

# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. 1.—54TH YEAR

SYDNEY, SATURDAY, APRIL 15, 1967

No. 15

## Table of Contents

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ORIGINAL ARTICLES—	Page	PUBLIC HEALTH—	Page
The Taipan ( <i>Oxyuranus scutellatus</i> ) and the Effect of its Bite, by C. H. Campbell .. . . . . .	735	Reports from Australian Virus Laboratories .. . . .	787
The Investigation and Treatment of Pituitary Dwarfism: Preliminary Experience with Human Growth Hormone, by H. G. Burger, Kevin Catt, J. F. Connelly, Bryan Hudson, F. I. R. Martin, Roger Mellick, H. P. Taft and H. N. B. Wettenhall .. . . . . .	739	<b>CORRESPONDENCE—</b>	
The Semantics of "Giddiness", by M. J. Eadie .. . . .	743	Press Editorial .. . . . . .	788
The Management of Polyps of the Colon and Rectum, by A. B. G. Carden .. . . . . .	746	Science and the Anaesthetist .. . . . . .	788
A Prospective Study of South Australian Blood Donors: I. Static Information, by R. W. Beal .. . . . . .	749	"Can These Bones Live?" .. . . . . .	788
Oculomotor Nerve Paralysis, by John I. Balla and J. B. Morley .. . . . . .	755	The Recognition of Coronary Proneness .. . . .	789
Fluphenazine ("Anafensol") in the Treatment of Disturbed Mentally Retarded Children, by Elizabeth Arnold and D. W. Maginn .. . . .	758	Five Cases of Unexplained Jaundice .. . . .	789
Experience with a Depot Phenothiazine in the Treatment of Schizophrenia, by William A. McIlraith .. . . . . .	760	Associate Positions in Hospitals .. . . . . .	789
<b>REVIEWS</b> .. . . . . .	762-764	Paget's Disease of Bone .. . . . . .	789
<b>LEADING ARTICLES—</b>		Oral Contraceptives .. . . . . .	789
"Partners in Health" .. . . . . .	765	The Puzzle of Heart Disease .. . . . . .	789
<b>COMMENTS AND ABSTRACTS—</b>		Type of Anaesthesia and Hyaline Membrane Disease .. . . .	790
Articular Sporotrichosis .. . . . . .	767	<b>ROYAL AUSTRALASIAN COLLEGE OF SURGEONS—</b>	
International Cooperation Against Cholera .. . . .	767	Primary Fellowship Examination, February/March, 1967 .. . . . . .	790
"Medicine in South Vietnam Today" .. . . . . .	768	Faculty of Anaesthetists: Primary Fellowship Examination, February/March, 1967 .. . . . . .	790
Shorter Abstracts: Medicine .. . . . . .	768	<b>THE AUSTRALIAN COLLEGE OF GENERAL PRACTITIONERS—</b>	
<b>THE WIDER VIEW—</b>		Melbourne Course for General Practitioners in June, 1967 .. . . . . .	790
Medicine in South Vietnam Today. Part 3: Saigon Again—The <i>Helgoland</i> , The Children's Hospital and Medical Education, by Allister Brass .. . . .	770	Queensland Faculty: Postgraduate Weekend .. . . .	790
<b>BRUSH UP YOUR MEDICINE—</b>		<b>UNIVERSITY INTELLIGENCE—</b>	
Genetics in Medical Practice, I, by C. B. Kerr .. . . .	778	University of Queensland .. . . . . .	791
<b>SPECIAL ARTICLES—</b>		Australian National University .. . . . . .	791
Quality of General Practice, by John M. Last .. . . .	780	<b>THE COLLEGE OF RADIOLOGISTS OF AUSTRALASIA—</b>	
"Survival Car" Built for Australian Conditions .. . . .	784	Membership Examination Results .. . . . . .	791
<b>POINTS OF VIEW—</b>		<b>POSTGRADUATE WORK—</b>	
An Australian Broadcasting Commission "Guest of Honour" Talk, by T. F. Main .. . . . . .	786	The Postgraduate Committee in Medicine in the University of Sydney .. . . . . .	791
		<b>NOTES AND NEWS</b> .. . . . . .	792
		<b>DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA</b> .. . . . . .	793
		<b>CORRIGENDUM—</b>	
		Australian Medical Association: Annual General Meeting .. . . . . .	794
		<b>NOMINATIONS AND ELECTIONS</b> .. . . . . .	794
		<b>DEATHS</b> .. . . . . .	794
		<b>NOTES FOR CONTRIBUTORS</b> .. . . . . .	794
		<b>CLASSIFIED ADVERTISEMENTS</b> .. . . . . .	794
		<b>SUBSCRIPTION RATES AND DELIVERY</b> .. . . . . .	794

