Measles is different from other virus diseases in that the susceptibility of the human species is extreme, but the adequate resistance of the healthy human being towards this aggression is no less striking. G. S. Wilson[1] remarked. "We have therefore the striking anomaly of a high degree of immunity to death associated with an apparent lack of immunity to attack. In this respect, as in certain others, measles is unique." This is so true of the Indian situation, where one encounters a distinct difference between the attacks of measles in high socioeconomic groups with that of lower socioeconomic groups, the attacks being much more severe in malnourished children with lowered resistance.

In my detailed study of 336 cases of measles from 1964 to 1966 at Hyderabad, India, 54% had pulmonary, bronchitic, and laryngeal infections; 37% had diarrhoeal illnesses (of which about 10% had associated rickets, whooping cough, mumps, and otitis media); and 2% had classical measles encephalopathy. One child had cutaneous and mucosal purpura accompanied by haemorrhages and distressing dyspnoea with predominant neurological and respiratory signs (the so-called "black measles"). In 7% there was *x*-ray evidence of reactivation of dormant tubercular focus with negative Mantoux test (an anergy, on average lasting 4-6 weeks). One child had classical tropical eosinophilia with primary complex and a severe attack of measles. In 6% hypoproteinemia was precipitated and the convalescence was prolonged with a ssociated diarrhoea. These secondary bacterial infections are doubtless due to the epithelial alteration (in the epithelium of the mouth and the respiratory and digestive tract) and to humoral and immunological disturbances.

Among the clinical manifestations, apart from the prodromal symptoms, photophobia is quite marked and blotched, oedematous, weepy facies is very characteristic of measles. Cough is dry, incessant, and tiring. Post-measles pigmentation is a constant feature (suggesting intracutaneous capillary haemorrhages) which invariably shows desquamation on face and trunk. Lastly, one has to take into cognizance the recently known problem that injection of an inactivated measles virus vaccine[2] creates a predisposition to serious clinical symptoms in cases of subsequent natural infection. The pathogenesis of this phenomenon so far remains obscure. These and many other factors are reminders that measles deserves much more vigilant management today.—I am, etc.,

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## Analgesics and the Kidney

SIR,—Your leading article (21 July, p. 123) might be taken to imply that renal papillary necrosis is the essential feature of the renal damage associated with analgesic abuse. However, Burry *et al.*,[1] whose observations you commend, found this lesion in no more than 20 of 69 patients who had taken at least 2 kg of phenacetin. Other renal lesions were found in 33 patients and for some of these lesions the statistical correlation with the cumulative dose of phenacetin was comparable to that of renal papillary necrosis (Burry *et al.*, table IV).

Since it is death of tissue in mass, renal papillary necrosis is an acute lesion, even when it develops in a patient who has been taking analgesics for many years. Only one zone of demarcation can be found between living and necrotic tissue, and evidence of previous, less extensive necrosis is not found in the necrotic papilla. In animals[2] renal papillary necrosis is not invariably followed by cortical damage, and where this supervenes an additional pathogenic factor is implicated. This finding is not restricted to experimental animals. We are building up a number of case histories in which analgesic-associated renal papillary necrosis is not accompanied by consequential cortical scarring. Other findings which suggest that renal papillary necrosis is not the sole primary lesion of analgesic renal damage are the incidence of neoplastic change[3] and the improvement or stabilization in the patient's condition when analgesics are stopped.[4]

It is extremely difficult to produce experimental renal papillary necrosis with analgesics, their metabolites, or related compounds. Many of these substances are nephrotoxic, some intensely so, but the site of the lesion is the proximal convoluted tubule.[5 6] The tubular necrosis is sometimes followed by a severe chronic interstitial inflammatory reaction.[7] Because acute necrosis of proximal convoluted tubules is produced by salicylates[8 9] there is some doubt that the renal papillary necrosis inconstantly produced by aspirin in long-term feeding experiments[10 11] represents a chemotoxic effect, and in any case epidemiological studies indicate that these experiments are not directly relevant to chemical analgesic renal damage.[12]

While the frequent incidence of renal papillary necrosis distinguishes the analgesic renal syndrome from other forms of nephrotoxic renal damage, the evidence we have adduced does not, in our view, suggest that it is the primary lesion. If we are correct, the retention of renal papillary necrosis as the criterion of the analgesic renal syndrome will continue to falsify concepts of its natural history and to obscure the chain of factors between cause and effect. There has been remarkably little success achieved by 20 years' investigation of what at first semeed a straightforward problem. Perhaps it would be opportune to reconsider the position and, as a first step, endeavour to define the natural history with a degree of precision closer to the standards of experimental medicine.—We are, etc.,

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## Irradiation Treatment of Rheumatoid Arthritis

SIR,—Your leading article on this subject (4 August, p. 247) certainly covers the English literature, but makes no mention of the vast Continental series. For instance, Menkes *et al.*[1] describe the results of 1,240 treatments in a whole variety of joints, with an overall improvement rate of 88% at one year, and with this number of treatments they are able to provide much in the way of analysis of favourable and unfavourable situations.

