

Chapter 1

THE 1966 PROPOSAL

On the evening of 20 June 1966 there was a meeting of the Senior Medical Staff at National Women's Hospital in Auckland. Among those present were a number of doctors whose names were to become more and more familiar as this Inquiry progressed. Eight matters were discussed that night, one a proposal tabled by Dr Herbert Green, Associate Professor in the Hospital's Obstetrics and Gynaecology Department.* The subject of the proposal was carcinoma in situ.

Dr Green's proposal, set out in full in the Minutes of the Senior Medical Staff meeting, read:

"Carcinoma in Situ

Associate Professor Green:

Up to December 1965, 503 cases of cervical carcinoma-in-situ have been treated, 68.2% of them by cone biopsy or lesser procedure. One case is alleged to have progressed to invasion but this woman had an extensive carcinoma of the vulva diagnosed at the same time as a doubtful cervical carcinoma-in-situ. One such case is approaching the expected incidence of invasive cervical cancer in any 500 women of this age group.

"Sixty cases with micro invasion have been treated, 40 of them by cone or ring biopsy. Four have been treated by punch biopsy alone.

"Many have had persistently positive smears including in one woman up to 8 years following the original cone. There have been 57 subsequent pregnancies.

"Cytology and the diagnosis of large numbers of carcinoma-in-situ have not accelerated the declining incidence of cervical cancer or favourably influenced mortality rates. It is considered that the time has come to diagnose and treat by lesser procedures than hitherto, a selected group of patients with positive (A3-A5) smears.

"Including the four 1965 cases, there are at present under clinical, colposcopic, and cytological observation, 8 patients who have not had a cone or ring biopsy. All of these continue to have positive smears at intervals. It is suggested that this should be extended to include all cases in women under the age of 35 with positive smears in which there is no clinical or colposcopic evidence of invasive cancer, ie

- a) The cervix shows nothing more than an eversion (erosion) on clinical inspection.
- b) There is no undue bleeding on probing the cervical canal.
- c) Colposcopic findings are consistent with carcinoma-in-situ only.

"In the interests of continuity of supervision and patient-confidence, it is suggested all such cases should be passed to the care of Professor Green whose conscience is clear and who could therefore accept complete responsibility for whatever happens, with Dr McIndoe to assist on the colposcopic and cytological aspects."

The Minutes then record the following discussion:

"Professor Green said that his aim was to attempt to prove that carcinoma-in-situ is not a pre-malignant disease. He also said that he had omitted to state

* Associate Professor Green chose to be addressed throughout the Inquiry as Dr Green.

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in this report that punch biopsy specimens would be taken. If at any stage concern was felt for the safety of a patient, a cone biopsy would be performed.

"There was a lengthy discussion during which Professor Green answered many questions.

"Mr McFarlane and Mr Grieve favoured retaining these patients under their respective teams but had no objection to handing over cases coming into the category stipulated by Professor Green to Professor Green for follow-up.

"The matter was then deferred for consideration by the Hospital Medical Committee."

In 1966 the Senior Medical Staff meetings were the forum through which matters of clinical interest and relationships between clinicians and the Postgraduate School were frequently discussed. It was an ideal opportunity to debate management of patients and consider new treatment options and implications. However, it had no direct duty or authority to approve Dr Green's study. It appears to have been constituted as an 'in-house' committee to inform members of the senior staff of management decisions and enable them to participate in the decision-making process.

As soon as the Senior Medical Staff (SMS) meeting concluded, a meeting of the National Women's Hospital Medical Committee (HMC) began. Whereas Dr Algar Warren, the Medical Superintendent, had chaired the previous meeting, this time the head of the Postgraduate School, Professor Dennis Bonham, was in the chair. There were 10 other doctors present, all of whom had attended the earlier SMS meeting.

The Hospital Medical Committee meeting lasted slightly more than two hours. A large number of topics were discussed, one of which was Dr Green's proposal on carcinoma in situ. On this occasion the Minutes record:

"The committee was of the opinion that cases considered suitable for this treatment by the consultants in charge of the cases, be referred to Associate Professor Green for followup.

Moved: Dr S

Seconded: Mr M

That: 'the Report of Associate Professor Green be received and the proposals contained therein be commended to the rest of the staff.'

Dr Green's proposal was put to the HMC as the body responsible for approving such projects. Since 1947 the Committee had been required to:

"...be responsible for the clinical organisation at National Women's Hospital in order that the professional and scientific work shall be properly carried out therein..."

At that time there appears to have been no written Hospital Board requirement that the HMC consider the ethics of research proposals. However, the Committee had chosen to assume that role. Dr Warren considered that the HMC had certain ethical duties. Professor Bonham held the same view when, in 1986, he responded as chairperson of the Hospital's Ethical Committee to an enquiry about the 1966 Proposal.

There was no other mechanism, either formal or informal, for dealing with ethical aspects of clinical practice or research. In fact, the Auckland Hospital Board does not appear to have considered this an important issue until about 1972 when the Medical Superintendent of National Women's Hospital, by memorandum, stated that the functions of an ethical committee were carried out by the Hospital Medical Committee.

A significant number of the people who were present at the Hospital Medical Committee meeting and the earlier SMS meeting gave evidence during this Inquiry. They were Professor Bonham, Dr Warren, Dr Malcolm McLean, Dr Green, Dr Bruce Grieve and Mr Bruce Faris. Another of those present at the SMS meeting was Dr Bill McIndoe. Although Dr McIndoe died before this Inquiry started, he was obviously a methodical man given to

recording his thoughts with great care and in considerable detail. I have a large volume of his hand-written and typed memoranda, correspondence and comments. They have all been authenticated by his daughter and the only doubt which remains is whether the documents accurately record the events of 1966 and subsequent years.

KNOWLEDGE OF THE INVASIVE POTENTIAL OF CERVICAL CARCINOMA IN SITU BEFORE 1966

Carcinoma in situ (CIS) is basically a symptomless condition. It is a lesion which is found on the surface of the epithelium (the lining or skin of the uterus or any area of the genital tract) and which has not invaded or spread beneath that layer. CIS is known as preinvasive or a cancer precursor. It will develop into cancer in an unknown number of cases over an unknown period of years. In order to discover its presence it is necessary to screen apparently well women.