## THE TAIPAN (*OXYURANUS SCUTELLATUS*) AND THE EFFECT OF ITS BITE

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The largest and most dangerous venomous snake found in Australia is without a doubt the taipan (*Oxyuranus scutellatus scutellatus* Peters) and, but for the king cobra (*Ophiophagus hannah*) of Asia, it could well lay claim to being the world's most venomous terrestrial reptile. A study of the cranial and dental characteristics of the taipan indicates that it is the closest relative of the cobra and may have evolved from that snake (Kinghorn, 1956).

The name taipan is a Cape York aboriginal vernacular name for the snake, which was known and feared by the

local Aboriginal people (Thompson, 1933). The snake was less well known to the local white population, but was feared by those who knew of it, for Garde (1890), writing from Maryborough, said that a Mr. Johnstone who had lived in northern Queensland had seen four out of seven people bitten by death adders recover, but he had attended the funerals of all 12 people who had been bitten by "brown snakes". Furthermore, whereas a fatal case of snake bite was an uncommon event in the practice of early medical practitioners in New South Wales (Bland, 1861) and Victoria (Thomas, 1869), it was not so uncommon in North Queensland where Byrne (1893), after only 18 months' residence at Mackay, had seen four fatal cases

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of snake bite, and Macdonald (1895) at Ingham had treated 60 cases of snake bite, six of which proved fatal.

Although the first specimen of a taipan was described from Rockhampton in 1867 as *Pseudechis scutellatus* by Peters, it is only over the last 45 years that the snake has been studied to any considerable extent. In 1923, Kinghorn received a large elapine snake (9 ft. 3 in. long with a girth of eight inches) captured by W. McLennan at Coen in the Cape York Peninsula which he thought, judging by external characters, to be nearly allied to *Pseudechis scutellatus*; but the dental and cranial characteristics proved different from those of any other genus and he described the snake as a new genus, *Oxyuranus maclelleni*. Thompson (1933) showed that these snakes were, in fact, identical, but agreed that the cranial and dental characteristics pointed out by Kinghorn were sufficient to justify the retention of the genus *Oxyuranus*.

#### CHARACTERISTICS OF THE SNAKE AND ITS DISTRIBUTION

The taipan is a large brown snake with the head distinct from the neck and a slender forebody. The average maximum length is 8 ft., but specimens up to 11 ft. long have been recorded (Worrell, 1963). On sight it cannot be easily

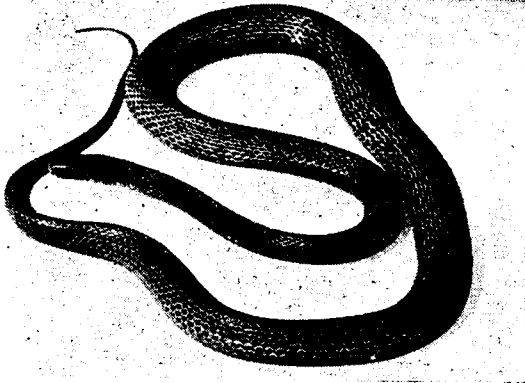


FIGURE 1: The Papuan taipan (*Oxyuranus scutellatus canni* Slater). (Photograph, K. R. Slater).

distinguished from a large brown snake (*Demansia textilis* Dumeril and Bibron) or from the mulga snake (*Pseudechis australis* Boulenger). The snake is active in the day time and early evening after sunset. It lives in openings or holes in the ground, under overhanging boulders, in hollow logs or under concrete or iron debris.

