The risk determination of geriatric problems

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Summary
Ten geriatric problems which eventually lead to impairment, disability or handicap with progressive deterioration of bodily structure and function are discussed.

At the geriatric clinic at Tygerberg Hospital, Parowvallei, CP, 1150 patients were examined to distinguish the low-risk patients with no serious impairment of health from those suffering from disabilities of moderate nature and severe life-threatening handicaps.

The increasing number of geriatric patients attending the clinic and the associated administrative problems have made this study necessary.

Ten problems are responsible for the majority of complaints and multiple lesions with which patients so often present at geriatric clinics.

Immobility
This is a frequent presenting symptom, with many causes. Psychologically, anxiety and fear are responsible for complete lack of confidence after a patient has suffered a cerebrovascular accident or fallen and sustained a fracture. The fear of falling again can so demoralize a frail patient that inertia eventually forms part of the clinical picture of depression and dementia.

Peripheral neuropathy due to diabetes, ischaemia, bronchial carcinoma, rheumatoid disease and drug toxicity increases the risk of falling when position sense is lost. Loss of balance, sometimes associated with postural hypotension due to autonomic nervous system disturbances, further complicates the issue.

Muscle pains with weakness, stiffness and rheumatism are commonly found in polymyalgia rheumatica. Intermittent claudication from muscle ischaemia affects the lower extremities, whereas the proximal limb girdle muscles are affected in neoplastic disease in the elderly.

Degenerative osteo-arthritis of the spine, shoulders, hips and knees is more common than the inflammatory condition of rheumatoid or septic arthritis. Gout, in its classic form or secondary to blood dyscrasia, affects both sexes in old age. Pseudogout most commonly affect the knees, with pyrophosphate crystals in the synovial tissue and fluid. Osteo-arthritis is common in old age, with obese patients particularly vulnerable. A variety of pain factors impair mobility and so cause a loss of independence. Grindind pains occur in knee joints when the bone surfaces no longer have the protection of joint cartilages, and spondylitic pains due to osteophytes pressing on the nerve roots radiate down the arms and legs. Night pains, due to increased vascularity in congested bones, result from immobility and frequently cause insomnia. Prostaglandins add inflammatory changes to the degenerative process already present and so aggravate the pain and discomfort. Neurogenic claudication causes extreme discomfort when local arthritic lesions compress the spinal arteries.

Bone diseases
Severe persistent pain, aggravated by movement and weight-bearing and often worse at night, seriously impairs the patient's mobility. Traumatic or pathological fractures, frequently misdiagnosed, are often responsible for continuing immobility.

Osteoporosis, much more common in the elderly female, can present with considerable loss of bone tissue as a result of prolonged bed rest, thyrotoxicosis, steroid therapy or Cushing's syndrome.

Osteomalacia may be due to a combination of factors such as dietary insufficiency, malabsorption after a gastrectomy, impaired metabolism of vitamin D resulting from abuse of liquid paraffin as a laxative, liver or renal disease, and anticonvulsant drug absorption. Softening of the bones is responsible for the painful immobility in this condition.

Paget's disease causes pain due to deformity and increased fragility of the bones of the lower extremity. Pathological rarefaction and sclerosis of the bone structure with fractures or sarcomatous changes further complicate the picture.

Metastatic spread from cancer of the lung, gut, thyroid, breast, prostate gland and skin can cause malignant bone disease in geriatric patients. The patient with multiple myeloma, a monoclonal gammopathy, often presents with a normal alkaline phosphatase value.

Drug-induced immobility
Iatrogenic impairment of mobility results from oversedation with phenothiazines, benzodiazepine tranquillizers and anticonvulsant drugs. The patient develops parkinsonian features or suffers from postural hypotension. Reserpine (rauwolfia), methyl-dopa and diuretics or laxatives can cause depression and hypokalaemia with weakness necessitating immobilization in bed after the patient has suffered 'drop attacks', faints, falls or even fits.