At the time that Dr Green put his Proposal to the Senior Medical Staff and Hospital Medical Committee, the accepted method for initial diagnosis was the Papanicolaou smear, a technique where cells are collected from the mouth of the cervix or from the vagina and their structure microscopically examined. However, the only rational basis for conducting a routine screen of women who usually displayed no symptoms of disease, was if carcinoma in situ did have a significant chance of developing into invasive cancer; and if it was possible to treat CIS effectively, so preventing its development to a more serious and life-threatening disease.

By the early 1960s most experts in Europe, the United States of America and Australia considered that CIS was a precursor of invasive cervical cancer. There was a growing body of research to support this belief. Professor Per Kolstad, now a Gynaecological Oncologist at the Norwegian Hydros Institute for Cancer Research and one of a number of specialists of international repute called by the Inquiry, cited studies from Norway and other parts of the world in illustrating examples of this research. He first gave three examples of indirect evidence of the invasive potential of CIS.

1. The observation that carcinoma in situ is more prevalent in populations with a high incidence of invasive cervical cancer and the fact that carcinoma in situ is seldom found among females with a low incidence of invasive cervical cancer.
2. The mean age for women with carcinoma in situ is 10 years lower than those with invasive carcinoma.
3. Carcinoma in situ is frequently found at the border of invasive cervical cancer, especially in the earlier stages 1B and 2A.

Professor Kolstad also gave direct evidence of the invasive potential of CIS.

1. In 1961 Professor Kolstad compiled a table of studies for the Norwegian Medical Society on the development of invasive carcinoma in untreated cases of carcinoma in situ from Paris, Copenhagen, Stockholm, Warsaw and from New York:

Development of invasive carcinoma in
untreated cases of CIS

Author	Observed Years	No. of Patients	Invasive Cancer No.	%
Funck-Brentano	9	124	41	30.2
Karlstedt	1-23	94	17	18.1
Kottmeier	3-10	40	9	22.4
Lange	1-10	100	24	24.0
Masterson	1-5	25	7	28.0
Petersen	8-22	127	39	30.7
Polahovsky	2-5	85	30	35.3
Total	1-23	595	167	28.3

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2. *"The internationally famous Gynaecological Oncologist, Meigs, from Harvard University said in 1956, 'One last plea is that all of us cease to allow patients to go without treatment after a diagnosis of cancer in situ has been made. I think it is careless, thoughtless and very reprehensible to follow such a procedure.'"*
3. *"Leopold Koss, another recognised expert on the development of cervical cancer, presented a study in 'Cancer', No 16 1963, in which he gave the following summary of his findings (the emphases are Koss's): 'The essence of a long-term study of early malignant lesions of epithelium of the uterine cervix are reported. This study encompassing 93 cases with follow-up periods ranging from six months to ten years, suggests the following conclusions:*
 1. *Carcinoma in situ is a lesion of the cervical epithelium that **beyond doubt**, is a precursor of invasive cervical cancer.*
 2. *Carcinoma in situ is very fragile and poorly established and may be readily eradicated by a variety of minor procedures. Its natural course may be profoundly modified even by small biopsies, drugs and possibly a physiological trauma such as delivery.*
 3. *Spontaneous disappearance of carcinoma in situ apparently does occur, **but it is an extraordinarily rare event.***
 4. *Lesions histologically less advanced classified as borderline atypia (dysplasias) behave similarly and may develop into carcinoma in situ and even invasive cervical cancer.*
 5. *Carcinoma in situ and the lesser but related lesions appear to have **an extraordinarily slow evolution.** It was well known in the early 1960's continuing over periods of many years. For this reason they should not be considered to be in the emergency category and may be treated more leisurely.*
 6. *The behaviour of carcinoma in situ and related lesions of the cervix is at marked variance with that of invasive cervix cancer. **This knowledge should not be used to minimise the importance of the lesion**, but rather to establish new concepts of early human cancer!"*

Professor Kolstad's evidence convinces me that by the early 1960s expert world opinion considered that carcinoma in situ was a precursor of invasive carcinoma.

MANAGEMENT OF CIS BEFORE 1966 – Outside New Zealand

According to Dr Joseph Jordan, Consultant Obstetrician and Gynaecologist at the Birmingham and Midlands Hospital for Women, Director of that hospital's Colposcopy Unit, and Director of Clinical Services in Obstetrics and Gynaecology to the central district of Birmingham:

"The standard treatment for premalignant disease of the cervix in 1966 was hysterectomy although in a small number of centres in North America and a larger number in Europe, cone biopsy was found to be effective in a high proportion of cases."

Dr Malcolm Coppleson, head of the Gynaecological Oncology Department, King George V Memorial Hospital, Royal Prince Alfred Hospital in Sydney, Australia, also spoke of the large numbers of hysterectomies being performed in the 1960s. He said that his perusal of the literature of the 1950s and 1960s

"points up the concern of some gynaecologists about this uncritical and radical approach, especially in young healthy women.

"Out of this concern were derived less traumatic and simpler diagnostic methods such as randomly directed four quadrant punch biopsies performed with the unaided eye and treatment of selected cases of carcinoma in situ by conization alone. Without colposcopy, trepidation persisted that invasive cancer might be missed."

Although colposcopy was very rarely used in the United Kingdom or the United States of America before 1966, the colposcope had been introduced in Norway as early as 1953. It allowed a change in treatment from relatively radical procedures like hysterectomy or radium irradiation to conization. Dr Coppleson:

"The use of colposcopy permitted a safer and greater rationalisation of therapy and the trend progressed to more conizations as definitive therapy and fewer hysterectomies. In our 1967 book, I wrote that conization of the cervix 'is the recommended treatment for the majority of women with carcinoma in situ'."

During this period, many gynaecologists worldwide had already moved from the radical treatment of CIS by hysterectomy to the more conservative cone biopsy. 'Conservative' is used here in the sense, 'to conserve'. In order to retain her fertility, no more of a woman's uterus was removed than was necessary.