Worrell (1963) and Slater (1961) both agree that the taipan's reputation as an aggressive reptile (Thompson, 1933; Kinghorn, 1956) is unjustified. They say it is a shy nervous snake that attempts to avoid man and flee from him. Slater states that it is fortunate that this is so, for he knows of "no other snake more formidable and adept in defence when at close quarters nor more capable of clearing the Papuan grasslands of man if it did adopt truly aggressive behaviour". When aroused it will strike without warning and with great rapidity over a long range.

The taipan is a snake of tropical Australia, frequenting the open country of the coast as well as the inland plains and savanna woodland, being principally found in the Cape York Peninsula and around the Gulf of Carpentaria. Its distribution extends south to Rockhampton, and possibly to Gympie, latitude 26° 13' S. (Morgan, 1956), and westward to Arnhem Land, Birdum and Melville Island (Worrell, 1963). Worrell (1963) thinks that the taipan will also be found in North West Australia as well.

Before 1952 the taipan had been reported only from the Fly River area of Papua (Boulenger, 1896), but in that year Slater saw but failed to capture near Port Moresby a fast-moving snake that was blackish in colour with a

bright orange streak along its back. After several more encounters with this snake, his Papuan assistant, Oroki, in 1953 captured the first live taipan in Papua (Slater, 1961). The Papuan taipan has distinctive colouring. Some specimens are brown, others are black, but they all have a characteristic orange or red streak on the back. Among the Papuans it is known as "the black snake with the red back". Slater (1956) described the Papuan form as a subspecies *Oxyuranus scutellatus canni* (Figure 1).

In Papua the taipan has a very restricted distribution and is found mainly in the two areas of savanna woodland vegetation—one in the Western District and the other in the coastal area of the Central District stretching from near Kukipi to just east of Marshal Lagoon. K. R. Slater (personal communication, 1960) could find no difference between these western and eastern races of the snake, and thinks that their distribution may possibly be continuous in the foothills behind the Gulf of Papua. The taipan does not extend deep into forest areas in Papua, but has been found at an altitude of 1,100 ft. near Sogeri, inland from Port Moresby.

#### BITING APPARATUS AND VENOM STUDIES

Whereas most of the Australian venomous snakes have short fangs, Kellaway (1932) stated that the taipan "had a truly magnificent biting apparatus". The fangs of large specimens are half an inch (13 mm.) in length.

The venom yields obtained by McLennan after killing two taipans were 475 and 356 mg. The average venom yield of the taipan obtained at the Commonwealth Serum Laboratories was 100 to 120 mg., and the maximum venom yield was 400 mg. (Trinca, 1959).

Kellaway and Williams (1929) studied the effects of the venom on laboratory animals. They used venom which had been kept for some years and may have undergone some deterioration for the certainly lethal dose (CLD) for 100 grammes of guinea-pig was found to be 0.008 mg. compared to 0.0025 mg. for fresh venom studied by Morgan (1956). After subcutaneous injection of the venom into monkeys, the animals developed a partial muscular paralysis and died from asphyxia. There were no circulatory collapse, no lesion at the site of injection and no significant findings at autopsy. Similar effects were noted in the rabbit, guinea-pig and rat. In-vitro experiments showed that the venom contained a thrombase which coagulated citrated plasma. The venom was feebly hæmolytic. Later work (Kellaway *et alii*, 1932) showed that the venom produced a curare-like paralysis in rabbits. The venom of the taipan was thus strongly neurotoxic, coagulant and weakly hæmolytic.

Studies on the venom of the Papuan taipan at the Commonwealth Serum Laboratories showed that it was very slightly more toxic than the Australian taipan venom (K. R. Slater, personal communication, 1960).

