

# RESEARCH IN THE CAPE TOWN MEDICAL SCHOOL 1912 - 1962

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During 50 years this school's research activities expanded in three stages. In the first 25 years only the *pre-clinical* sciences carried out research as a faculty function. Then there was a great step forward with the foundation of organized *clinical* research between 1937 and 1950. Thereafter remarkable *overall* expansion and achievement made the school internationally known as a centre of comprehensive research. The following survey attempts to outline the history of this progress; it can only mention some of the work to indicate the trends, spectrum and significance of research here.<sup>1</sup>

## 1912-1937 : PRE-CLINICAL RESEARCH

In October 1911 Professor Jolly arrived to start the work of the school.<sup>2</sup> He was enthusiastic in doing research and in encouraging others. He erected South Africa's first electrocardiogram, and his work soon made him

famous. In 1912 Prof. R. B. Thomson started the anatomy department's researches in embryology and anthropology with particular reference to indigenous population groups. In the 1920s Professor Drennan began his long career in these preserves. He won early recognition with his studies of the famous Cape Flats skull and of Bushman morphology, and a student, Solly Zuckerman, shone in research on baboon skulls. In physiology, during the same decade, Drs. Bosman and L. Mirvish probed aspects of calcium metabolism and Dr. Zwarenstein began exploring the endocrines of *Xenopus laevis*. The latter work became internationally known in 1933 through the Zwarenstein-Shapiro pregnancy test.<sup>3</sup>

In 1919 Professor Clark did the earliest part of his famous pharmacology research on the actions of drugs on cells. In the 1920s his successor, Professor Gunn, examined digitalis and plant poisons—a field which Dr.

Sapeika entered from the mid-1930s. In chemical pathology Drs. Linder and Vadas pioneered from 1929 with investigations of rickets, osteomalacia, and the cerebrospinal fluid. Research in bacteriology and pathology started late, but in the 1930s Professor Campbell studied brucellosis and in 1937 Dr. van den Ende attempted to produce Hodgkin's disease in rabbits—a poignant recall.

Meanwhile the clinical departments concentrated on teaching and patient-care; as in many overseas schools at this time there was no faculty programme or facility for clinical research.<sup>4</sup>

A few clinicians went somewhat further but only in personal pursuits. Among these, Dr. Berelowitz 'experimented' with anaesthetic techniques,<sup>5</sup> Dr. Wood personally sectioned all his surgical material, and Dr. van Zijl gained the first Ch.M. degree of this school.

It must be emphasized that a number of clinical teachers here, though not participating in research, have been invaluable to it. No graduate who was taught by the original 'big three'—Professors Falconer, Saint and Crichton—will ever forget their insistence on using the enquiring mind and observing eye, the essentials in research. And none of the researchers here, 90% of whom were taught by Professor Forman, will fail to acknowledge his value as a critical and responsive stimulator and as a distributor of new ideas.

#### 1937-1950 : CLINICAL RESEARCH FOUNDATIONS

The momentous feature of this stage was the start of *clinical* research as a faculty function. In 1937 a peripheral vascular diseases unit was formed under Professor Saint with Dr. Goetz in charge. His outstanding work soon won recognition. Among early achievements he initiated the clinical applications of optical digital plethysmography. In 1947 he was appointed Research Associate Professor in Surgery. In 1938 Professor Brock laid the first foundations of organized research in clinical medicine with studies of nutrition problems in Cape Town. He started with an allocation of £100 and a makeshift laboratory set up in an unused operation theatre.<sup>6</sup> Soon gaining sponsors, he extended his activities and became internationally known as an authority in nutrition and other medicosociologic fields. His various efforts had profound effects in promoting and catalyzing much of the future advance.

Another feature of this period was the entry of young clinicians—mostly candidates for M.D. or Ch.M. degrees—who formed a remarkable nucleus of talent for clinical research.

