areas were within normal limits. All the "tropical transplants" tested had been in a cold climate for over five years and if they were under 40 (females) or 50 (males) showed no hypertension. Twelve such persons were checked and one 10-year-old girl showed hypercholesterolaemia and a uric acid level of 9·5 mg/100 ml, which was considered to be unrelated to the environmental change.

I suspect there is a causal relationship between hyperaldosteronism and acclimatization to a sodium-leaching environment, with persistence of the hormonal conservation mechanism on transplanting to a cold climate and consequent sodium retention with its usual sequelae. One patient had a weight change overnight of up to 5 lb (2·3 kg), and this occurred every night. Radioisotope studies were entirely normal but chronic asymptomatic *Enteramoeba histolytica* infestation was found and treated successfully. No change was observed in the weight pattern. Another patient was unable to compensate so well and at present takes a daily diuretic which controls his water retention and an anti-aldosterone (Aldactazide).

Should there be any readers involved in projects dealing with these matters in a scientific way I would be happy to hear from them, as my own clinical observations and impressions lead me to the strong inclination to propose a definite syndrome of the "Indian Colonel" of the old comic stories—plethoric, irascible, hypertensive, acclimatized in youth to heavy strain on the milieu interne, and then repatriated in late middle life to a cold climate. Perhaps such a syndrome has already been described.—I am, etc.,

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Bronchospasm following Althesin Anaesthesia

SIR,—Althesin is a recently introduced steroid anaesthetic agent and as such it received considerable attention at the 5th World Congress of Anaesthesiologists in September 1972. Since then it has been taken into widespread use. While the drug has several advantages, it is beginning to become apparent that in some patients quite severe bronchospasm can complicate its use. Among others, Avery and Evans[1] reported five cases and Hester[2] one case of bronchospasm after Althesin. We would like to report the following case:

A 28-year-old 70-kg man was given an uneventful anaesthetic for examination of his knee. The technique used was that of thiopentone induction, intubation using succinylcholine, maintenance on intermittent positive pressure ventilation with alcuronium, and reversal of the muscle relaxant at the end of the operation with atropine and neostigmine in the usual way.

A few days later he was premedicated with papaveretum and hyoscine 75 minutes before the induction of anaesthesia for repair of the medial ligament of the knee. Induction was with Althesin 4 ml followed immediately by pancuronium 6 mg, and the patient's lungs were inflated with a nitrous oxide/oxygen mixture. Intubation after about a minute was followed by considerable bucking and coughing, which rapidly settled.

Over the next few minutes the lungs became more and more difficult to inflate. A further 2 mg of pancuronium was given with no effects and airway suction produced no secretions. Auscultation showed very poor air entry to all areas, and after dismissing an initial tentative diagnosis of bilateral tension pneumothorax, such had been the suddenness of onset, it became obvious that one was dealing with a severe bronchospasm. This was successfully treated by inflating the lungs with considerable difficulty using a 50:50 nitrous oxide/oxygen mixture plus 1% halothane. The spasm relaxed completely over the next 20 minutes, and the operation was concluded normally with no residual damage to the patient. A further anaesthetic using a thiopentone, nitrous oxide/oxygen, halothane regimen was carried out subsequently with no problem. It is perhaps relevant to relate that, though the patient had denied anything but the most robust health before the first anaesthetic, on further questioning later he admitted to mild asthma in childhood.

Dundee and Clarke[3] have asked for reports of idiosyncrasy to any anaesthetic agent to be reported to them in order to make a detailed evaluation of the extent of this problem, and this case has been so reported.—We are, etc.,

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J. ANDERSON
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1 Avery, A. F., and Evans, A., *British Journal of Anaesthesia*, 1973, **45**, 301.
2 Hester, J. B., *British Journal of Anaesthesia*, 1973, **45**, 304.
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Actinomycin D for Wilms's tumour

