood—venereal disease reference laboratory (V.D.R.L.) positive; cerebrospinal fluid—Wassermann reaction positive; protein 300 mg./100 ml.; and 30 mononuclear cells.

Our records showed that in 1947 this patient had received several courses of penicillin injections for a syphilitic infection in the secondary stage, and the cerebrospinal fluid in 1948 was normal, although blood serology remained and was still positive when last examined in 1963. Anti-specific treatment was not advised, and the patient's symptoms gradually responded to steroids. Examination of cerebrospinal fluid four weeks later showed: cells to be less than 1; protein 200 mg./100 ml.; Wassermann reaction positive; *Treponema pallidum* immobilization (T.P.I.), Reiter test, and V.D.R.L. all negative.

It was thought that the positive Wassermann reaction was probably a false biological result related to the increased protein in the cerebrospinal fluid, and a further cerebrospinal fluid specimen obtained four weeks later was completely normal with a negative Wassermann reaction.

Of the seven cases reported, apart from Case 5, a burnt-out tabes, and Case 7, a juvenile neurosyphilis, I would hesitate to attribute the symptoms to a syphilitic infection of the central nervous system unless the C.S.F. T.P.I. test was positive, and apparently this test was not performed in all the cases reported. Furthermore, even if the T.P.I. test is positive it is well to remember that syphilis can involve the central nervous system asymptotically. The suggestion that the "Wassermann reaction today is of even greater importance than in the past" deserves some qualification. It is well known that many diseases and conditions other than syphilis can produce positive Wassermann reactions, and if this test is relied on alone to diagnose syphilis many patients will be treated unnecessarily for this disease, and, perhaps more important, the true diagnosis may be delayed.

A 46-year-old married woman, under investigation for bilateral pleural effusion, was referred in October 1967 because serological tests performed on a specimen of her blood showed the following results: venereal disease reference laboratory, positive 1:4; Wassermann reaction, positive; Reiter test, negative. There was no historical or clinical evidence of syphilis, and a negative *Treponema pallidum* immobilization test from a further specimen of blood sent for examination confirmed that the positive Wassermann reaction and V.D.R.L. tests were due to false biological reactions.

Many V.D. clinics nowadays, when investigating difficult diagnostic cases, use the V.D.R.L., W.R., and Reiter tests as a screening procedure, and then confirm or refute the diagnosis of syphilis on the result of the T.P.I. and/or fluorescent treponemal antibody test.—I am, etc.,

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BASIL LEVY.

Oral Contraceptives and Thromboembolic Disease

SIR,—The articles by Drs. W. H. W. Inman and M. P. Vessey, and M. P. Vessey and Richard Doll (27 April, pp. 193 and 199) concerning the increased incidence of venous thrombosis and embolism in women seem to indicate that oral contraceptives are more dangerous than other forms of contraception and should not be prescribed unless absolutely necessary.

However, it has been my impression that the incidence of carcinoma of the uterine cervix is much less in those women who have been taking an oral contraceptive. I think that it might be of considerable interest to compare statistics of carcinoma of the cervix in these same groups of women to see if their overall incidence of significant disease (vascular and cancer) might actually have been lower than expected, because there was far less cancer in this group.—I am, etc.,

JOHN P. CANBY.

Consulate General of the United
States of America,
Melbourne, Australia.

Smoking, Sputum, and Lung Cancer

SIR,—It has been pointed out to me that a difference in the prevalence of lung cancer between those reporting and those not reporting persistent respiratory symptoms (23 March, p. 732) might be attributable substantially to differences of age distribution. This is because respiratory symptoms might be expected to be reported more frequently by older individuals among whom the prevalence of lung cancer is greater.

In preparing the data for publication the available age range had been divided into those aged 40 to 59 years and those aged 60 years and over, and an examination of this division seems to indicate that the differences in prevalence of lung cancer between those with and those without chronic sputum production were too great to be accounted for by

differences in age. However, the data have been re-examined, using a finer (quinquennial) age distribution, and age-standardized prevalences have been calculated for those with and for those without chronic sputum production within each smoking category.

The Table shows actual and age-standardized prevalences of lung cancer, as well as the ratio between the rate for those with and the rate for those without chronic sputum production, both for the actual prevalence rates and the standardized prevalence rates. It will be seen that, although standardization has reduced the extremely high ratio of the prevalences in those with and those without chronic sputum among the ex-smokers and pipe smokers, the reduction in the ratios among the cigarette smokers is

trivial, and in one consumption category the ratio is in fact increased.

The conclusion, therefore, would seem to be that any differences in prevalences of lung cancer between those with and those without chronic sputum production is substantially due to differences other than age.—I am, etc.,

J. RIMINGTON.

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St. Thomas's Hospital,
Stockport, Cheshire.

Record Sales of Cigarettes

SIR,—I am encouraged by Dr. E. H. L. Harries (2 March, p. 576) and by the publication of two recent reports to comment further on the subject of smoking.

On 22 February the *Daily Telegraph* reported: "Record sales in Britain last year of 119,100 million cigarettes." A week later came the report: "British fire losses reach new peak—£90,000,000—10% higher than in 1966." (*Times of Malta*, 29 February).

It is apparent from the first report that the findings of top scientists of the Medical Research Council, checked repeatedly and independently, that cigarette-smoking is highly carcinogenic and responsible for a great many other morbid states, have been, for all practical purposes, thrown on the scrap-heap. Can it be doubted, moreover, that the astronomical number of naked lights and smouldering cigarette butts which derive from smoking are mainly responsible for the figure in the second report?

And, unless I am utterly wrong in my basic thinking, we of the medical profession are 100% responsible for this appalling state of affairs, because tobacco-smoking is a disease, a drug addiction, which, like opium smoking, is wholly preventable, and it is our sole function to eliminate disease.—I am, etc.,

Marsascala,
Malta.

LENNOX JOHNSTON.

Recurrent Tetanus

SIR,—The extreme rarity of tetanus recurring or relapsing was stressed by Mr. S. Y. D. C. Wickramasinghe and Dr. Malinie Fernando (2 December 1967, p. 530), and rightly so. This prompts me to report a case from my records.

A 20-year-old male was admitted to the hospital at Calicut, India, in September 1963 with an unmistakable clinical picture of tetanus. A chronic ulcer near the left ankle was thought to be the route of infection. *Clostridium tetani* was demonstrated in a swab taken from the ulcer.

Rates of Lung Cancer per 1,000 Males aged 40 years or more

	Non-smokers		Cigarette Smokers								Ex-smokers		Pipe Smokers		All Subjects	
			1-9		10-19		20 +		All							
	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S
Actual rates ..	0	0	0.73	6.25	0.91	4.96	1.87	5.01	1.30	5.09	0.24	10.13	0.97	13.76	0.84	6.29
Age-standardized rates	0	0	0.64	4.63	0.90	5.81	2.67	4.66	1.73	5.96	0.53	9.26	1.77	12.82	1.31	7.84
Ratio $\frac{(S)}{(NS)}$ actual rates ..			8.333		5.451		2.679		3.915		42.208		14.186		7.488	
Ratio $\frac{(S)}{(NS)}$ standardized rates			7.198		6.418		1.743		3.441		17.468		7.231		5.971	

S denotes volunteers claiming daily sputum for a minimum of 5 years and NS denotes those not claiming this symptom.