The cone biopsy was a valuable diagnostic technique which had also come to be accepted as treatment for CIS, particularly in cases involving younger women. By using colposcopy, the gynaecologist was able to shape a cone to follow and encompass the abnormality. A hysterectomy was performed if the lesion had not been completely removed by a cone biopsy, and in cases involving older women for whom the reproductive function was not important and whose lesion was not fully visible with the aid of the colposcope.

MANAGEMENT OF CIS BEFORE 1966 – at National Women's Hospital

The gynaecologists at National Women's Hospital were not unaware of world opinion on the nature of CIS and the trends towards its more conservative management. As early as March 1955 the Senior Medical Staff unanimously supported the formation of a cancer team under the control of Mr Harbutt, to which all cases of carcinoma of the cervix were to be referred for treatment. The aim was to improve the standard of treatment as additional experience was gained.

It is possible to infer from discussion at a Senior Medical Staff meeting in June 1955, that CIS (Stage O Carcinoma) was to be referred to this team also. The meeting discussed the formulation of a policy for the treatment of carcinoma of the cervix and uterine body and defines Stage O as:

"Carcinoma in situ – also known as preinvasive carcinoma, intraepithelial carcinoma – and similar conditions."

The meeting agreed that:

"CIS should be treated by hysterectomy except in cases where it is desirable to conserve reproductive function when amputation of the cervix should be carried out."

In October 1955 the Senior Staff agreed that the taking of cervical smears was the only means of diagnosing carcinoma of the cervix at Stage O and fixed a policy that all patients over 35 years of age attending the out-patients' department, or admitted to gynaecological wards, were to have a cervical smear taken.

Over the next 10 years the Senior Medical Staff and Hospital Medical Committee

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regularly reviewed and discussed diagnosis and treatment procedures for CIS and invasive cervical cancer and agreed on general policies in procedure. For instance, in March 1957 it became general policy where CIS was diagnosed from a positive smear and a ring biopsy, that the cervix should be amputated for further histological diagnosis before proceeding to a total hysterectomy. The meeting also agreed that there was "no place for wedge biopsy in the diagnosis of CIS".

A month later it was agreed that in investigating cervical carcinoma in situ the first step should be to take a ring biopsy which aimed to encompass completely the squamocolumnar junction and an area as high as 2cm up into the endocervical canal. However, the decision to amputate the cervix was to be taken now only where the pathologist required additional material for examination or the clinician considered that there was a good indication for this procedure. At the same meeting, Dr Sullivan, reporting on his study leave in the USA, said that:

"At the three centres visited [CIS] was discussed with the pathologists, all of whom were agreed that carcinoma in situ is an early progressive malignant lesion, which if untreated, will eventually become invasive."

In May 1958 the Minutes of the Hospital Medical Committee state:

"The official Hospital policy regarding the treatment of carcinoma of the cervix Stage O, [carcinoma in situ] should be adequate cone biopsy ... provided the immediate follow-up is negative and ... the pathologist is satisfied that the cone biopsy has included all the carcinomatous tissue."

The importance of regular follow-ups was raised in 1959 and again early in 1963 when Dr Green told staff that in his view check-ups were just as important after a hysterectomy as after a cone biopsy.

In October 1963 at a full staff meeting, the factors indicating the need for a cone biopsy were discussed and enumerated: all A3 smears or above, or three A2 smears. All these cases were to have a follow-up smear once a year. At this same meeting Dr Green was given permission to collect samples of cervical mucus from A3 to A5 smears and from known cases of CIS for biochemical testing.

Management of CIS by Dr Green prior to 1966

In 1949-1950, as part of the pre-requisite to Dr Green's admission as a member of the Royal College of Obstetrics and Gynaecology, he wrote a paper on the early diagnosis of cervical cancer. It was obviously an interest which he pursued from that time until he joined National Women's Hospital in 1956. Indeed it is clear from his evidence that a motive for joining NWH was to enable him to work with cervical cancer patients and those with carcinoma in situ. Given this intense interest in the disease and its management, it is not surprising that Dr Green began writing of his findings during the course of treating women diagnosed with CIS. He was also increasingly concerned at the number of young women undergoing hysterectomy for the disease, which he regarded as unnecessarily radical.

In his evidence he spoke of reading papers such as that by Krieger, Lawrence and McCormack from Cleveland, Ohio, which caused him to ponder on the need for total hysterectomy as a treatment for carcinoma in situ. He spoke of Kottmeier and many others who, during the 1950s, had written up their experiences of CIS and carcinoma of the female genital tract for scientific journals and books.

There were also discussions on treatment of CIS among consultants at the Hospital at that time and Dr Green mentions in particular, Dr Grieve and Dr Harbutt, Mr Faris, Dr Macfarlane and Professor Liggins, all of whom were respected consultants at NWH.

The active encouragement of research at the Postgraduate School, Dr Green's particular interest in the disease, his age, his reading and his discussions with colleagues made a more formal study of carcinoma in situ almost inevitable. He had begun writing and presenting papers soon after he arrived at NWI and presented a paper, which was the forerunner to the 1962 article, 'Carcinoma In Situ of the Uterine Cervix,'¹ as early as 1958. In the 1962 paper he said:

"When, in 1956, it was apparent that an increasing number of young women with small families were being subjected to hysterectomy for carcinoma in situ, it seemed worthwhile to consider a more conservative approach to treatment.... At first, conservative treatment in this Hospital was applied only to young women (under 35 years of age) and then only if more children were desired. Later, the illogical nature of this view was realised – if local excision is good enough for a young woman why should it not be so for her near-menopausal sister whose cervix is likely to suffer much less trauma? The policy of local excision was then extended by the author to the older patients."

At the time he wrote that, Dr Green was obviously concerned about conducting unnecessarily extensive surgery on women whose disease did not necessarily warrant it. He was reviewing, as had Dr Coppleson, the need to treat carcinoma in situ by hysterectomy, and particularly by radical hysterectomy. Some centres were beginning to use a cone biopsy (known when it is used for treatment purposes as conization) as an effective treatment for CIS.

A hysterectomy was an extreme measure to take unless it was thought critical for the health or survival of the woman concerned. Hysterectomy was regarded by some doctors as a mutilating operation with psychological effects. It not only interfered with a woman's reproductive system, but subsequent pathological examination also found that CIS had not always been present. Moves to a more conservative treatment protocol were not, therefore, unique to Dr Green or National Women's Hospital.