Dr. Elliott was the first; in 1941 he gained the first M.D. degree awarded here. In the early 1940s there were Drs. Berk, G. Bull and Budtz-Olsen. From the end of the war 16 others came on the staff as physicians or surgeons. Later many of these held senior posts and, as will be told, contributed notable research here.

Meanwhile, *pre-clinical* research advanced. Professor Drennan investigated biologic aspects of pre-history, Dr. Sapeika studied alkaloids and animal and plant poisons, and Drs. Linder and Zwarenstein continued in their respective fields. Other fronts opened by newcomers included Professor Irving's well-known physiology researches on tooth nutrition and caries and on the anti-rachitic value of sunshine, Dr. J. A. Keen's work on cranial morphology and the anatomy of hearing, Dr. Budtz-

Olsen's clot-retraction studies, and Dr. Singer's serological anthropology and genetic investigations starting in 1949. Adding to this progress there was Professor van den Ende's great contribution in establishing virus research. He started this project in 1946 and from soon thereafter, with the help of Dr. Polson (biophysicist), Dr. Mead (biochemist) and Dr. Selzer, it succeeded so fast that by 1950 it was a CSIR unit and a feature of the school.

#### 1951-1962 : RAPID PROGRESS THROUGHOUT

This stage was marked by progressive acceleration and expansion of research which brought the school into international medicine's front line. All pre-clinical departments contributed; obstetrics and gynaecology research began; and in surgery and medicine the excellent but restricted foundations of the 1940s flourished into a remarkable complex of wide-ranging and productive activities.

The multiple reasons for this progress cannot be analysed fully here. The prime enabling factor was the CSIR policy of establishing units around highly promising researchers. (The first were the virus unit and the clinical nutrition unit.) Secondly, the Joint Medical Service, starting in 1951, attracted talented specialists who could from then on do research with the tools provided by the CSIR. Thirdly, as progress outstripped these generous facilities, further essential sponsorship was gained. From the 1950s, mainly through the indefatigable efforts of Professor Brock, large grants were obtained from the US Public Health Service and several US Foundations for research in various departments. The Nuffield and Wellcome Foundations of Great Britain also contributed, and the US Navy helped Research Associate Professor Goetz. In 1957 local industry and commerce, with insurance companies in the lead, donated a large fund to establish the fine laboratories of the department of medicine. There was further help from bequests and funds (some of which contributed from long before, e.g. the J. S. Marais Memorial Research fund for surgery, the C. L. Hermann and Fourcade bequests, the Nkana-Chingola-Kitwe fund for virus research) and many other public and private bodies, trusts and individuals.

#### Anatomy

This department has had exciting years with many interesting and significant projects. Spectacular and important fossil finds, including the famous Saldanha skull,<sup>7</sup> provided the focus for massive researches by Dr. Singer (Associate Professor, 1960),<sup>8</sup> helped by Professors Drennan and Wells and Dr. E. N. Keen. This attracted universal attention and the collaboration of leading scientists of Europe and America.

Professor Drennan developed his work on growth and racial differentiation. Professor Wells took up problems of human stature. Dr. Singer broke new ground in comparative haematology and serology; in association with Oxford, Harvard and other universities he made extensive surveys to determine the biologic structure of indigenous population groups in Southern Africa. Other notable work included researches in cardiovascular embryology and arterial distribution patterns by Prof. J. A. Keen and Drs. E. N. Keen, Van der Horst and Jarvis. The latter also made new approaches to the anatomy of hearing by studying aquatic and underground mammals.

#### Physiology and Pharmacology

Professor Sloan started studies of the physical fitness of students here in comparison with overseas counterparts, and took up work in phonocardiography. Dr. Zwarenstein (Associate Professor, 1954) investigated aspects of liver

glycogen, and Dr. Sapeika (Associate Professor, 1956) researched on anticoagulant and other drugs and on poisons.

In 1954 Dr. Budtz-Olsen helped in a comparative haematology survey in Madagascar and later assisted in giraffe researches. Other departmental projects concerned thyroid hormones, plasma-volume expanders, assisted ventilation, hepatic secretory functions, serum lipids and gastric acid secretions.