#### CLINICAL OBSERVATIONS

Published cases of taipan bite have all been reported from coastal areas of North Queensland—Cooktown (two cases) and Cairns (one case). Cases of possible taipan bite have occurred at Atherton (one case), Cairns (three cases), Mossman (three cases) and Port Douglas (one case).

Dr. H. Flecker, who stimulated local interest in the problem of snake bite in the Cairns district, published the first reports of cases of taipan bite: three in 1940 and three in 1944. These cases were observed by different practitioners in North Queensland and in no case was the identity of the snake inflicting the bite established with certainty. The rapid onset of unconsciousness or convulsions within 2 to 90 minutes of the bite was the first sign of fatal envenomation in three of the cases.

The cases reported by Reid and Flecker (1950), Benn (1951) and Lester (1957) are of more value, for the dead snake was identified as a taipan in each case.

Reid and Flecker's patient experienced difficulty in opening the eyes followed by nausea, the possible occur-

rence of vomiting and the onset of unconsciousness within 30 minutes of the bite. These symptoms were followed subsequently by a partial muscle paralysis. The patient recovered.

Benn (1951) recorded the onset of blurred vision four and a half hours after the bite of a taipan in a man aged 20 years who was admitted to the Cairns Hospital. This symptom was followed by vomiting, severe headache and generalized muscular paresis leading to death by respiratory failure. Black tissue resembling gangrene was present for a quarter-inch area around the wound at autopsy, but a tourniquet had been kept on for half an hour without release and the radial pulse had been obliterated during this period.

The patient ("D") from Cooktown reported by Lester (1957) vomited "cohee grounds" and bright blood, later developed ptosis and generalized paralysis and subsequently died in the tank respirator. Lester also reported two other cases in which the snake was not positively identified but was thought to be a taipan. One patient, a boy aged 10 years, became unconscious within a few minutes of the bite and subsequently developed ptosis, vomited and complained of abdominal pain. The bite wound continued to ooze blood for some time and generalized muscle weakness developed from which the patient subsequently recovered. The other patient developed the first signs of generalized muscle paralysis four hours after the bite and died in the tank respirator 12 hours after the bite.

From the reported cases, it would appear that the taipan may give rise to the following symptoms and signs: wounds that bleed, vomiting, vomiting of blood, abdominal pain, headache, sudden loss of consciousness, convulsions, difficulty in seeing and speaking, and generalized muscle paralysis.

Two of three definite cases and six of the eight doubtful cases of taipan bite were fatal.

PRESENT STUDY

The clinical details of six patients, who were thought to have been bitten by taipans and who were seen at the Port Moresby General Hospital over a six-year period (1960 to 1965), are summarized in Table 1. (Details of two of these patients were included in an earlier paper—Campbell, 1964.)

Two patients brought in the dead snake. The other four patients were bitten by black snakes with red backs. It is admitted that colour is an unsatisfactory means of identifying snakes as a rule, but the red back of the Papuan taipan appears to be a constant characteristic.

distinguishing the taipan from the Papuan black snake, the only other highly venomous snake with which it is likely to be confused. Papuans belonging to different coastal groups can separate the Papuan black snake from the taipan.

Five patients were bitten while within 15 miles of Port Moresby. The sixth patient was bitten near Marshall Lagoon. Four patients did not see the snake before it struck; one man trod on the snake which bit him twice on the ankle. The snake usually let go after biting and vanished quickly. In three cases the wound had been incised; two patients had two puncture wounds visible and one had only one tiny bleeding puncture wound, but when the blood was wiped away no wound could be seen. There was no pain, œdema or tenderness around the wound in any patient.

Report of a Case

One patient, whose hospital number was 30447, worked with the Department of Agriculture in Port Moresby at a laboratory which for some years had collected taipans and Papuan black snakes. He was a reliable man and well aware of the differences between a taipan and a Papuan black snake. He stated quite definitely that the snake which bit him was a taipan. He was bitten as he walked back after the "knock-off" bell had rung, so that the time relationship of his symptoms and signs to the time of bite is well established.