Your statement that "yttrium-90 appears to be more effective and less dangerous than Au-198" must surely be in the context of the knee or major joints only, as the very powerful beta emission of yttrium-90 has produced radionecrosis of the skin when used in finger joints,[1] and Virkkunen *et al.*,[2] cited by you, noted radiation burns after using gold-198 in finger joints. The French workers now use yttrium-90 in the knees, rhenium-186 in other large joints, and erbium-169 in finger joints.[1 3 4]

One other point of importance has been the renewed emphasis on resting or immobilizing the joint after injection. You mention the reduction in chromosome damage with immobilization of the knee after injection, but there is also a very definite reduction in the extra-articular spread of radiocolloid, especially to lymph nodes, with rest and immobilization.[5] Others have shown that the colloid is better retained in the treated joint with bed rest.[6] —I am, etc.,

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## Survival in Coalworkers' Pneumoconiosis

SIR,—In a recent article Dr. A. L. Cochrane (2 June, p. 532) suggests that "there is no appreciable disability or loss of expectation of life (in 20 years) associated with any category of coalworkers' pneumoconiosis except categories B and C"—that is, the most severe. He concludes this from a 20-year follow-up of the male population of the Rhonda Fach, but unfortunately there seem to be several points which are open to dispute.

Dr. Cochrane gives the percentage of the original population surviving 20 years, broken down by age and by category of

pneumoconiosis. He judges that category A has a similar survival rate to less severe categories, but his method of measurement may disguise the effects of the disease. A pneumoconiosis sufferer may perhaps change from face work to surface work or slow down his life in general. He may therefore survive longer, but only at the expense of loss of earnings and enjoyment of life. Observed survival rates and expectation of life may then be similar to those of non-sufferers, but only through this slowing down.

There is also some difficulty about the actual data presented. One would expect the first age group, probably also the second, to survive 20 years even with category A pneumoconiosis. Survival rates for these groups should not lend weight to conclusions for older groups, and since the last age group has so few subjects in many of its categories, it can be discarded. The evidence appears to be shrinking.

The 55-65-year age group does show a significantly lower survival rate in category A; at 15% it is lower than in the less severe cases, which range from 22 to 30%. Also the remaining two age groups display some strange variations. In the 45-55-year group there is a low (50%) survival rate for miners and ex-miners without pneumoconiosis and a very high rate (67%) for category 3. With such variation within the group it seems difficult to conclude that category A has the same survival rate as the other, less severe categories. In the 65-75-year age group category A shows the highest survival of all at 24%, which is strange when there does seem to be a downward progression for the other categories.

My final point is that the figures might also be explained in terms of the substantial reduction in the manpower of the coal industry since 1951. If a significant number of those in category A in 1951 left mining, they would have lived longer; the survival rate for category A may thus appear similar to those for less severe categories, but again the effects of the disease may be disguised.

In conclusion, Dr. Cochrane's "reasonable suggestion" seems at best premature, and at worst positively misleading. There are serious doubts as to whether his figures support his views, and so further evidence is required. —I am, etc.,

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## Edrophonium in Diagnosis of Cholinergic Crisis

SIR,—I think Dr. C. W. H. Havard (25 August, p. 439) underestimates the hazards of injecting 10 mg edrophonium intravenously as a diagnostic test of cholinergic crisis in myasthenia gravis. The possibility of a cholinergic crisis usually arises in severely affected patients taking more than 20 anticholinesterase tablets daily, who become suddenly weaker over a matter of hours. If this weakness is due to undertreatment, 2 or 3 mg edrophonium is usually enough to obtain an improvement, and the absence of improvement after 5 mg (except in the few patients already known to need a higher dose) is good evidence that the sudden weakness is not due to underdosage. Giving 10 mg edrophonium to a patient who is already close to paralysis from overdosage may cause failure of respiratory and bulbar muscles, combined with an outpouring of saliva and bronchial secretions, that can asphyxiate him. Even a patient who is underdosed, so that edrophonium improves his respiration, may expire two minutes later when the edrophonium wears off leaving the chest full of seretions. In these circumstances I think atropine should always be given intravenously before the edrophonium test and facilities for immediate endotracheal intubation must be at the bedside. These complications may theoretically be "unlikely," but even in units in which myasthenia is frequently seen they do occur.—I am, etc.,

