In the case of children undergoing preliminary skin-grafting for burns or scalds, intubation is rarely necessary. At the Fleming Memorial Hospital for Children, Newcastle upon Tyne, such cases are given "nepenthe" intramuscularly or orally two or three hours before operation, and a blood transfusion is set up; apart from the nepenthe, no further sedation is given unless the child is exceptionally apprehensive. During the operation a light anaesthetic with nitrous oxide and oxygen plus a minimal amount of halothane given intermittently is all that is required. Post-operative recovery is extremely rapid, so that the problems of aftercare and feeding are made much easier from the nursing point of view.—I am, etc.,

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PHILIP AYRE.

Toxicity of Methaqualone

SIR,—A statement to the effect that serious toxic effects have not been reported for methaqualone appeared in your "To-day's Drugs" section (January 12, p. 107). It should be noted, however, that a record of toxicity from this drug appears in the July, 1962, issue of the Registry on Blood Dyscrasias of the American Medical Association Council on Drugs.

The Registry lists one case of aplastic anaemia with pancytopenia due to methaqualone. In addition there are listed two cases of thrombocytopenia due to ethinamate.—I am, etc.,

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Pulmonary Hypertension after Pregnancy

SIR,—It is unfortunate that the second leader in the redesigned *Journal* (January 5, p. 3) on "Pulmonary Hypertension after Pregnancy" should omit to mention an important cause of this condition. The article rightly emphasizes the mechanism and diagnostic features of thrombo-embolism, but it fails to indicate that following pregnancy, whether full-term, abortive, or molar, the thrombo-emboli may consist of or may contain trophoblastic tissue.¹⁻⁵ This embolic trophoblastic tissue may be choriocarcinoma or histologically benign hydatidiform mole, or an intermediate form. Any of these neoplastic forms if left untreated in the pulmonary arteries can kill the patient.

Since the amount of trophoblastic tissue in a particular pulmonary thrombus may be very small it can be missed at necropsy. The absence of a typical tumour mass in the pelvis may add to the diagnostic mimicry of ordinary thrombo-embolism. The source of the emboli in these cases is trophoblastic tissue lying in the uterus or in pelvic veins, where its presence may also be hidden by thrombus. Such patients may have few if any gynaecological symptoms, pelvic examination may show no abnormality and uterine curettings are normal.

Clinical and radiological examination of the cardiopulmonary system will not distinguish these two forms of thrombo-embolism, nor will the most sophisticated cardio-respiratory function studies. This is not surprising since the functional disturbance is identical in both forms. The distinction between the two forms is important therapeutically. Those due to trophoblastic disease do not respond to anticoagulant therapy alone, but they do respond to specific cytotoxic therapy.

The trophoblastic cases can only be recognized by testing for chorionic gonadotrophin. This can be done initially by the routine pregnancy tests, and if pregnancy has been excluded a valid positive test establishes the

presence of trophoblastic disease. If negative, trophoblastic disease is still not excluded, since the amount of hormone being produced may be insufficient to give a positive test. In these cases sensitive quantitative tests for chorionic gonadotrophin must be performed. Similar sensitive and quantitative assays are essential for the proper management and treatment of all forms of abnormal trophoblastic proliferation. It is not known how frequently the trophoblastic form of post-pregnancy thrombo-embolism occurs, but, like other things, it will only be found if it is looked for.—I am, etc.,

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D.N.A. and the Chromosomes

SIR,—It is with great interest that I have read papers by Drs. N. B. Atkin and B. M. Richards concerning the D.N.A. content of cervical carcinoma. I am afraid, however, that their latest preliminary report (December 1, p. 1445) will be a source of confusion with respect to the karyology of cervical cancer.

The terms "diploid" and "tetraploid" as used in this article are not consistent in meaning with previous, comparable studies based on precise chromosome analysis. To my knowledge there is no microspectrophotometric technique which allows the accurate determination of chromosome number, particularly when working with old histological sections as the authors describe. In cancerous cells there is only a close relationship between D.N.A. measurements and chromosome number.¹ Based on my own observations, I will estimate that less than 10% of the tumours in the diploid class actually have exactly 46 chromosomes. Yet it is the clear implication of the article, as evidenced by the editorial comment in the same issue, that these tumours are diploid; that they have 46 chromosomes.