He had very early minor symptoms—slight headache, nausea and slight tenderness of the regional lymph nodes. The symptoms appeared within half an hour of the bite and were transient (disappearing within an hour) and might have easily been disregarded, had not blood tests been performed which showed that significant envenomation had occurred. One hour after the bite the white cell count (7.200 per cubic millimetre with 45% neutrophils) and the erythrocyte sedimentation rate (1 mm. in the first hour—Wintrobe) were normal, but the whole blood clotting time (Lee and White) was 3.5 minutes (normal range 3.00 to 5.75 minutes—Booth and MacGregor, 1965) and the bleeding time (Duke) was 7.25 minutes (normal range 1.25 to 3.75 minutes). Clot retraction was defective and the clot was friable. The rabbit anti-fibrin test, a flocculation test for human fibrin degradation products (Ferreira and Murat, 1963), gave strongly positive results. The fibrinogen titre (Sharp *et alii*, 1958) was nil. The prothrombin index was 20%. Haemolysis was evident on inspection and spectroscopic examination of the patient's serum.

Two hours after the bite the patient's blood would not clot. The addition of epsilon aminocaproic acid did not alter the fibrinogen titre, which was still nil. Tests on unheated and heated human fibrin plates showed evidence of slight fibrinolytic activity. Nine and one half hours after the administration of 24,000 units of taipan antivenene the clotting time was 4.75 minutes, the prothrombin index 71% and the fibrinogen titre was 1 in 2. Forty hours after the antivenene was injected the blood tests gave normal results.

TABLE 1  
Summary of the Clinical Details of Six Patients with Taipán Bites

Hospital Number	Sex	Approximate Age (Years)	Time of Bite	Month	Site of Bite	Symptoms <sup>1</sup>	Signs	Treatment and Response <sup>1</sup>
7,847	M.	10	12 noon	August	Middle third of leg	Vomited twice 1.5 to 2 hours a.b.	Tender regional lymph glands; mild degree muscular paralysis	Slight progression after antivenene administration
12,129	M.	20	12 noon	June	Ankle	None	None (5 ft. 8 in. taipan brought in)	No progression after antivenene administration
12,448	M.	35	2 p.m.	June	Ankle	Fell unconscious 0.5 hour a.b.; vomited 6.5 hours a.b.; transient abdominal pain for 0.5 hour	Continued bleeding from bruised face; complete muscle paralysis	Progression after antivenene administration; tracheotomy; A.R. for 10 days with eventual recovery
15,372	M.	20	4 p.m.	December	Foot	Vomited once; epigastric pain	Abdominal tenderness; snake brought in	No progression after antivenene administration
30,447	M.	40	4 p.m.	January	Ankle	Slight headache 0.5 hour a.b.; nauseated 1 hour a.b.	Slightly tender regional lymph glands; haemoglobinuria and heavy albuminuria 2.5 hours a.b.; blood incoagulable; no fibrin	No progression after antivenene administration
31,521	F.	20	10 a.m.	March	Lower third of leg	Vomited; slight pain in groin; headache; difficulty in speaking	Tender regional lymph glands; generalized muscular paralysis	No response to antivenene administration; tracheotomy and A.R.; recovered

<sup>1</sup> Key: a.b., after bite; A.R., artificial respiration.

The patient passed urine one hour after the bite and this contained no albumin or blood, but two and one quarter hours after the bite he passed dark brown urine which contained hæmoglobin, many red cells and a large amount of albumin (one half). The hæmoglobin persisted in the urine for four to eight hours. No paralysis developed.

### DISCUSSION

The taipan is a large snake with an efficient biting apparatus and a large yield of potent venom. It is indeed a formidable snake. The average venom yield is three times that of the Australian mainland tiger snake and the venom of these two snakes is of approximately equal potency (the CLD of tiger snake venom per 100 grammes of guinea-pig is 0.002 mg.—Morgan, 1956). Taipen venom is much less toxic than Reevesby Island tiger snake venom, which is two and a third times as potent as the venom of the mainland tiger snake and is thus the most potent terrestrial snake venom known (Morgan, 1938), but the average venom yield of the Reevesby Island tiger snake is, however, only 20.8 mg. (one-fifth of that of the taipan), and the biting apparatus of the tiger snake is inferior to that of the taipan.