Weakness
Weakness or a feeling of intense tiredness or fatigue is a term very often used imprecisely by patients trying to explain their discomfort. Weakness is a prominent symptom of any serious disease, very difficult for patients to describe and equally difficult for doctors to assess.

Autonomic dysfunction
Autonomic dysfunction is commonly seen in the elderly as disturbances of baroreceptor reflex control. Postural hypoten-

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sion, hypothermia, disturbances of oesophageal and gastrointestinal mobility, urinary retention, incontinence and impotence are some of the common clinical manifestations.

Endocrine derangements

After diabetes mellitus, thyroid disorders are the most important causes of weakness. With hyperactivity, myopathy and proximal muscle weakness may often be the only clinical abnormality. In myxoedema immobility is most likely to be secondary to a general slowing down and a loss of initiative. The patient with apathetic thyrotoxicosis presents atypically with apathy, depression, lethargy, profound weight loss and uncontrolled atrial fibrillation. Both hyper- and hypo-activity of the adrenal glands are associated with weakness. In Cushing’s syndrome there may be proximal muscle wasting with hypokalaemia, whereas in Addison’s disease the weakness is more vague and generalized.4

Blood diseases

Dyspnoea, dizziness and tiredness with accompanying heart failure are frequently found in severe anaemia. Iron deficiency is central to the vast majority of anaemias in the elderly, but lack of the other haematinic factors, vitamin B12, and folate, is also common.

Patients with acute or chronic leukaemia, polycythaemia vera and multiple myeloma often present with the same nonspecific symptoms of fatigue and weakness.5

Diseases of the heart and circulation

Among the most frequent symptoms of heart disease in old people is a feeling of extreme exhaustion. This complaint is so commonly associated with other disorders that its significance may be missed or receive only scant attention. The symptom probably arises from a reduction in the output of the heart and chronic reduction in the blood flow to the brain.

The classic picture of acute myocardial infarction is not the rule in the geriatric patient. Many patients present with dyspnoea, but a silent cardiac infarction is also common; otherwise the patient can exhibit minor symptoms of weakness, confusion, syncope, transient ischaemia or stroke but without chest pain.6

Angina pectoris in some patients is not due to ischaemic heart disease but to aortic valve disease or hypertension. The pain may not be very severe, but its nature and site, the presence of dyspnoea, and the association of the pain with exercise and its relief by rest are typical.

Abrupt changes in rhythm in an elderly patient can lead to cardiac syncope, transient ischaemic attacks and possibly dementia. Arrhythmias should be suspected as the cause of a fall, particularly if it was preceded by dizziness and not related to a change in posture.

The patient with congestive heart failure resulting from ischaemic or hypertensive heart disease often exhibits the cardinal sign of breathlessness masked by confusion, agitation, nausea or coughing. There may simply be a history of the patient having become bed-bound, incontinent, and no longer able to cope at home.

Respiratory and cardiac failure in the elderly are so closely related to cardiac function that it is difficult to distinguish the relative importance of the cardiac and respiratory contributions. There may be very few pointers to the lungs as the source of trouble, and much of the respiratory distress of chronic bronchitis, emphysema or late-onset asthma in the elderly is cardiac in origin. True respiratory failure can be mainly silent, masked by cardiac failure with massive oedema, or cause acute confusion, stupor, fits or profound lassitude.

Neurological disorders

Cerebrovascular disease is the biggest single physical cause of hospital admission of the elderly in the UK, accounting for 20% of bed occupancy. The patient is usually hypertensive and often overweight, a heavy smoker, suffers from ischaemic or valvular heart disease, and presents with marked loss of power in the arms and legs. In addition there may be sensory impairment, asteagnosia, proprioceptive loss, visual disturbances, aphasia, apraxia, reduction of intellectual capacity and impairment of memory.7 During rehabilitation the patient has to overcome the following barriers to independence — motor paresis with spasms and contractures, sensory losses, communication problems, balance disturbances, depression, and dementia.8

The patient with parkinsonism, the most frequent neurological disorder of the elderly other than stroke, presents with muscular weakness, immobility, rigidity and tremor, which slow down body movements and interfere with physiological functions. Poor food intake leads to weight loss, poor nutrition and wasting which may be so great as to raise suspicions of neoplastic disease. The side effects of levodopa and other dopaminergic drugs (nausea, vomiting, orthostatic hypotension, cardiac arrhythmias, dyskinetic syndromes and mental disturbance) further weaken the patient.