#### *Pathology, Chemical Pathology and Bacteriology*

The CSIR *virus research* unit developed considerably and fulfilled its early high promise with Professor van den Ende in the lead. After his tragic death in 1957 Professor Kipps became head; Drs. Polson, Mead and Selzer were in the team throughout, and others helped later. The unit made notable contributions to fundamental knowledge of the ultrastructure of viruses and other macromolecules of biologic importance and interest. Its early work gave one of the first indications of the existence and importance of soluble antigens. Intensive studies have been made on these antigens as well as on serum antibodies, inhibitors and many viruses.

The latter include some viruses causing important diseases in man, e.g. poliomyelitis and influenza. Others were chosen for their value in fundamental research, e.g. the viruses of blue-tongue, plant diseases and a sea-bird epizootic. Many ingenious new techniques have been devised by Drs. Polson and Mead. An immunological test, developed by Dr. Selzer, enables diagnosis and typing of poliovirus to be made within days instead of 6 weeks as required previously.

Research in *bacteriology* was done by Professors van den Ende and Kipps and Dr. Don, with Dr. Naude and others assisting later. Research on bacteriophage-typing of staphylococci aims at getting information for dealing with hospital cross-infections. The results of serological studies on *Pseudomonas aeruginosae* are of value in the epidemiology of pseudomonas infections. In *pathology* various organ cancers are being examined by Prof. J. G. Thomson and Dr. Uys, and the former is also studying asbestosis and the carcinogenic action of iron. Dr. Campbell produced cirrhosis in rats by intravenous egg-yolk and is observing effects of adrenalectomy. In *chemical pathology* Professor Linder studied primary aldosteronism and renal failure. He was succeeded by Professor Kench, who has initiated important team research on problems of protein metabolism, enzyme chemistry and haemoglobin degradation.

#### *Obstetrics and Gynaecology*

Starting in the 1950s Prof. J. T. Louw and others worked on various problems, including aspects of pregnancy toxemia and genital cancer.

Dr. Marais demonstrated lesions in placental spiral vessels in accidental haemorrhage. Dr. Benjamin found diabetes in a high percentage of cases of uterine corpus cancer or dysfunctional bleeding. In 1957 the University's first M.D. degree in obstetrics was awarded to Dr. Jordaan.

#### *Surgery*

Until 1958 Research Associate Professor Goetz continued his renowned work here. His giraffe studies with Drs. Singer and Budtz-Olsen were another manifestation of his originality and scientific enterprise. In the early 1950s Professor Erasmus contributed studies on pain,

while Dr. du Plessis resumed his work on the parotid and turned to gastric problems. Prof. J. H. Louw concentrated on studies of congenital abnormalities and problems in vascular surgery. His earlier work with Dr. Barnard on intestinal atresia made a new approach to this condition. In 1958 the return of Dr. Barnard, as Director of Surgical Research, was a landmark; now 'Americanized', he galvanized his unit into crescendo activity, and within a few years it was internationally known for achievements in *cardiovascular surgery*. He was promoted Associate Professor in 1962.

Valve surgery is a major research project. Several mitral and aortic valves have been designed and manufactured here and used successfully in patients. The value of pericardial tissue for valve reconstruction is being assessed by Dr. Frater. Extracorporeal circulation techniques have been studied by Associate Professor Barnard and his team and applied in many cardiac operations. They also developed methods of inducing profound hypothermia and used them in cardiac, aortic, hepatic and neurosurgical procedures. Many other units and departments (cardiac, child health, anaesthetics, bacteriology, medicine) and services (hospitals and blood transfusion) are indispensable collaborators. Massive homo-transplantation has been a spectacular study here, and coronary artery disease is being investigated with a view to developing surgical treatment.

Many widely-ranging problems in *general surgery* are also being studied.