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## Sterility after Vasectomy

SIR,—Two recent reports have added to the controversy of post-vasectomy management. On the one hand, Professor J. P. Blandy and Mr. A. Halim (14 July, p. 110) have stressed that surgeons should be cautious in their interpretation of the findings of occasional non-motile spermatozoa in semen examined after this procedure, since vital staining has shown that not all immotile sperm are dead. On the other hand, Mr. D. Urquhart-Hay (18 August, p. 378) in describing the effect of irrigating the vas with a 1:1,000 solution of euflavine, has reported that semen analysis is unnecessary since no motile sperm were found in specimens examined by light microscopy.

Professor Blandy and Mr. Halim also refer to the fact that sperm in frozen semen used for artificial insemination are never motile after thawing. However, it may be incorrect to draw a direct analogy with the situation after vasectomy, for in those individuals who have occasional non-motile spermatozoa present for months afterwards the numbers present are so few that accurate total counts are not worthwhile. The question raised is whether occasional immotile spermatozoa, dead or alive, have a practical fertile potential when present in such small numbers, since the association between male infertility and oligospermia is accepted.

It is still our contention that this finding is likely to be of little significance, provided the operation has been performed correctly and the procedures undertaken have minimized the possibility of recanalization occuring, since we are unaware of pregnancies resulting from men who have failed to provide specimens at three months for analysis, or from a group of men who had an occasional non-motile spermatozoon reported for several months and then abandoned contraceptive precautions. It was these aspects that prompted the provocative suggestion[1] that post-vasectomy counts may be unnecessary provided 20 ejaculations have occured, since there is an association between the frequency of emission and the number of sperm present.[2] This policy is rational if it can be ascertained that the number of sperm present following this are invariably so few that total counts are not significant and that any sperm present are not effectively fertile in such numbers.

As far as irrigation of the vas is concerned, we have previously reported[3] that this procedure, using distilled water, effectively reduces the number of positive counts found three months later. An extension of this study has shown that two-thirds of individuals are sterile as soon as four weeks after operation as assessed by failure to demonstrate sperm in a plain film of semen.[4] Mr. Urquhart-Hay, using euflavine, failed to show motile sperm in all specimens, examined within two hours of emission using the same technique of analysis reported in our study.[3] However, semen was not examined at set times but at varying intervals up to 158 days. The total counts reported were in excess of 20 million/mm$^3$ in 13% of subjects and above 5 million/mm$^3$ in an additional 7%, but we assume these were examined soon after the operation or in subjects who had ejaculated infrequently. Despite this, immediate sterility was claimed.

We share the caution expressed by others in considering those with excessive counts to be infertile if a reasonable percentage of immotile sperm are viable, until such time as further studies fail to show pregnancies resulting following this procedure, or until the significance of immotile viable spermatozoa in varying numbers is demonstrated.

The value and acceptability of vasectomy is that in general it is a simple surgical procedure, but it has obvious ilimitations in some instances if long term surveillance is considered necessary before sterility is pronounced, especially if the criteria used to assess this are based on inaccurate premises. Therefore, we still feel there is a need for interested bodies to decide on the most rational approach to post-vasectomy management.

The medicolegal implications of not performing sperm counts when a spermicidal preparation is used for irrigation are of obvious importance, for at present two consecutive negative counts are generally considered desirable. Previously, we obtained an indication that examination of a plain film of semen, rather than of a centrifuged deposit, is legally acceptable,[5] provided this is the practice of a body of responsible surgeons. If the policy undertaken by Mr. Urquhart-Hay is generally adopted by other surgeons, will this then have the same validity?—We are, etc.,

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SIR,—Mr. D. Urquhart-Hay states in his interesting paper (18 August, p. 378) that irrigation of each vas with 2·5 ml of 1/1,000 solution of euflavine destroys all sperms and "eliminates the necessity for examining two consecutive specimens of semen for azoospermia after operation." However, sperm counts three months after "vasectomy" are occasionally within the normal range.