SIR,—My previous letter (17 February, p. 420) was intentionally provocative and I am pleased to see that it has stimulated the publication of results from Liverpool by Professor P. P. Rickham (14 April, p. 114), from Toronto by Dr. R. D. T. Jenkin (26 May, p. 485), and from Melbourne by Dr. T. F. Sandeman (26 May, p. 485). All these results are very impressive when compared with those from Birmingham, but it should be noted that they all quote three-year survival (unqualified), whereas the Birmingham results were for three-year survival *free of disease*. If one adds on children still alive at three years despite recurrence or metastases the results appear to be better. This is yet another way in which the comparison of results from different centres may be misleading. If all survivors are included regardless of the presence or absence of disease, the three-year results in the Birmingham region for the years 1965-9 for patients who received actinomycin D initially are increased from 6/29 to 9/29 (31%) and for those who did not receive actinomycin D they are increased from 7/17 to 8/17 (47%).

The results presented by my former colleague Dr. Sandeman are particularly striking, and though the groups were not contemporaneous I agree that his figures make it difficult to defend a controlled trial involving the omission of any initial chemotherapy. Nevertheless, the conflicting Birmingham results remain unexplained.

A number of correspondents have emphasized the importance of a centralized service for the treatment of Wilms's tumour so that the paediatrician, surgeon and radiotherapist can work as a team with a common policy and seeing a sufficient number of patients each year. With this I am in full agreement. It is probably a matter of greater importance than the use of chemotherapy. Though until 1970 there was no surgeon practising exclusively paediatric surgery in the Birmingham region, there were a number of surgeons with great experience of paediatric work. In 1965 a policy was established within the United Birmingham Hospitals whereby all children diagnosed as having Wilms's tumour were treated at one hospital by one surgeon and by one radiotherapist who also gave chemotherapy. The three-year survivals free of disease were worse prior to 1965 and the figures for 1950-64 for the whole Birmingham region are given for comparison:

Stage I	9/20
Stage II	4/15
Stage III	1/28
Stages IV and V	0/14
Stage unknown	2/5
Total	16/82

Thus the results for all stages were 19% compared with 28% for the years 1965-). It so happened that actinomycin D was first used in Birmingham at about the same time as the paediatric oncological team was set up. It is difficult to be certain which factor improved the results, but I doubt if actinomycin D had any great influence. Unfortunately, though the team was set up in 1965 the majority of children with Wilms's tumour continue to be treated at other hospitals scattered throughout the region. In the years 1965-9 the three-year survival for children treated solely at the Queen Elizabeth Hospital, Birmingham, was 5/11 (45%), for those referred for radiotherapy but who had surgery elsewhere it was 5/13 (38%), and for those treated entirely at other hospitals it was 7/22 (32%).—I am, etc.,

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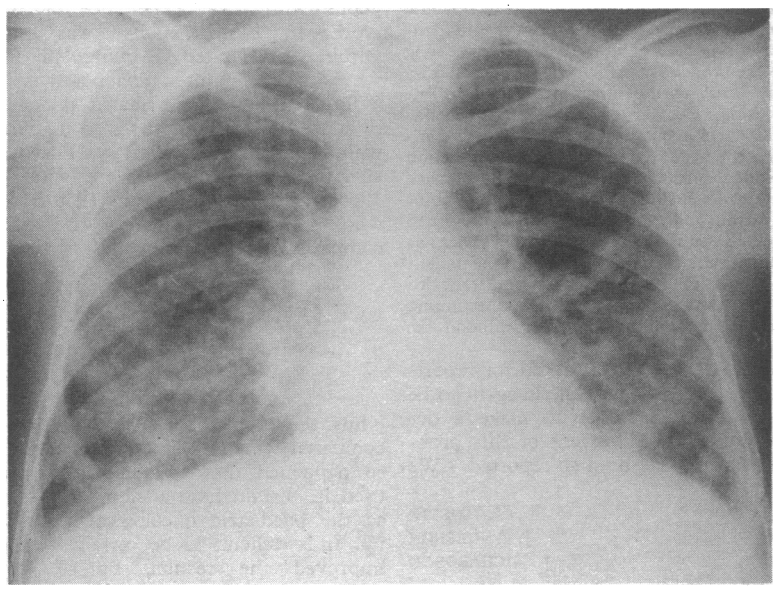
Drug-induced Respiratory Disorders