There were then, as there are now, limitations on the use of the more conservative treatment approach. A number of expert medical witnesses stressed that this treatment was more appropriate in younger women, that invasive cancer must be excluded by a histological diagnosis and that follow-up cytology must satisfy the clinician that the disease has been eradicated. Dr Green, writing in 1962, was clearly setting out a conservative treatment policy which he had already formulated. In that 1962 paper, Dr Green referred to the conservative management by cone biopsy (80), ring biopsy (1) and amputation of the cervix (3) of 84 patients who had been diagnosed as having CIS up to 1960. This conservative management had already been extended to patients where there was doubt about the completeness of the excision and to patients over the age of 35.

In his evidence, Dr Grieve said that Dr Green was the only clinician at National Women's Hospital treating CIS by less than cone biopsy before 1966. All the others were performing hysterectomies or cone biopsies. The 1966 Proposal itself, and an article by Dr Green published the same year, gave further details of patients managed conservatively.

It appears, therefore, that in the early 1960s, a significant number of patients with CIS, including some over the age of 35, were managed by Dr Green by diagnostic procedures and by cone biopsy. It was evident that Dr Green was already content to follow some patients with positive smears without eradicating the lesion.

DIAGNOSTIC TECHNIQUES IN 1966

As CIS is basically a symptomless disease, the clinician cannot expect to gain any information from the woman herself. Taking her history will be useful only if the woman reports symptoms consistent with invasive cancer. The clinician is able to detect invasive cancer with the naked eye; but CIS would normally pass unnoticed. Consequently the

clinician's role is to ensure that the diagnostic techniques of the cytopathologist and histopathologist are used where appropriate, and to ensure that no symptom which might mean invasive disease is overlooked.

Cytology and the Papanicolaou smear test

A cytologist studies the structure of cells under a microscope. In genital tract cancer precursors and invasive cancer, the cells are collected from the mouth of the cervix or from the vagina by a technique commonly known as the Papanicolaou smear or the smear test. When Papanicolaou smear tests were introduced to National Women's Hospital during the 1950s, they were used with enthusiasm by the consultant staff employed there, Dr Green included. Every woman (aged 30 and over to begin with) who attended the Hospital for an obstetrical or gynaecological examination was offered this simple test. Mrs Barnes, a Senior Nurse at NWH until 1962 when she left nursing, said:

"At the time I was working in the Clinic, the Papsmear test was one of Associate Professor Green's greatest enthusiasms and we used to jokingly suggest that a woman could hardly get past the appointment counter without having her pants off and a smear taken. So there was a great deal of excitement and enthusiasm concerning the procedure and its prospects, and we couldn't wait to share our knowledge with the patients.

"There was certainly no question of in any way withholding what we thought about their condition and their prospects. Really, we were rejoicing with these women because they had, at such an early stage, been discovered to have the potential for invasive cancer."

Mrs Barnes' evidence confirmed both the early emphasis placed on the value of cytology and the recognition of those who worked at the Hospital of the invasive potential of CIS.

In Papanicolaou's original classification cytologic findings were graded into five classes:

- Class 1 Absence of atypical or abnormal cells
- Class 2 Atypical cytology but no evidence of malignancy
- Class 3 Cytology suggestive of, but not conclusive for malignancy
- Class 4 Cytology strongly suggestive of malignancy
- Class 5 Cytology conclusive for malignancy.

This classification is used by a minority of pathologists now, but a modified Papanicolaou system was used at National Women's Hospital until 1983. Part of that system was an additional category – Grade (Class) 2R. According to Michael Churchouse, the Charge Technologist in the Cytology Laboratory at NWH, Grade 2R had a specific meaning in the Hospital laboratory:

"Dr McIndoe had gone to great trouble to ensure that the clinicians knew what a 2R was. A 2R was 'I don't know' category. It is neither one thing nor the other. It clearly has to be either repeated or a biopsy. It has to have some further investigation.

"Over the years, started by Dr Darby with his special stamp and culminating in Dr McIndoe putting very special stickers and even changing the word to 'Atypical', he was attempting to make the clinicians heed this report to repeat. What I want to make very clear here is that we were doing malignancy screening. All that was required of us at that time, over that period of time, was to say, 'This patient has a malignancy.' 'This patient we think might have a malignancy, it needs further investigation.'

"This was very clear to everybody but it appeared from time to time that they took less notice than we would have wished of the 2Rs and so we went to the stickers, the changing of the wording, the emphasising that this was not a negative, this was something that had to be, this was cytologically significant, and had to be very clearly and carefully investigated."

It appears that at National Women's Hospital during the 1960s and 1970s a Grade 2R smear was not being adopted as a management suggestion "at least by Dr Green".

The Papanicolaou smear test is an extremely useful means of detecting precancerous conditions or early invasive cancer. It is, however, an inexact test and has never been used as a precise diagnostic technique. While cytology can warn the gynaecologist of the possibility of disease, it is a starting point only. But by the same token, it should not be ignored.

Colposcopy

(a) Basic use of the Colposcope

A colposcope is a binocular microscope with a strong light. It provides a magnified view (10 to 40 times) of the surface structures of the cervix. The patient is examined on a normal examination table or in a specially designed reclining chair. The instrument was developed in Germany in the 1930s to study the early stages of cervical neoplasia. From the 1950s onwards, groups in Norway (Professor Kolstad), Czechoslovakia (Dr Staffl) and Australia (Dr Coppleson) began expanding the technique.

Dr Coppleson said that the colposcope started to allow "a more generalised enquiry into the meaning of all the other features of the colposcopic image, other than topography, such as colour, surface configuration and blood vessel changes as well as temporal changes in appearances as might constitute a life history of the normal and the diseased organ". This further development assisted the expert colposcopist in excluding the presence of invasive cancer by examining the cervix and taking small biopsies of the most abnormal areas. However, Dr Coppleson said that until the early seventies, very little of this new knowledge was available outside the research centres where it was developed.

(b) Colposcopy at NWH in 1966

Professor Carey's enthusiasm for the value of cytology had resulted in the introduction of Papanicolaou smear tests at National Women's Hospital. It appears that he was also responsible for ordering the Hospital's first colposcope. It lay unused until Dr Warren arrived as Medical Superintendent at the Hospital in September of 1960 and came upon it in storage.