Peripheral neuropathy is very common in the elderly; weakness and wasting of the thigh muscles and a sensory or mixed sensorimotor peripheral neuropathy is commonly found. The complications of ischaemia, trauma, sepsis, pain in the lower limbs, loss of bladder control and the threat of gangrene all add to the patient’s feeling of weakness.

Epilepsy in old age demands a thorough assessment of the cardiovascular and nervous systems for cerebrovascular and heart disease resulting in sudden changes in cerebral perfusion pressure. Cardiac dysrhythmias, a cerebral tumour, hypoglycaemia, uraemia or drugs may precipitate the seizures. Anticonvulsants interact among themselves or with other commonly used drugs and toxicity increases the frequency of epileptic attacks. Paroxysmal pain down the paretic side of a hemiplegic patient, bouts of mental confusion and sudden akinetic attacks can all be epileptic phenomena.

Metabolic disturbances

Metabolic disturbances, whether endocrine, nutritional, genetic or dystrophic in nature, are liable to put severe strain upon almost every tissue of the body, eventually leading to progressive disablement. Patients often exhibit apathy, depression and mental and physical slowing, or entirely nonspecific deterioration. Refined foods taken in excess are in some way responsible for cholelithiasis, hiatus hernia and diverticulitis of the colon occurring in the same patient, thus complicating the picture of obesity. This syndrome, known as Saint’s triad, often leads to problems in the differential diagnosis of ischaemic heart disease, oesophageal discomfort and pains, and gallbladder or liver disorders.9

Vomiting, diarrhoea, confusion, weakness, general malaise and restlessness are often the only presenting features of fluid deficiency and electrolyte disturbances. The elderly are often disinclined to take fluids for fear of incontinence, and the hypostatic oedema of their immobile legs is often ascribed to the presence of too much water in their bodies.

The malabsorption syndrome becomes increasingly prevalent in old age. This may be due to small-bowel ischaemia, gluten sensitivity or abnormal bacterial colonization. The absorption of fat and fat-soluble vitamins, folic acid and vitamin B12 is mainly affected.
Renal diseases

The two most important factors likely to cause damage to the kidneys in old age are infection and back pressure due to obstruction. Pyelonephritis can present in the undramatic, rather non-specific way so typical in geriatric medicine, and confusion and incontinence should arouse suspicion of its presence.

The clinical features of analgesic nephropathy are indistinguishable from those of chronic pyelonephritis, and the continued ingestion of analgesics will eventually lead to renal failure. Obstructive nephropathy, resulting from enlargement of the prostate gland, urethral stricture, pelvic tumour or stones or neurogenic in origin, leads to pyonephrosis and destruction of the kidney parenchyma.

Liver disease, especially cirrhosis, cholestatic or drug-induced jaundice and carcinoma, which are the most common liver disorders, may be symptomless. The lowered sensitivity to pain in some old people can cause diagnostic problems, since the onset of painless jaundice tends to suggest a neoplastic cause.

Abnormal catabolism

Because of the very high incidence of so many different forms of cancer in old age, the possibility of malignant disease must always be kept in mind. Apart from anorexia, nausea, vomiting, gastro-intestinal blood loss, rectal bleeding and anaemia (due to multiple factors) the presentation may be completely non-descript. The patient is observed to be 'falling apart at the seams' with general decline, extreme weakness, mental depression, a toxic confusional state, or dementia as a metabolic complication of cerebral metastasis.

Infections

Localizing signs of acute infections may be absent or minimal in geriatric patients, and even general disturbances such as fever may be conspicuous by their absence. Infections of the respiratory and urinary tracts are particularly likely to cause confusion of sudden onset. Cultures of sputum, urine, and blood and a careful search for possible sites of infection are necessary in all such patients.