SIR,—In your leading article on this subject (12 May, p. 320) you mention especially aspirin, sulphonamides, and nitrofurantoin as causes of pulmonary eosinophilia—"an allergic manifestation in which eosinophilic infiltrations of the lung are accompanied by fever, cough, sputum, dyspnoea, and crepitations." We would like to add niridazole (Ambilhar) to the list of drugs that can cause severe pulmonary sensitivity reactions. Since reporting the occurrence of this syndrome in two patients treated with niridazole in 1972[1] we have seen it develop, in varying severity, in at least 10 more patients. The following case illustrates how dangerous and serious the reaction may become if ignored.

An 18-year-old farmer was admitted for treatment of *Schistosoma mansoni* infection. He was started on oral niridazole at a dose of 12·5 mg/kg daily for 12 days; on the sixth day of treatment he developed severe dyspnoea and on auscultation there were widespread crepitations over both lungs. A chest radiograph performed next day showed widespread large scattered pulmonary infiltrations (see figure). The total white blood count was 6,200/mm³ and the eosinophil count had risen from 7% to 22%. He responded rapidly to oral chlorpheniramine. Two months later (because he was still passing live eggs of *S. mansoni*) he was restarted on oral niridazole. Within one hour of having received half a tablet he developed a severe asthmatic attack. On auscultation there was severe wheezing with widespread crepitations, and a chest radiograph showed a recurrence of scattered, rounded patches



of opacity all over the right and left lung fields. The asthmatic attack was relieved only after giving 100 mg of hydrocortisone sodium succinate intravenously.—We are, etc.,

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1 Farid, Z., *et al.*, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 1972, **66**, 119.

Propranolol and the Hyperactive Carotid Sinus Reflex Syndrome

SIR,—The hyperactive carotid sinus reflex syndrome is a physiopathological condition in which syncope, originating in the carotid sinus and mediated through a cardiac and/or a peripheral vascular effect, develops on compression of the carotid sinus. The carotid sinus syndrome is an analogous physiopathological condition but of a higher grade as it manifests itself spontaneously.[1]

The existence of a carotid sinus syndrome is a contraindication for the administration of beta-adrenergic blocking agents as these drugs inhibit sympathetic stimulation, important whenever vagal tone is increased.[2] As the existence of a hyperactive carotid reflex syndrome might also be a contraindication for any therapy with beta-adrenergic blocking drugs, all the patients from our outpatient department who are to be put under treatment with propranolol are previously tested for a hyperactive carotid sinus reflex syndrome was diagnosed. A test dose Franke's procedure.[3,4]

A 62-year-old man with grade III chronic coronary insufficiency was to be treated with propranolol in an initial daily dose of 120 mg. On compression of the right carotid sinus he was found to develop a brief syncope and marked bradycardia resulting from sinus arrest followed by junctional escapes (see fig., A). Thus a hyperactive carotid sinus reflex syndrome was diagnosed. A test dose of 2 mg of propranolol was administered intravenously as a bolus injection and 10 minutes later hyperextension of the head provoked a more prolonged syncope and a more marked bradycardia than previously. Thus the hyperactive carotid sinus reflex syndrome had been transformed into a carotid sinus syndrome after propranolol. Digital compression of the carotid sinus for a shorter period than previously provoked a much more lasting sinus arrest 15 minutes after propranolol (see fig., B).

