

Staff Meeting Bulletin  
Hospitals of the » » »  
University of Minnesota



The  
Undescended  
Testis

November 12, 1937

To the Alumni of the Medical School:

It is a privilege to extend a word of welcome from the faculty of this Medical School to the alumni who have returned for the 1937 Homecoming. We hope that you are finding the clinics and lectures interesting and valuable, and that you will take time while here to visit your former instructors and to make the acquaintance of the new members of our faculty.

Those of you who were graduated ten or more years ago will note great changes in the physical plant, with improvements of laboratory and clinical facilities. More recent graduates will find the external appearances of the School unchanged but, if they will delve below the surface, they will discover significant improvements in teaching programs, in facilities and in staff.

Time keeps robbing us of the teachers and investigators who have built the name of our Medical School, but the younger men who are taking their places are carrying on with the ability and the loyalty which insures continued progress for the future. We are proud of our alumni and can assure them that they can be increasingly proud of their School.

The faculty appreciates your visit and would like to greet and visit personally with as many of you as possible.

Sincerely yours,

Harold S. Diehl

STAFF MEETING BULLETIN  
HOSPITALS OF THE . . .  
UNIVERSITY OF MINNESOTA

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Volume IX

Friday, November 12, 1937

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Published for the General Staff Meeting each week  
during the school year, October to May, inclusive.

Financed by the Citizens Aid Society

William A. O'Brien, M.D.

I. LAST WEEK

Date: November 5, 1937

Place: Recreation Room,  
Nurses' Hall

Time: 12:20 to 1:30

Program: Movie: "Rhapsody in Steel"

Announcements

Ovarian Abdominal Hemorrhage  
Charles E. McLennan  
W. A. O'Brien

Discussion: R. W. Koucky  
L. A. Lang  
Ruth Boynton  
Leo T. Samuels  
J. F. McClendon  
I. M. Goldberg  
C. E. Rea  
Charles E. McLennan

Present: 145

Special Guests:  
Physicians registered in  
the Institute for Surgical  
Diagnosis and Treatment.

Gertrude Gunn,  
Record Librarian

- - - - -

II. MOVIE

Title: Colorful Bombay

Released by: M-G-M

- - -

III. GOSSIP

Combe-Saunders-Abercrombie-Crohn-Ginzburg-Oppenheimer's disease is regional ileitis.....Two years ago one of our well known medical alumni in Northern Minnesota made elaborate preparations to come back for the Homecoming Game - in other words, he bought a new suit.

In due time the sartorial creation arrived and was admired by all. It showed a few wrinkles which were rather disturbing to our good friend so he sent it to the next town to be pressed as his town did not boast such an establishment. It was returned just a short time before he left home and when he opened the box, it had changed into an old fashioned gentleman's old fashioned greenish black outfit. The clothes presser had sent the doctor's suit to an undertaker who had buried it on an old man the previous day. And the suit is still there.....The Center for Continuation Study celebrated its first birthday Tuesday, November 9, with a dinner in the dining hall. Sir Walter H. Moberly, (and Lady), Chairman of the Committee of Award of the British Commonwealth Fund Fellowships was the guest of honor. It was a most successful first year, said the "pediatric" advisory committee of representatives of all the colleges of the University.....According to one of the surgeons from Emmetsburg, Iowa, who was registered at the institute on Surgical Diagnosis and Treatment last week, Larry O. Doyle, the sage of Southeast Minneapolis, is known in his home town as Oscar.....One of our departmental heads looked so "cute" in his shorts when he and his wife were dressing for dinner that she gave him a big hug and broke one of his ribs.....

..Outpatient Surgeon James Hayes is president elect of the Minnesota State Medical Association. His arrangements committee has been at work since early in the fall planning the program for next July in Duluth. In his undergraduate days at Carleton College he was a star athlete. Internist Wesley W. Spink is also a Carleton great in athletics. Associate Professor of Medicine Cecil Watson's father, Dr. J. A. Watson, was born in Ireland. Although the elder Watson and Chief Ophthalmologist Frank Burch have been close friends for years, Dr. Burch did not connect the two Watsons because Cecil did not speak with a brogue.....The Hennepin County Medical Society, the Ramsey County Medical Society and the Medical Faculty will sponsor a private preview of the new film "The Birth of a Baby" at Northrop Memorial Auditorium Monday, November 29, at 8:30 P.M. Complimentary tickets will be given to the staff.....The Minnesota

State Medical Association and the Minnesota Public Health Association are again sponsoring the College Health Lecture Series. Eighty lectures are planned for 20 colleges, to be given by a staff selected from the Medical School, Mayo Foundation and the Speakers' Bureau of the Minnesota State Medical Association..