In *orthopaedic surgery* Professor Allen developed the well-known 'UCT Artificial Limb', and he has extended the principles to construct prostheses for children born without legs. In *plastic surgery* Dr. Davies Snr. invented a simple dermatome of much value in treating burns in children, and Dr. Davies Jnr. evolved a successful new method of hare-lip repair. In *neurosurgery* the fields of research include intracranial haematoma and cerebral angiography.

#### *Anaesthetics*

The staff commenced fundamental research in the 1950s and many problems are being explored. Halothane techniques, now as a routine used here in cardiac surgery, were elaborated by Dr. A. Bull (Associate Professor, 1963) and others, and his work with Dr. Smythe on intermittent positive-pressure respiration treatment of tetanus neonatorum was a major advance in this field.

#### *Radiology*

The radiotherapy section under Dr. Grieve (Associate Professor, 1959) devised improved appliances and dosimetry techniques. Large surveys on cancer and long-term evaluations of therapeutic regimes are being made. The radiodiagnostic section collaborates with other units in their researches.

#### *Medicine*

The glimpses of this department's massive researches must be even more fragmentary than those already given of other work.

During the period under review team-projects have been developed by 44 departmental physicians, of whom 70% have held full-time university-hospital appointments and the

majority have worked here for 5 years or more. Most of the research is done by teams dealing with different fields in medicine, members often joining in some projects of other teams. Four of the teams form CSIR research units or groups.

1. *Clinical Nutrition Unit.* Under the leadership of Professor Brock, this unit (one of the first set up by the CSIR) has studied many facets of malnutrition—the two most important having been *protein malnutrition*, particularly kwashiorkor, and the relationship between *dietary fat and ischaemic heart disease*. Professor Brock, Dr. Hansen (Associate Professor, 1962) and others made major advances by establishing the primacy of amino-acid deficiency in kwashiorkor. This work is continuing in association with the Department of Child Health. The dietary fat researches started with a survey made by Dr. Bronte-Stewart with Dr. Ancel Keys. It achieved a major break-through in establishing the different effects of saturated and unsaturated fats on serum lipids. Dr. Eales (Associate Professor, 1957) was closely associated with the early work in protein and lipid metabolism; he was assistant-director of this unit for some years.

Among many subsequent researches, the sociological aspects of differing rates of ischaemic heart disease in Cape racial groups are being studied by unit workers including Miss Moodie. Genetic aspects of the interracial studies have been taken up recently by Dr. Gordon.

2. *Endocrine Research Group.* Dr. Jackson, in charge of endocrine research laboratories, was active throughout in many endocrine studies. His development of the concept of 'pre-diabetes' has aroused much interest; he and others, including Professor Linder, have studied many aspects of diabetes. Original observations on gonadal dysgenesis were made by him and Dr. Hoffenberg, who has been mainly concerned with thyroid researches, particularly on thyrotrophic hormones.

Dr. Jackson worked on the Fanconi syndrome and various bone diseases. Down the years, since early physiology days, workers here have been interested in calcium and phosphorus metabolism in rickets and other conditions. Recently steroid hormones have been investigated in this unit which has been recognized as a CSIR research group.

3. *Cardio-pulmonary Research Group.* In 1951 the 'cardiac clinic' was founded in Groote Schuur Hospital by Dr. V. Schrire with the early help of Dr. Nellen. Its activities expanded greatly and it was created a CSIR research unit. The group has produced internationally-known contributions in cardiology. Members collaborate extensively with other units, in particular Associate Professor Barnard's team.

A new auscultatory sign differentiating certain tachycardias, and original observations on second-sound splitting, were reported by Drs. Schrire and Vogelpoel. These workers, with Drs. Nellen and Swanepoel, established the value of the simple amyl nitrite test in distinguishing certain murmurs; they also, with Dr. Beck, demonstrated the use of phenylephrine. Arising out of Dr. Schrire's observation of the rarity of ECG evidence of myocardial infarction in Cape Town Bantu, an interracial study revealed its frequency in Whites and Coloureds and that hypertension is common in all three groups. Recently an ingenious simple technique for accurate arterial puncture was devised by Drs. Schrire and Kaplan.