Dr McIndoe obviously chose to become skilled in this technique. For many years he was the only formally trained colposcopist in this country. He had joined the Hospital as a Registrar in the late 1950s and after becoming a fellow of the Royal College of Surgeons in 1961 he had been appointed a cytologist. During 1963 he spent three months training in colposcopy, a part of that time with Dr Coppleson in Sydney. Dr Coppleson remembers:

"Dr McIndoe came to Sydney in the mid or early 60s to learn the technique and its newer findings. My recall of this visit is poor but sufficient to reach the conclusion that his grasp of the technique, its meaning, potential, and detail, not surprisingly, were indifferent, and in retrospect unquestionably too vestigial to apply to such an intrepid venture."

(The 'intrepid venture' to which Dr Coppleson refers is the 1966 Proposal.)

In September 1962, as part of a report on the Thames Cervical Cytology Survey, Dr McIndoe had informed a full staff meeting that he had examined 23 patients with positive and

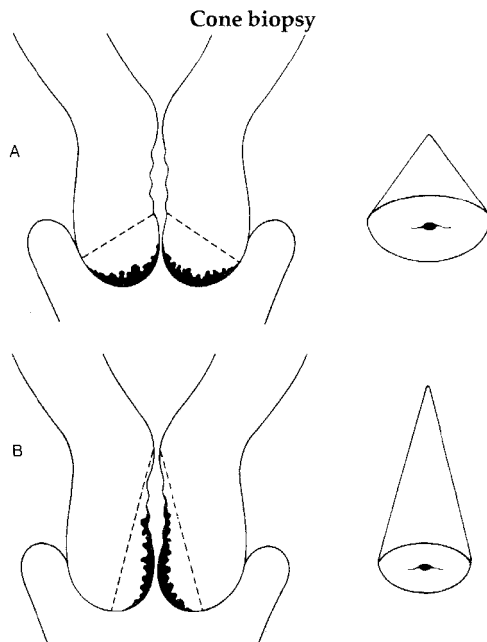
A2 repeat smear results. He said that he could now "handle the instrument quite well and [has] had some experience with it". However, he noted that he had not had sufficient experience with a wide enough range of patients to be able to submit any conclusions.

Dr McIndoe took up an appointment in colposcopy at NWH in 1965, having been appointed to a half-time position in cytology earlier that year. The technique was still in its infancy and the many uses of colposcopy and the range of its possibilities were in their early stages of development. In this environment, despite a growing confidence with the technique, Dr McIndoe's skills could have been no more than elementary in 1966, and he would have been the first to agree.

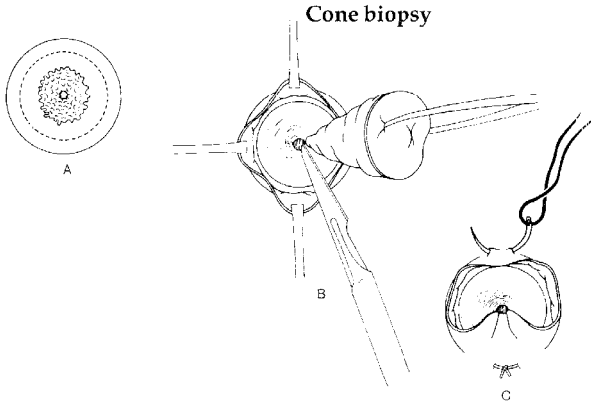
As Dr Coppleson said, there was a "paucity of published work, especially the detail on the subject and nascency of our ideas on the topic. At the time, few colposcopists even understood the concept let alone had the necessary expertise and confidence to grade lesions". It was Dr Coppleson's opinion that while Dr McIndoe would have been exposed to the new approach to colposcopy which "permitted the differentiation of appearances that were prospectively serious from the majority which were demonstrably insignificant", he doubted "his [McIndoe's] grasp of its significance".

Histopathology

In the 1950s and 1960s before colposcopy was available, when a positive smear was reported and there was no clinical evidence of invasive cancer, the next step in the procedure was to take a biopsy of tissue from the woman's cervix or other affected part of the genital tract. By far the most common form of biopsy then was the cone biopsy.



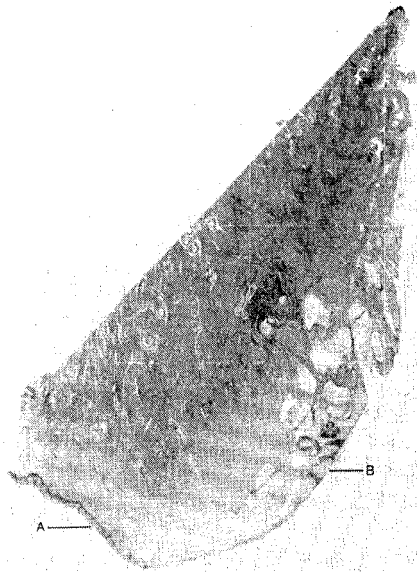
Conization is the removal of a cone-shaped wedge of tissue from the cervix. The specimen should include uninvolved endocervical epithelium above the abnormal lesion and uninvolved ectocervix below. In postmenopausal patients the squamocolumnar junction is more often located in the endocervical canal, requiring the narrow type of cone specimen B.



- A Surface of the endocervix which will form the base of the cone. The dotted line indicates the line of incision clear of the abnormal areas defined by colposcopy.
- B Excision of cone-shaped specimen.
- C The denuded cervical tissue is then covered with flaps of surrounding epithelium.

This tissue was then examined by a histopathologist. A large piece of tissue, such as that taken with a cone biopsy, will include parts of the underlying stroma (the tissue beneath the surface layer or epithelium). In order to diagnose or exclude invasive cancer it is essential to have a tissue sample of this depth available for histopathological examination. The pathologist then reports the presence or absence of disease to the gynaecologist.

Section of a cone biopsy



- A Original (native) squamous epithelium of the ectocervix.
- B Area of CIS arising in the transformation zone, which lies mainly in the endocervical canal in this patient.