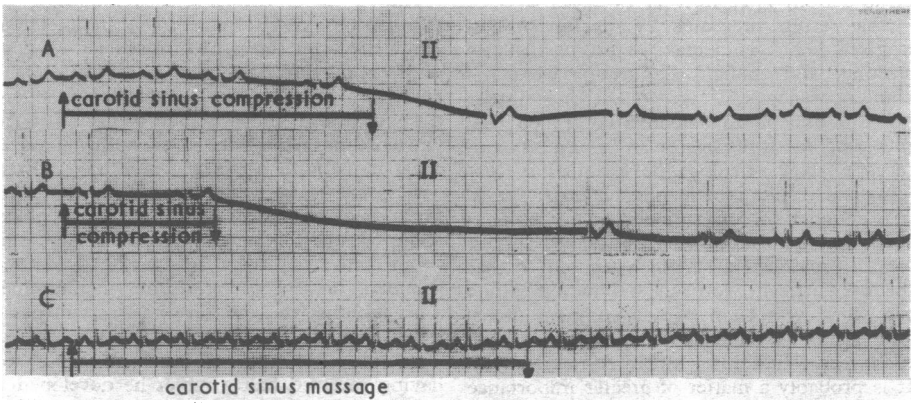
Twenty minutes after propranolol 1 mg of atropine was injected intravenously; five minutes later the right carotid sinus was massaged for several seconds. No effect was observed either on the electrical activity of the heart (see fig., C) or on the clinical condition of the patient. This last procedure and the corresponding result show the innocuity of our methods.

It is imperative to search for a hyperactive carotid sinus reflex syndrome in every patient who is to be treated with beta-adrenergic blocking drugs and this therapy avoided if the syndrome is diagnosed and the participation of a central cardiac mechanism in it demonstrated.—I am, etc.,

ARIEL J. REYES

Fundacion Procardias,
Durazno 2025,
Montevideo, Uruguay

1 Thomas, J. E., *Mayo Clinic Proceedings*, 1969, **44**, 127.
2 Isasi, E. J., Reyes, A. J., and de Bayarres, M. A., *Arquivos Brasileiros de Cardiologia*, 1969, **22**, 215.
3 Franke, H., *Deutsche medizinische Wochenschrift*, 1967, **92**, 1155.
4 Grand, A., and Lapicorey, G., *Coeur et Médecine Interne*, 1972, **11**, 265.



Electrocardiograms (lead II) from patient with hyperactive carotid sinus reflex syndrome. A. Right carotid sinus compression: sinus arrest and junctional escapes. B. Carotid sinus compression after propranolol: cardiac inhibition is enhanced. C. Carotid sinus massage after atropine: no effect on cardiac activity.

New Ideas on Vitamin D

SIR,—Professor Iain MacIntyre (14 April, p. 120) referred to our point of view regarding the role of parathyroid hormone in the regulation of 1,25 dihydroxycholecalciferol (1,25-$(OH)_2D_3$) biosynthesis. The statement which he attributed to me is at best only partially correct.

Except under the abnormal hypophosphataemic state, we believe that the parathyroid glands do play an important determining role in the regulation of 1,25-$(OH)_2D_3$ synthesis. Our experiments[1] have been completely verified by Fraser and Kodicek,[2] by Hill and Mawer,[3] and by Rasmussen *et al.*[4] If animals are made hypophosphataemic, the parathyroid hormone is no longer required to stimulate 1,25-$(OH)_2D_3$ synthesis.[5] Of course we do not know the molecular events involved in the regulation, nor does anyone else to my knowledge. Though it is possible that the parathyroid hormone may stimulate 1,25-$(OH)_2D_3$ synthesis by changing ionic concentrations in the renal cell, the fact remains that under normal physiological circumstances (excluding hypophosphataemia), as far as we can presently surmise, the parathyroid hormone plays a major role in the stimulation of 1,25-$(OH)_2D_3$ synthesis. We know of no other points of view which have adequate experimental support.—I am, etc.,

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2 Fraser, D. R., and Kodicek, E., *Nature New Biology*, 1973, **241**, 163.
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Malignancy of Bronchial Adenoma

SIR,—With reference to your leading article on this subject (19 May, p. 378), there must be others like myself who were surprised to read that bronchial adenomas are white. Possibly some are in some circumstances,