Bronchopneumonia is still the most frequent chest infection in an old person and the possibility of tuberculosis, particularly in old men, must always be kept in mind. A few diseases are more acute. Appendicitis in the older patient has a fulminating course with rapid development of gangrene and peritonitis. This, a typical clinical picture, is mainly due to atrophy of lymphoid tissue and thrombosed arteriosclerotic mesenteric vessels.

Instability

Falls may occur so often that independent life in the patient's home becomes impossible. Cardiovascular causes of falls include myocardial infarction, and it must be kept in mind that the classic picture with characteristic chest pain is rare, affecting only about 20% of victims. Almost 10% of the remainder will present with a syncopal attack due to inadequate cerebral blood flow.

Hypertensive patients on potent antihypertensive drugs often suffer from postural hypotension. This is a common cause of falls, and also occurs during an attack of myocardial infarction when there is a sudden drop in blood pressure. Concealed bleeding, especially in the gastro-intestinal tract, and pulmonary emboli from venous thrombosis in immobile legs are other causes of sudden reduction in blood pressure.

Atherosclerosis and ischaemic heart disease are responsible for changes in cardiac rhythm, marked sinus bradycardia, complete heart block with Stokes Adams attacks, or a tachyarrhythmia-like atrial fibrillation.

The patient with chronic anaemia, whose haemoglobin level is 10 g/dl or less, often experiences episodes of transient cerebral ischaemia. Transient ischaemic attacks may be caused by acute or chronic diarrhoea, by the defaecation syndrome in constipated patients straining at stool, or by straining to urinate.

Cervical spondylosis with osteo-arthritis and osteoporotic changes in the vertebrae can compress the vertical arteries with interference of the cerebral blood flow during neck movements. Musculoskeletal causes include unstable joints resulting from degenerative disease and weak ligaments and musculature, with joints just giving away beneath the patient.

Spasticity and sensory disturbances in the brain or spinal cord, defects in the special sense organs, peripheral neuropathy or weakness of the nerves, also all expose the patient to greater instability.

Immobility and weakness as causes of instability have already been dealt with.

Confusion

Delirium, an acute confusional state like fever in a child, is an indicator of the presence of an illness and not a diagnosis in itself. Clouding of consciousness, sleepiness and hallucinations can occur but the intellect is intact, the condition reversible and the prognosis good. Chronic brain failure or dementia is a state of irreversible impairment of intellectual function due to brain cell damage. Basically the problem is loss of short-term memory. It is usual to distinguish between the senile and atherosclerotic forms, but the two varieties coexist in about 20% of patients.

Other causes of confusion are uncommon. They include: drugs — antiparkinsonian, anticholinergic, anti-epileptic and antihypertensive medications; emotional or neurotic pseudodementia; metabolic disturbances such as myxoedema and vitamin B12 deficiency; epilepsy, electrolyte disturbances and endocrine abnormality; nutritional disturbances such as pellagra; trauma, tumours or toxins (alcohol and barbiturates); infections of the respiratory and urinary tracts; atrial fibrillation; and silent myocardial infarction, strokes with minor episodes of cerebral infarction in the silent areas of the cortex, and faecal impaction coming on unexpectedly.

Incontinence

Urinary and faecal incontinence may be reversible or established. Normal mental function will favour a reversible cause, which should be carefully sought and may include psychological factors and disorientation in strange surroundings, diuresis and intestinal hurry, infective conditions, or mechanical factors such as retention and overflow from prostatic obstruction or faecal impaction. A toxic confusional state causing incontinence can be induced by a great many drugs, especially sedatives and the unnecessary employment of powerful irritating purgatives or diuretics. Disturbances of fluid and electrolyte balance will further complicate matters.