4. *Renal-Metabolic Research Unit.* Since the 1940s Associate Professor Eales has been mainly interested in the fluid and electrolyte exchanges in nutritional oedema

and renal disorders and in porphyrin metabolism. He has made distinguished original contributions in these fields, in addition to his notable work in nutrition. Recently this unit has been accorded CSIR recognition.

Associate Professor Eales has put the earlier (clinical, demographical and biochemical) work on South African porphyria on a sound experimental basis. Recently, with Drs. Dowdle, Sweeney and others, he has studied its treatment with chloroquin and its production in rats by feeding hexachlorobenzene. Arising out of Drs. Horwitz and Sougin-Mibashan's observation that gout is common in Cape Town, this condition was investigated by the latter who made original observations on the uricosuric effect of ethyl biscoumacetate.

5. *Haematology Section.* Dr. Merskey, whose work in bleeding disorders is internationally known, led researches with Dr. Sougin-Mibashan and others on blood coagulability in coronary thrombosis; and with Dr. Lackner they studied fibrinolytic activity in various conditions. With Associate Professor Sapeika, Dr. Uys and others, Dr. Merskey also investigated the effects of phenindione on experimental atheroma.

#### Child Health

Starting research in 1952 with a small-scale study of kwashiorkor by Drs. Suckling and Hansen (then under Professor Brock), much progress followed Professor Ford's arrival and the opening of the Red Cross Hospital. Its metabolic unit, under Associate Professor Hansen, has collaborated in notable work with the clinical nutrition unit and with Dr. Smythe and others at Groote Schuur Hospital. Various projects have been investigated, often in association with other units. The treatment of tetanus neonatorum has been greatly improved by the work of Dr. Smythe and Associate Professor Bull, as already told, and neonatal Cocksackie infection has been intensively studied by the department.

It has indeed been a fruitful journey to this point from the days of Professor Jolly and his string galvanometer. The catholicity, enthusiasm and high scientific standard of all the work in the school justify the expectation of a great deal more to come.

<sup>1</sup> In the past decade alone over 1,000 research papers have emanated from this school and 50 M.D. projects have been completed. Most of these and numerous current researches cannot even be mentioned here. Nor can tribute be paid to all—teachers, administrators, sponsors and technicians—whose work has been invaluable. A book on the history of the school and its teaching hospitals is in preparation.

<sup>2</sup> He started in the South African College Physiological Laboratories which officially opened in 1912. In 1926 these became part of the University's Wernher and Beit laboratories at Mowbray.

<sup>3</sup> In the 1930s Dr. Zwarenstein led students in their research work for the Ph.D. degree. Prof. Lancelot Hogben, of the Zoology Department, was another potent stimulator of medical researchers from the 1920s.

<sup>4</sup> The Robinson Chair in Radiology was founded in 1935, but it did not yet function in research.

<sup>5</sup> Louw, J. H. (1962): S.Afr. Med. J., 36, 667.

<sup>6</sup> Groote Schuur Hospital, opened in 1938, had no provision for laboratories (other than ward side-rooms)—an example of lack of facilities throughout the faculty, persisting until the 1950s.

<sup>7</sup> The first fragments were found in 1953 by Mr. Keith Jolly, son of Professor Jolly, while working with Dr. Singer and a field team.

<sup>8</sup> Since 1954 the University has promoted senior academic staff *ad hoc* Associate Professors in recognition of 'scholarship and ability to do outstanding research and creative work'. The promotions and dates are indicated in this paper.

<sup>9</sup> Since 1947 the University has awarded Fellowships to the following in recognition of 'distinguished original academic work': Professors Irving (1948), van den Ende (1953), Brock (1956), Drs. Merskey (1956), Jackson (1957), V. Schrire (1959), Prof. J. H. Louw (1961) and Associate Professor Eales (1962).