Smaller punch biopsies were performed at National Women's Hospital at this time. Both punch and wedge biopsies were largely employed when a target site was identified. Ring biopsies were also performed at NWH during this period. They were smaller, shallower versions of the cone biopsy and were between 1.5 and 2cm deep.

Co-operation in diagnosis

Even before the introduction of colposcopy, it was essential for the gynaecologist, the cytopathologist and the histopathologist to work together to detect and treat the presence of carcinoma in situ or invasive disease. Gynaecologists cannot detect precancerous abnormalities with the naked eye. They have to rely on the skills of their colleagues to help them detect, pinpoint and grade the severity of the disease. Therefore close co-operation among these specialists has always been essential. The same need for reliance and co-operation is true of the work of the specialist colposcopist.

During the 1960s Dr McLean, as pathologist in charge, Dr McIndoe, as gynaecological colposcopist, and Dr Green as gynaecologist, all had specialist training and skills. Each would have a knowledge and understanding of the other's work, but none could reliably undertake the highly specialised work of any other member of the team. This dependence of the clinician on information from other specialists highlights the dangers for patients if there is mistrust or lack of cooperation.

DISCUSSION OF THE 1966 PROPOSAL BY THE SMS AND HMC

Discussion of the 1966 Proposal was recorded both in the Senior Medical Staff and Hospital Medical Committee Minutes. Parts of these records came under close scrutiny during the Inquiry. Although the SMS Minutes record that, "Professor Green said that his aim was to attempt to prove that carcinoma in situ is not a premalignant disease", in his evidence, supported by Professor Bonham, he said that this was an inaccurate report of his remarks. Had his aim been so stated, he felt sure his colleagues would not have approved the Proposal. The record ought to have stated that his aim was:

"To attempt to prove that carcinoma in situ is not invariably a premalignant disease" (my emphasis).

(a) Was the word 'invariably' part of the stated aim?

To a lay person recording the Minutes, the omission of the word "invariably" may not seem of much significance. Nonetheless, there has been no evidence to suggest that the person who took the Minutes was anything other than a careful and meticulous assistant. Indeed the accurate recording of discussion in the Minutes was seen as of such importance that in a jointly signed memorandum of 20 September 1961 concerning the Hospital Medical Committee, the Medical Superintendent and the Head of the School of Obstetrics and Gynaecology agreed that

"(3) – the Stenographer to read back to the meeting the full text of each resolution and matters leading up to the resolution and then any corrections made by the meeting. No alterations to be made to the minutes after such corrections have been made by the meeting."

Unless a different philosophy prevailed at the SMS meetings, it is likely that there was a similar procedure.

By 1966 scientific literature confirmed the possibility of progression from CIS to invasion. Dr Green's decision to repeat this research, by attempting to prove that CIS is not invariably a premalignant disease, was very very dangerous for the patients involved.

To **disprove** invariable progression to invasive cancer, every woman included in the trial would have to progress to invasion. Professor David Skegg, Professor of Preventive and Social Medicine and Director of the Hugh Adam cancer epidemiology unit at the University of Otago, commenting on the possibility that the word "invariably" was part of the stated aim, said

"It would be an extraordinary thing to have embarked on this study if it were really believed that the purpose was to prove that it does not invariably progress. I hope that the Minutes are correct and that Professor Bonham's memory is incorrect because if he says the purpose was to show that carcinoma in situ does not invariably progress, that means that it was thought justified to prove that point, to withhold treatment from the proportion of women in whom it would progress, and in fact to prove that it does not invariably progress, one would have to go on until every single woman had developed invasive cancer."

The only other possible interpretation is that Dr Green held a fixed belief that he was setting out to **prove**. If that was so, then he was ignoring virtually all the existing literature which assessed the likelihood of progression to invasion. Even if he considered that the use of colposcopy would help him to exclude the possibility of invasive cancer, before allowing positive smears to remain untreated or under-treated, he should have known that there was a possibility that his belief was inaccurate.

I have come to believe that Dr Green was in fact trying to prove a personal belief. It cannot be just a coincidence that an interview with Dr Green, published in the New Zealand Herald on 24 January 1970, quoted him as saying:

"In situ cancer is not a forerunner of invasive cancer."

Two years later in the Auckland Star (21 June 1972), the identical statement appears with the addendum "and the smear test is overrated". It is also possible that Dr Green, as part of this belief, felt that CIS was a normal condition for most women. There was striking evidence for this theory in the interviews of two patients, both of whom were included in the 1966 Proposal group.

Patient Code 4F1 knew that the results of her smear tests were not normal. She said:

"He [Dr Green] told me that there was nine out of 10 women have cancer and he said that in my case, if I went to my normal GP they would panic. Mr Faris told me the same. That they would panic, they would be rushing me into hospital."

"But he did say that they would panic and he said in cases like that, it does lie dormant, it doesn't sort of – it can go one way or the other and just assured me that why they were keeping a close eye on things, having smears every six months, that if it turned the other way, then they would have to do something."

Dr Green repeated this observation to Patient Code 4S, when he told her that she had to understand:

"Every person is normally born with the cancer, but it is the type of cancer that is dormant and that's all I could understand because he was using all sorts of words that you don't understand. I'd like to have been told or gone into it more thorough.... He said sometimes it just flares up every now and then, but he told me what I had was nothing to really worry about because he said it would never kill me, but it is still in the back of your mind."

I have not been told whether there is a scientific basis for the proposition that the majority of people harbour cancer of some type. As a description of carcinoma in situ, however, it is inaccurate and misleading.