Established faecal incontinence is much less frequent than irreversible urinary incontinence. Causes include neuropathic (neurogenic) bladder and rectum; destruction of the second to the fourth sacral segments of the cauda equina by tumours, toxins or trauma (painless distension with overflow incontinence results and there is loss of both motor and sensory functions); and lesions of the posterior nerve roots or posterior horn cells in diabetes mellitus, tabes dorsalis and subacute combined degeneration of the cord (loss of sensation causes chronic bladder distension with retention and overflow). A lesion between the sacral segments of the cord and the higher centres of the brain

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leads to loss of sensation and muscular incoordination with high intraluminal pressures and muscular instability. When there is damage to the higher centre or its connections in the cerebral cortex, sensation is retained but the ability to inhibit reflex contractions of the bladder and rectum is lost. Immediate evacuation occurs when the patient becomes aware of the discomfort in the pelvis.

Local lesions of the pelvic floor resulting in prolapse or destruction of sphincters, or malignant infiltration of tissues, are all recognizable causes of incontinence.

Impairment of homeostasis

The concept of homeostasis is basically concerned with the actions of brain hormones (enkephalins and endorphins) and the hypothalamus, hypophysis and adrenal glands. In stress, the enemy of both homeostasis and restoration, the factors of disturbance are greater than the factors of resistance. Important stresses in elderly people are cold, malnutrition, surgery, and acute or chronic illnesses including infections, strokes and depression.

Metabolic acidosis, resulting in changes in blood glucose levels, plasma pH, plasma volume and osmotic pressure, develops as a reaction to stress when homeostasis of the internal environment is impaired. In the elderly, dehydration and disturbances of electrolyte balance are frequently associated with large-bowel lesions.

Energy homeostasis maintains a dynamic balance between nutrient intake and energy expenditure. Physical inactivity, adiposity, the presence of physical disorders and certain drugs all influence the diminishing homeostatic mechanisms of the elderly. The maintenance of protein homeostasis is a complex phenomenon but a central requirement in conditions of protein energy deprivation where nutrition is only marginally adequate.

The metabolic elements are homeostatically controlled, primarily through their absorption from the intestine, followed by enterohypothalamic circulation and very little renal excretion. The trace metals, zinc, copper, chromium and cadmium are implicated in most of the major degenerative diseases, and evidence is accumulating that deficiencies of these elements are particularly prevalent in our geriatric population.

The hypothalamus is directly involved in the feedback mechanisms controlling many pituitary hormones in a whole variety of homeostatic mechanisms (blood pressure, temperature regulation, sleep and metabolism) which often fail in the elderly. Vascular and age-related histological changes in these glands could impair or reduce the hypothalamic-pituitary target organ's functional capacity to control stress while retaining the ability to maintain basal hormonal levels. Physical and psychological stresses are sometimes associated with features which could implicate the pituitary gland, e.g., hyperthermia, lack of pyrexia in infections and hypotension. Hypothermia is also likely in vascular and neoplastic lesions involving the third ventricle or the hypothalamus itself.

Iatrogenic or iatropathic problems

A thorough investigation of geriatric patients reveals the silent existence of many conditions; multiple lesions are the rule rather than the exception. Treatment of these multiple disorders has, however, led to new problems resulting from the administration of a number of powerful drugs which can produce a variety of ill-effects. Adherence to several principles is essential if therapeutic hazards are to be avoided and optimum benefit is to be obtained from drug treatment in the elderly.

Having made the diagnosis, the doctor should aim to improve the quality of the patient's life, using the minimum number of drugs in the simplest possible way. A full assessment of these patients is essential as they are less tolerant of adverse effects because of generally higher blood levels of the drugs and impaired homeostasis.

Interactions often occur when two or more drugs are given concurrently; the drugs, the disease itself, or an idiosyncrasy on the part of the patient may be responsible. Common examples of indirect adverse effects are the unmasking of latent disease such as diabetes by steroids and thiazide diuretics, the precipitation of acute gout by thiazides, and the reactivation of chronic tuberculosis by steroid therapy. A good deal of morbidity in the elderly is attributable to overmedication. Errors in self-medication by patients at home can only be reduced by careful supervision by members of the community. Non-compliance is extremely difficult to assess, but according to published studies 25 - 50% of patients do not take their medicine at all.