It is to be hoped that in the future the author will avoid the term "diploid" when referring to those cancerous cells whose D.N.A. content lies in the range of normal cells. I have also noted that the conclusions of this preliminary report are contrary to De's observations,² which were based on chromosome analysis.—I am, etc.,

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Ataxic Neurological Syndrome

SIR,—As Dr. D. R. W. Haddock and his colleagues point out in their account (December 1, p. 1442) of an ataxic syndrome in Tanganyika, prevailing conditions in East Africa may lead to further cases and should be carefully watched for. Such multiple neuropathies of obscure aetiology are probably more common than is realized. The writer reported¹ an outbreak of pellagra in Lake Province, Tanganyika, with evidence of multiple deficiencies of the vitamin B complex. One case besides having an atrophic glossitis, styes, and dyssebacea (see

picture) responding to riboflavin had also marked ataxia with loss of co-ordination, light touch, and vibration sense in the legs. All the skin and mucous membrane changes rapidly cleared, but despite intensive B-complex vitamin therapy the neurological signs remained with neither amelioration nor deterioration for at least three years after the original admission. Money's three cases in Kampala² of "obscure funicular myelopathy" had certain features in common with those now reported. Diminished visual acuity in the absence of optic disk changes, unaffected by thiamine or riboflavin but apparently responding dramatically to vitamin B₁₂ injections (50 micrograms daily for one week), was reported³ in three patients at Mwanza with no other neurological signs.

Investigation of future cases should include closer examination of the diet, therapeutic trial with specific vitamins of the B complex, examination for scotomata,

contraction of the visual fields, measurement of vitamin B₁₂ in the blood, and riboflavin, thiamine, and N-methylnicotinamide in the urine.—I am, etc.,

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Tuberculosis in the Elderly

SIR,—The considerable decline in the incidence of pulmonary tuberculosis has exposed many complex problems, and, as indicated in your leading article (December 29, p. 1737), not the least important is the unabated significance of the disease in middle-aged and elderly men. Control is prejudiced by uncertain knowledge, but the report of the Joint Tuberculosis Council, with its identification of the abrupt clinical course in many of these patients, has great interest.

During the mass radiography campaign in Glasgow (1957), unfortunately but unavoidably because of the excessive demands of the occasion, tuberculin tests were not undertaken in conjunction with the pulmonary radiograph, but it was possible to determine "radiological" attack rates in those patients notified during 1958 whose radiograph was normal in 1957. The miniature films were rescruited by dual independent examination, and, while agreement with the interpretation of the medical directors (1957) was good, a film was only accepted as normal (no primary or reinfection lesion) where there was agreement between all three readers.

Alternate notifications (1958) were examined; 98 men over 45 years (24% of the total notifications in that age group) whose disease was identified in 1958 had a normal radiograph in 1957 (an annual "radiological" attack rate of 0.9 per 1,000 of those judged normal in 1957); in men aged 15–24 the figures and rates were 72 (52% of the total notifications in the age group and an attack rate of 1.2 per 1,000).

The quality of the disease in each group is recorded in the following Table:

M.M.R. Campaign			
All Clear 1957			
Pulmonary Tuberculosis 1958			
	Males 15–24		Males over 45
		%	%
No infiltration	..	10.3	4.9
Unilateral 1 zone	..	50.0	37.7
Unilateral 2–3 zones ..	..	23.5	21.3
Bilateral 2–3 zones ..	..	8.8	24.6
Bilateral 4–6 zones ..	..	7.4	11.5
<i>Bacteriology</i>			
Positive	..	51.5	43.8
Negative	..	38.2	43.8
No information	..	10.3	12.4

The results are consistent with the substantial observations from the Joint Tuberculosis Council that in many of these middle-aged men symptoms are of recent development and suggest the intriguing probability that the disease is "primary" in character within the context that its incidence is highest in those whose allergy has been dissipated.

The contribution made to the 1958 notifications in Glasgow by men over 45 years whose x-ray was normal in 1957 was therefore considerable. The evidence accumulates, as you suggest, that a significant, although not necessarily dominant, incidence of the disease develops in men who have no previous radiological evidence of primary or reinfection tuberculosis, but unfortunately destroys the familiar contention that a single x-ray survey of men over 45 would identify all or most of those at risk.

The results of the 1958 survey determined an approach to the local medical committee in Glasgow who sponsored a scheme which had as its purpose the annual x-ray of all men over 45 on the lists of the general practitioners (the "Over 45 Scheme"). The scheme was at once a success but also, alas, a failure; a success in that an incidence of 10.8 per 1,000 of active, previously unknown, pulmonary tuberculosis was discovered, but a tiresome failure in that only 0.7% of the selected group were referred for examination.

The eradication of tuberculosis—an attainable goal if not bunkered by the monetary or spiritual economy of regional boards—must depend on intensive case detection and on techniques based on a more exact knowledge of the natural evolution of the disease. The failure of our Over 45 Scheme was not, I imagine, determined primarily by poor co-operation, but by our