CERVICAL CANCER REPORT

There was further support that Dr Green held the theory that CIS is a natural condition after the issue of vaginal swabs from neonate infants was raised during the course of the Inquiry. In an affidavit on this study Dr Green said:

- “3. *Around about 1963, I thought of the possibility that abnormal cytology in women later developing CIS or invasive cancer may have been present at birth; this was because many pathologists and clinicians whom I consulted, diagnosed dysplasia or CIS in autopsy specimens of cervixes of stillborn infants.*
4. *To test this particular theory I thought of examining vaginal swabs from infants in the hope that abnormal looking cells exfoliated from the cervix might be found in the lower vagina....*
7. *Soon after this particular study commenced, I realised that the study was totally unsatisfactory because the enormous number of normal squamous cells shed into the vagina from the vaginal epithelium effectively ‘drowned’ any possibility of finding cervical cells coming from much further up the vagina.*
8. *I can recall that 2 or possibly 3 swabs were reported as having ‘abnormal’ cells and I thought that this suggested some evidence that confirmed the hypothesis that abnormal cervical cells were present at birth, however I soon realised that they were from a thinner than usual vaginal epithelium caused by relative deficiency of placental estrogen. Once this was realised, I lost interest in the study.”*

There is additional evidence that Dr Green did not accept the usual view that cervical carcinoma in situ is a potential precursor of invasive cancer. In his paper ‘Cervical Carcinoma in Situ: True Cancer or Non-invasive Lesion?’², the title itself hints at the hypothesis reported in the Senior Medical Staff Minutes. In that paper Dr Green questioned “the commonly accepted view that cervical carcinoma in situ is necessarily a precursor of invasive cancer”, and presented evidence to support his contention that CIS may pursue a benign course in a large proportion of patients. In 1965, in his paper entitled ‘Cervical Cytology and Carcinoma in Situ’³, Dr Green again presented evidence that CIS “may in a fair proportion of cases be a benign lesion”. This reasoning could also be inferred from a sub-heading in the same paper, What is Cytology Mainly Revealing? Early True Cancer or Not?

In 1966 Dr Green presented a paper, ‘Is Cervical Carcinoma in Situ a Significant Lesion?’, which was subsequently published.⁴ Although Dr Green said that it was presented to provoke discussion, there is a consistent theme running through all these early papers. The content of those papers, which had been researched and completed before his Proposal was put to the SMS and HMC persuades me that in 1966 he was sceptical of the progression theory.

Conclusions: I cannot believe that Dr Green would be so cynical as to attempt to prove an hypothesis that carcinoma in situ is not **invariably** a premalignant disease. I am satisfied that the discussion recorded in the Minutes of the Senior Medical Staff was accurate and that it was Dr Green’s intention to prove the hypothesis as stated:

“To attempt to prove that carcinoma in situ is not a premalignant disease.”

b) Other comments on the SMS discussion

At the time the Proposal was discussed, specialists at NWH had for some years acknowledged that CIS was “an early progressive malignant lesion which, if untreated, will eventually become invasive”, (Dr Sullivan 1957) and had agreed that the protocol for treatment “should be adequate cone biopsy...provided the immediate follow-up is

negative and...the pathologist is satisfied that the cone biopsy has included all the carcinomatous tissue”.

In the light of this knowledge, the evaluation of the Proposal as set out in the discussion is of great significance. There are a number of statements made during the discussion of the 1966 Proposal and recorded in the Minutes which help clarify Dr Green's intentions for the study and other senior staff members' response to it.

1. “He also said that he had omitted to state in this report that punch biopsy specimens would be taken.”

This statement represents the only indication that Dr Green was to rely in any way on histology as part of the diagnostic procedure. Punch biopsy was mentioned in the Proposal itself, but only as a form of treatment. In Dr McIndoe's memorandum (to which I shall refer in more detail later) to that meeting, he says:

“In the present case inadequate tissue diagnosis, which can be the only description of the type of biopsy I at present perform (if this is to be the only biopsy done) and follow-up only taking further steps if there is clinical or colposcopic evidence of invasion, would seem to me the type of care that should not be followed.”

In my view Dr Green's comment on the use of punch biopsy in the discussion is likely to have been in response to Dr McIndoe's concern about the failure to rely on histology in the Proposal as it was originally set out.

2. “If at any stage concern was felt for the safety of the patient, a cone biopsy would be performed.”

It is not clear from this record of the discussion whether Dr Green intended a cone biopsy to be a form of treatment or a form of diagnosis if invasive cancer was suspected. On all the evidence, however, it is more likely that “concern” related to the possibility that invasive cancer might be present and that the biopsy was for diagnostic purposes.

In the light of that, it is my view that this part of the discussion confirms that Dr Green intended a study which involved no treatment or under-treatment of women with positive smears.

3. “There was a lengthy discussion during which Professor Green answered many questions.”

Although I have grave concerns about the fact that this Proposal was not vetoed at either meeting, at least this statement shows that there was debate about it.

4. “Mr McFarlane and Mr Grieve favoured retaining these patients under their respective teams but had no objection to handing over cases coming into the category stipulated by Professor Green to Professor Green to follow-up.”

Until Dr Grieve's evidence I had inferred that he and Mr Macfarlane preferred to retain their own patients diagnosed with CIS for treatment; but that if any displayed persistent positive cytology they would be passed to Dr Green for inclusion in his study. This was an incorrect assumption. In fact Dr Grieve said:

“We handed over the majority of patients...to Professor Green, patients that came into this category.”

Question: ...Might the reality have been that at this stage you were reserving your position and expecting to retain patients in your respective teams...but in practice it didn't work out that way?

Dr Grieve: I don't know whether it worked out quite like that. I think...patients which we admitted from our own practice we preferred to maintain the management of...under our own teams and that they were not transferred.

Question: *So you retained your own private patients and those stayed under your care?*

Dr Grieve: *I think that in general that would be so.*

Question: *...The patients that you treated subsequent to June 1966, did you allow those to proceed with positive cytology without some kind of definitive treatment aimed at eradicating the source of the positive smears?*

Dr Grieve: *No.*

Question: *Why...not...?*

Dr Grieve: *I preferred to carry out what I considered was the established treatment at the time. On the other hand...I wasn't absolutely positive, far from it, that my treatment was the correct one. ...Professor Green was undertaking a study which we considered well worthwhile and might well be beneficial."*

The statement from the Minutes of the discussion therefore, resulted in patients referred from clinicians' private practice being offered 'established treatment' which at that time, according to Dr Grieve, was surgery less radical than hysterectomy – usually a cone biopsy. He said that:

"Surgery was advocated by me and others on the understanding that the patient's condition could be monitored closely by cytology screening and colposcopic examinations."

The other patients entering National Women's Hospital, unconnected to a particular consultant's practice, were those passed to Dr Green for inclusion in the 1966 Proposal.

5. "The matter was then deferred for consideration by the Hospital Medical Committee."