The following approach may help in minimizing non-compliance. A regimen containing only three drugs is said to be a reasonable maximum for an old person to manage. A simple explanation of the treatment should be given. Help in supervision can be sought from a neighbour, relative or health visitor. The necessity for compliance should be emphasized and the instructions repeated at follow-up. Containers should be easy to open and instructions clearly typed, and as few doses as possible should be prescribed.

Neurotic disturbances

A neurotic disorder in old age either arises de novo or as an exacerbation of a longstanding condition. It has always to be seen as a combination of personal predisposition, life experience, and the stresses met in later life. Statements volunteered by elderly patients attending clinics often include various losses as the cause of their neurotic disorder.

Physical health, social status, economic security, compulsory retirement, bereavement, and an adverse home environment are the most common complaints.

To the younger observer, the lives of elderly people seem to be so full of unpleasant experiences that symptoms of anxiety, phobias, obsessive hypochondriacal preoccupations and depressive reactions are sufficiently explained. A thorough medical history, physical examination and appropriate investigations are perhaps not considered necessary and are not systematically explored. The result is a lack of a body of knowledge, expertise and understanding of the neuroses and personality problems. This robs us of one of the few possibilities in treating the brain-damaged elderly person and preventing the breakdown of the supporting network which keeps him or her in the community as long as possible.

Psychotic problems

True depression is the master of disguise in geriatric medicine and the great imitator of other diseases. Moderate to severe depression occurs in approximately 15% of the elderly population, with suicide a serious hazard. The 65-and-over age group represents 10 - 15% of the general population but is responsible for at least 38% of all known suicides. There is frequently a history of manic-depressive illness, but the manic phase is less usual. In old people the mood swing is more often down than the reverse.

Paranoid reactions are usually mild and transitory rather than disabling. Many are related to increasing deafness or failing vision, but they are also seen in dementia or depression and occasionally as side-effects of drugs such as steroids or L-dopa. Paranoid psychoses (paraphrenia) account for 10% of admissions of elderly patients to hospitals with either a typical schizophrenic syndrome, paranoid delusions or auditory hallucinations alone.
They typically occur in socially isolated women with severe bilateral conductive deafness.22

Social problems
Old people especially at risk are the socially isolated and those with physical disability, including impairment of the special senses, which contributes to isolation. The housebound (nearly 8%) of old people living in their homes) constitute the largest group at risk. Other vulnerable groups include the recently bereaved, very old men living alone, and those with mental disorders, particularly depression. The application of preventive measures to these smaller groups rather than to the entire elderly population is a much more practical proposition.23

Risk determination
The following disturbances and disadvantages are experienced by geriatric patients as a result of the above ten problems.

1. An impairment or disturbance of body structure or functioning progressing slowly and not posing a serious hazard to the patient’s well-being (low risk).
2. A disability results when an impairment is actively progressing slowly and not posing a serious hazard to the patient’s well-being (low risk).
3. A handicap is present when subacute or chronic deterioration of the disabled patient progresses until he or she can no longer conform to the expectation of the social group owing to the disadvantages experienced from impairment and disability (high risk). This group needs special care as urgent life-saving remedial measures may suddenly become necessary.24,25 Acute deterioration of the health of the severely handicapped patient is an emergency requiring immediate hospitalization.

A risk analysis was carried out in 1981 on 1 150 patients at the geriatric clinic at Tygerberg Hospital, Parowvallei, CP, to assess well-being by taking into account all the complaints, symptoms and signs and the results of special investigations. The results are shown in Table I.

According to these figures low-risk patients accounted for almost half those examined (46.5%). The number of emergency hospital admissions from the geriatric clinic was also constant at this low rate (2%). The area in which examiners initially differed widely was in the determination of moderate- and high-risk patients. This discrepancy was found to be due to consideration of the various clinical manifestations rather than concentration on the main problems with which the patients presented.