The estimated CLD of taipan venom for a man weighing 70 kg. would be approximately 7 mg. (Kellaway, 1929; Morgan, 1956). With an average venom yield of 100 mg. and a maximum yield of 400 mg., the chances of a taipan bite being fatal are very high. Fortunately, even when biting with relatively full venom glands, snakes appear to be able to exert a considerable degree of control over the amount of venom injected and it is not common for the total content of venom in the glands to be injected. In the case of tiger snakes and death adders, as much as four-fifths of the venom may be held in reserve (Fairley and Splatt, 1929). This means that although the chances of receiving a massive dose of potent venom are reduced, the bite of a taipan must be regarded as potentially lethal at all times no matter how many times it has bitten previously.

In the cases of probable taipan bite reported by Flecker (1940, 1944) in which the bite was followed by sudden loss of consciousness and death in a few hours, the patients must have received massive doses of venom or the venom may have entered a vein. In such cases other toxic factors in the venom than the neurotoxin play a part in causing death. The thrombase may lead to rapid intravascular coagulation, and this or other toxic factors in the venom may affect the circulation producing severe hypotension. The patient may be found pulseless and unconscious.

However, unconsciousness after snake bite does occur in the absence of hypotension and is a well-documented symptom of Australian venomous snake bite. Eades has said that he was knocked out "as by a blow" half an hour after the bite of an ornamented snake (*Denisonia maculata* Steind) (Kellaway, 1934), and K. R. Slater (personal communication, 1960) has used almost identical words to describe the effects of the bite of the brown snake (*Demansia textilis* Dumeril and Bibron) which "knocked me unconscious and caused temporary blindness". This unconsciousness may come within half an hour of the bite and may last up to 12 hours.

As recovery occurs, it is important to distinguish a patient in this state from one who is unconscious from the effects of anoxia due to respiratory obstruction or the peripheral failure of the muscles of respiration. The patient in the former state may recover spontaneously without antivenene administration, but the patient in the latter state will possibly die without antivenene and other supportive treatment. It is not known what toxic factor in the venom is responsible for this loss of consciousness.

The other early symptoms of the taipan bite may be quite mild, and indeed, if one is not familiar with the clinical manifestations of snake bite, they can easily be disregarded. The headache may be absent or mild and evanescent, lasting only one to two hours. The patient may only feel nauseated, or he may vomit. (The importance of vomiting as an early symptom and sign of venomous snake

bite cannot be overstressed.) The patient may either vomit once or several times. Pain in the abdomen and pain in the regional lymph nodes may occur, but in the cases studied so far these symptoms have been less pronounced than they are in the case of Papuan black snake bites.

It must be stressed that these symptoms appear and may disappear within one or more hours, when everything then appears normal; but if their significance is overlooked and the apparent well-being of the patient misleads the doctor so that antivenene is not administered, they will be succeeded in most cases by the development of muscle paralysis which may progress to a fatal issue.

The patient reported by Lester (1957) vomited blood, and in one of the cases of possible taipan bite he described the patient had a local wound that continued to bleed. One of the patients (hospital number, 12,129) reported here, had badly contused lips (injured when he fell unconscious on his face) which oozed blood for 24 hours. The results of studies on the blood of another patient (hospital number, 30,447) indicated that a fibrinogenopenia is produced by the thrombase and that fibrinolytic activity is minimal. The hæmolysis observed in this patient was the first clinical evidence that hæmolysis may occur after a taipan bite. The patient's red cells were not glucose-6-phosphate dehydrogenase deficient.

Clinical work thus confirms that the venom of the taipan is highly neurotoxic. Complete peripheral paralysis of all voluntary muscles may be produced, and this is the usual cause of death. If death does not occur, recovery from the paralysis takes place over a two-day to seven-day period. The venom is probably more highly coagulant than Kellaway and Williams (1929) thought, and under some as yet undefined circumstances it is also hæmolytic. There is no clinical evidence of any hæmorrhagin activity.