There is in fact no discussion recorded in the Minutes of the Hospital Medical Committee that night although, of course, all 11 Committee members had been present at the previous meeting of senior staff.

SAFEGUARDS IN THE 1966 PROPOSAL

The Proposal includes the statement:

"It is considered that the time has come to diagnose and treat by lesser procedures than hitherto, a selected group of patients with positive (A3-A5) smears."

At first sight, in the context of the Proposal, it appears that Dr Green was proposing to manage this group of women by diagnostic punch biopsy alone. He was specifically asked during the Inquiry what he had intended by the term "lesser procedures". He replied:

"Cone biopsy rather than hysterectomy, ring biopsy rather than cone biopsy and singular or multiple punch biopsies rather than ring biopsies."

The Proposal itself does not specify this. It stipulated punch biopsies. The fact that cone biopsies would be used as a safeguard if there was any concern about the patient's condition only emerged during the course of the discussion which followed its tabling.

If this dialogue had not been recorded, there would be no permanent documentation giving greater detail of what Dr Green was proposing. However, it was possible to ascertain some of the safeguards that those present saw as implicit in the 1966 Proposal or that they drew from discussion at the meetings, from the evidence of Professor Bonham, Mr Faris, Dr Warren, Dr Grieve, Mr Wright and Dr McLean. These safeguards were:

1. Reliance on Dr Green's expertise

Dr Green was considered by his colleagues to be an expert in this field. Mr Faris said that he was also considered to be "fairly knowledgeable in respect of histology and cytology". Furthermore, as Professor Cole said, when breaking new ground in medical research "a degree of trust has to be achieved"; and when speaking of Dr Green's colleagues who approved the 1966 Proposal he said, "I concede that when they discussed this matter in 1966, his colleagues trusted Dr Green.... They trusted him with the best knowledge they had and they were experienced clinicians."

2. Exclusion of invasive cancer

The possibility that the patient suffered from invasive carcinoma was to be assessed before she was included in the study. If she had invasive cancer, then she must be treated for that. If, however, her condition was precancerous, then she was eligible to be included in the group.

3. Colposcopy

Mr Faris identified this technique as a means of ensuring that "there would be no signs or evidence of abnormality of the cervix beyond a mild erosion". In the 1966 Proposal, however, the role of colposcopy was to delineate preinvasive (CIS) and invasive disease.

4. Cone biopsy

If there was concern for the patient then a cone biopsy was to be performed.

5. Age of women to be included

Treatment would be restricted to those women under the age of 35. Although that precise age has no special significance, Dr Green's colleagues were aware that as a woman gets older it becomes more difficult to view the entire area of abnormality. Dr Jordan said:

"There is a further problem with the over 35s. As the woman gets older, the squamocolumnar junction is more likely to lie in the endocervical canal and therefore be invisible to the colposcopist. Since the colposcopist may not be able to see the lesion in its entirety, he is therefore unable to comment on whether or not that part of the lesion in the endocervical canal is suspicious of invasive carcinoma or not.

"Also he is unable to take a representative biopsy from the endocervical canal without performing a cone biopsy. It is for these reasons that women in the over 35 group are more likely to end up with a cone biopsy than local destructive methods, and are more likely to have unsuspected invasive carcinoma than the younger woman."

6. Clinical signs

There were to be no clinical signs of invasive carcinoma.

After hearing their evidence I accept that, when approving the Proposal, some members of the Committees believed adequate safeguards had been put in place, given their knowledge of CIS and its management in 1966. Had they evaluated the Proposal more carefully, however, they would have realised that most of the "safeguards" were illusory. And had they required a formal review of the Proposal once it was in effect, they would have been forced to acknowledge that those safeguards were not working.

Were there, then, any true safeguards? In my opinion the only protection offered to the patient was Dr Green's expertise in eliminating the possibility of invasive cancer by confirming the absence of symptoms and the checking of the clinical appearance of the cervix by colposcopic examination.

CONCLUSIONS

(a) Management of CIS before the 1966 Proposal

The Minutes from the two meetings on the evening of 20 June 1966, together with Minutes from Senior Medical Staff, Hospital Medical Committee and full staff meetings between March 1955 and the end of 1964, have led me to draw the following conclusions on the management of CIS at National Women's Hospital prior to 1966:

1. Carcinoma in situ (Stage 0 carcinoma of the cervix) was regarded at National Women's Hospital as a precancerous condition and its invasive potential was also known.
2. Cone biopsy was accepted as appropriate treatment for CIS as early as May 1958, provided that the excision was complete, follow-up was conscientious and there was no evidence of disease.
3. The use of the colposcope was still in its infancy.
4. The Hospital Medical Committee and Senior Medical Staff were familiar with the possible risks that CIS would progress to invasion if untreated. The 1966 Proposal should, therefore, have been considered with great care when it was put to the two meetings for approval. Furthermore, for some years there had been a move from the more radical treatment of hysterectomy to cone biopsy. The 1966 Proposal was not part of this trend.
5. It is clear that prior to 1966 the SMS and HMC regularly reviewed treatment and management procedures. Unfortunately this practice seems to have lapsed in the years that followed the acceptance of Dr Green's 1966 Proposal.

(b) What was the 1966 Proposal?

The 1966 Proposal was put in place to monitor the condition of women with positive smears who were not suspected clinically or colposcopically of harbouring invasive disease. No treatment was to be offered to those women unless at a later stage symptoms or examination disclosed the possibility of invasive carcinoma of the cervix.

The Proposal depended on a belief that carcinoma in situ was rarely if ever a cancer precursor. In 1966 Dr Green and his colleagues on the Hospital Medical Committee were well aware of the world view that CIS was a precancerous condition. This was obvious from the Minutes recorded before 1966 and from the manner in which clinicians other than Dr Green managed their private patients at this time. Furthermore, at least some private patients continued to be treated by generally accepted methods in the years that followed.

1. The Australian & New Zealand Journal of Obstetrics & Gynaecology, June 1962, Vol 2, No 2.
2. Aust.N.Z.J. Obstet Gynaec. (1964) 4:165
3. Journal of Obstetrics & Gynaecology of the British Commonwealth 1965, 72:13
4. International Surgery, June 1967, Vol 47, No 6, 511.