For the sake of a more uniform evaluation of the severely disabled geriatric patient, the following more acceptable criteria were recommended and accepted as standards for risk determination:
1. A sudden deterioration in health since the patient’s last attendance at the clinic 12 weeks before.
2. A serious setback within the last 12 weeks, e.g. a transient ischaemic attack, thrombosis, embolism, haemorrhage or metabolic upset.
3. Persistent undue weakness after recent hospitalization.
4. Continuing decline in spite of all medical, surgical or psychiatric measures.
5. Sudden collapse of the patient’s social structure.

The study was undertaken at the request of Professor C. L. Wicht, Head of the Department of Community Health at Tygerberg Hospital, for the following reasons:
1. The rapid increase in the number of geriatric patients referred to the clinic from other hospital departments.
2. A chronic shortage of personnel (medical and nursing) to deal with all the patients, especially those in wheelchairs and on stretchers.
3. The inconvenience caused to geriatric patients who have to be ready at 07h00 to be picked up and taken to the clinic. Some feel so well that they consider 12-weekly follow-up examinations unnecessary.
4. The long wait at the hospital before their examination and later at the pharmacy for their medications often proves too exhausting for some elderly patients.
5. The unnecessary drug and transport expenses on the pharmacy personnel could be reduced by less frequent examination of low-risk patients.
6. Unnecessary drug and transport expenses are proving to be a burden to patients as well as to the Cape Provincial Administration.

I would like to express my sincere thanks to Professor Wicht for his guidance and encouragement with this project. Thanks are also due to the personnel, Department of Community Health, Tygerberg Hospital, for their expert assistance and constant interest.

REFERENCES
The effect of paraquat on the incorporation of radiolabelled proline into acid-extractable lung proteins and collagens

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Summary

In this comparative study we describe the influence of paraquat on the rate of $\text{L-2,3-}^3\text{H-proline}$ incorporation into the acid-extractable proteins and into newly synthesized protropocollagen molecules from the lungs of rats and rabbits. Exposure to paraquat took two forms: (a) addition of paraquat in vitro to lung tissue taken from rats and rabbits, and (b) intraperitoneal injection of paraquat prior to death.

Paraquat (0.5 - 1.0 mM) added in vitro significantly slowed the rates of $^3\text{H-proline}$ incorporation into the acid-extractable proteins and into newly synthesized protropocollagen in both rat and rabbit lung tissue.

Paraquat administered intraperitoneally (27 mg/kg) to rabbits did not markedly influence the rate of $^3\text{H-proline}$ incorporation into acid-extractable proteins and collagen assessed in vitro 24, 48 and 96 hours after injection.

Paraquat injected intraperitoneally into rats induced no significant difference in synthesis rates of acid-soluble proteins up to 48 hours after injection. During the same period, the collagen synthesis rate of rat lung tissue was reduced. At 96 hours an increase was found when the rate of synthesis was expressed as cpm/mg DNA and as cpm/μg hydroxyproline.

Collagen has an important role in the development, structure and mechanical properties of lung tissue and in the pathogenesis of a wide spectrum of lung diseases, including fibrotic disorders. Collagen is distributed throughout the lung, including the tracheobronchial tree, the blood vessels and the alveolar interstitium and constitutes about 20% of the dry weight of the adult human lung. In the normal adult lung, collagen synthesis proceeds at a constant level, representing 4-5% of the total amino acid incorporation into lung proteins. Collagen constitutes 10-15% of the proteins synthesized by cultures of rabbit lung cells and fibroblasts.

Five major types of collagen have been identified in lung tissue. It appears that almost all tissues contain several types of collagen, although in different proportions. There are over 40 cell types in the lung and it is therefore extremely difficult to identify the types of collagen in lung tissue and specifically the cells responsible for synthesis of each type. Fibroblasts are involved in the synthesis and secretion of type I and type III collagen: the latter accounts for a small proportion varying from 5% to 30% of the total secreted procollagen. Type II collagen is mostly produced by tracheal and bronchial chondrocytes. Smooth-muscle cells synthesize a higher proportion of type III compared with type I collagen than do fibroblasts. Small amounts of type V and a pepsin-resistant fragment, probably

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