Taipan antivenene, if given early enough, will prevent the development of serious signs of poisoning, but in the small number of cases reported here it did not reverse severe paralysis.

### SUMMARY

1. The early literature dealing with Australia's most venomous snake, the taipan, is reviewed.
2. The clinical details of six Papuan patients who were thought to have been bitten by taipans are summarized.
3. Clinical work has shown that the venom of the taipan is powerfully neurotoxic, strongly coagulant and feebly hæmolytic.

### ACKNOWLEDGEMENTS

I wish to thank Dr. Peter Booth and Mr. A. MacGregor of the Australian Red Cross Blood Bank in Port Moresby for carrying out the tests on blood coagulation, and Dr. R. K. Arthur for permission to publish details of one of the cases. I am also grateful to Professor R. H. Black of the School of Public Health and Tropical Medicine, University of Sydney, and Mr. H. G. Cogger of the Australian Museum, Sydney, for their helpful comments on the article, and to Mr. K. R. Slater for information about the Papuan taipan. Mr. Slater also kindly provided the photograph of the taipan. The paper is published with the permission of Dr. R. F. R. Scragg, Director of Public Health, Territory of Papua and New Guinea.

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## THE INVESTIGATION AND TREATMENT OF PITUITARY DWARFISM: PRELIMINARY EXPERIENCE WITH HUMAN GROWTH HORMONE<sup>1</sup>

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EARLY attempts to treat dwarfism resulting from a deficiency of pituitary growth hormone with growth hormone obtained from animals were unsuccessful. Raben reported the first successful use of human growth hormone (HGH), extracted from human pituitary glands, in the treatment of a hypopituitary dwarf (Raben, 1958), and other investigators have since confirmed the efficacy of this hormone in restoring growth rate towards normal in appropriate patients (Raben, 1960; Prader *et alii*, 1964; Soyka *et alii*, 1964; Wright *et alii*, 1965). As supplies of human growth hormone are limited, extensive investigations are and will continue to be necessary to select for treatment those children most likely to benefit (Brasel *et alii*, 1965). These investigations should be designed to establish the diagnosis of growth hormone deficiency and to predict the likelihood of a response to growth hormone treatment in the individual patient.

Because of the many problems involved in both the production of human growth hormone and the detailed study of dwarfed subjects, those interested in these problems in Melbourne have worked together as a group. This report describes the preliminary experience of this group in the treatment of eight patients with human growth hormone, and our criteria for selection for such treatment.

### SELECTION OF PATIENTS

As will be noted, the first three patients treated were not studied as completely as the other five. This was

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because of the gradual development of our present method of assessment, which is described below.

### Preliminary Investigations

Before detailed studies were started patients were required to satisfy the following criteria: (i) growth retardation—height less than third percentile for age with a measured growth rate of less than 4 cm. in 12 months; (ii) open epiphyses with bone age delayed by more than three years; (iii) absence of puberty; (iv) absence of systemic disease, no obvious genetic tendency to short stature and appropriate chromosomal sex.

In cases in which these criteria were fulfilled additional studies were performed, including the measurement of serum alkaline phosphatase, cholesterol, calcium, phosphate and urea levels.

### Detailed Investigations of Pituitary Function

These are listed below.

X-ray examination of skull and pituitary fossa.

Urinary hydroxycorticosteroid and ketosteroid estimations before and after the administration of metapyrone.

Plasma cortisol level estimation.

Serum protein-bound iodine level estimation before and after the administration of thyroid stimulating hormone (TSH).

Estimation of total gonadotrophin content of urine.

Insulin tolerance test with measurements of plasma growth hormone levels before and after the induction of hypoglycaemia.

Those patients with evidence of pituitary disease, as assessed by the tests listed above, and who showed an abnormally low rise of HGH levels in plasma in response to hypoglycaemia proceeded to the third stage of investigation, an acute trial of HGH.