...Last year in Springfield at the annual meeting of the Illinois State Funeral Directors' Association, our demonstration of postmortem embalming technique went on at the scheduled time because a body was obtained at the last minute in St. Louis. It was flown to the convention by airplane. "Time" wrote up the incident under the heading "Tickets to Heaven".....The epidemic of arms in slings in our younger generation is just a case of hero worship - playing that they are star halfback Andy Uram.....Internist Fritzie Scheaf gets in shape for the hunting season by climbing the stairs to his office on the 18th floor of the Medical Arts Building in Minneapolis.....When General Practitioner Ed Simons of Swanville saw a patient with primary carcinoma of the lung, he became so interested in the disease that he looked into the matter. In his garage he did some experimental work on attempted reproduction of the disease in animals. The more he studied the question the more interested he became. His investigations won for him the prize offered by the Minnesota Society of Internal Medicine. The monograph now appears in book form and is said to be the most exhaustive treatise on the subject ever written as it analyzes more than 5,000 microscopically proved cases. It is a publication of the Year Book Publishers, 304 South Dearborn Street, Chicago, Illinois. The foreword is by our own J. Arthur Myers; E. T. Bell, L. G. Rigler and O. H. Wangensteen reviewed their respective fields of interest. And there are those who say that physicians in general practice do not see interesting cases.....And speaking of books, Chief Surgeon Owen H. Wangensteen's monograph on "The Therapeutic Problem in Bowel Obstructions" is also off the press of Charles C. Thomas, Springfield, Illinois and Baltimore, Maryland. The first section of the book is the essay for which the author was awarded the Samuel D. Gross Prize for 1935 by the Philadelphia Academy of Surgery. The balance repre-

sents additional ideas and the prevailing viewpoint of the clinic at the University of Minnesota Hospitals. Associates Scott, Sperling, Hibbard, Paine and Rea, research assistants from 1931 to 1935, Chief Radiologist on Leave Leo G. Rigler and Miss Hirsch (Art), all get the nod for valuable assistance.....

..At the Homecoming Clinic program this morning, Drs. Henry Michelson, Cecil Watson, O. S. Wyatt, Jennings C. Litzenberg, Irvine McQuarrie, Owen Wangensteen and Wallace Cole were scheduled to appear for half hour demonstrations. The visiting alumni are our guests for the balance of the day. We trust that their day will be pleasant. It is always good to have the alumni come back, even though it takes a special athletic event to bring them in. With the development of the new Center for Continuation Study visiting alumni will no longer have to feel like visitors.....Dermatologist James Tedder has been made Assistant Professor of Dermatology in Louisiana State University. Jim is one of our old interns of happy memory. His wife is from Minneapolis. While here he taught us a great deal about lymphogranuloma inguinale as a result of previous experience in the South.....Mrs. E. P. Lyon, the "mother" of the Medical School of the University of Minnesota, left for her winter home in Florida last week. This brave little woman, who has more than kept her chin up since the Dean went on, astounded her relatives and friends by making the trip by airplane.....When Urologist Ernie Meland practiced in the country before going to the Mayo Foundation for his graduate work, he had a very interesting time. He was located at a little town called Dalton in Northwestern Minnesota. In the few years that he was there the people grew to like him so much that they had a public going-away party for him. Although Dalton is only a town of a few hundred population, nearly 1500 came to bid Ernie farewell. Their purse to him was made up of a sum in which every person in the community had his share. You may be very certain that this information was not obtained from Ernie.....

Better luck tomorrow, Minnesota!

IV. THE UNDESCENDED TESTIS

Chas. E. Rea

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I. Introduction

The purpose of this summary is to review our experience with the treatment of the undescended testis.

II. General Considerations1. Etiology

The cause of non-descent of the testis is unknown. Factors said to bring about retention of the gonad have been classified by Eccles as abnormalities of the mesorchium of the testis and its component parts, the gubernaculum, the cremaster, or the route along which the testis must pass. To these causative factors probably should be added endocrine imbalance.

McGregor believes that ectopy of the testis can be explained on anatomical grounds. He states that one or more of the following congenital factors are present: (1) anomalies or absence of what he calls the "third inguinal ring," (2) fascial pockets, (3) fascial ridges. His careful dissections well explain the four varieties of undescended testes; namely, the inguinal, the pubopenile, the perineal, and the crural or femoral. Like most present day authors, he doubts the gubernacular theory of descent. His own studies failed to demonstrate any subdivisions of the gubernaculum, nor did they determine what stimulus causes descent.

2. Histology

John Hunter believed that the undescended testis failed to reach the scrotum because of its inherent imperfection. This cannot be wholly true, at least from an anatomical point of view, because up to puberty it is impossible to distinguish histologically between a normal and a retained testis.

The histology of the retained gonad has been reviewed by Eccles, Branca and Felizet, Rawlings, Moore, Southam and Cooper, Pace, Wangenstein, and others. Wangenstein has summarized the findings as follows: The normal testis grows but slightly from birth to puberty, during which time there are few histologic changes. The undescended testis before puberty resembles the scrotal gland in both weight and minute anatomy. With the onset of puberty, however, the normal testis shows a sharp increase in weight due to the elaboration of mature epithelium and the appearance of spermatozoa. The undescended testis exhibits these changes to a lesser degree. Wangenstein has never seen spermatazoa in the seminiferous tubules in the undescended testis after puberty. This agrees with the observations of Felizet and Branca, who found that while a few undescended testes contained spermatozoa and spermatocytes, only two of 51 contained spermatids, and none had spermatozoa.

Southam and Cooper believe that the further the pre-adolescent testis descends, the more closely it corresponds to the normally located gland of the same age. However, a large series of cases would be necessary to verify this statement. Certainly, the histologic picture of an abdominal gonad is often indistinguishable from that of an inguinal testis. The time factor is probably just as important as the degree of descent in determining the histologic picture, barring any congenital malformation.

In this laboratory, the histology of the congenitally undescended testis of the pig, dog, horse, and bull has been studied. Cryptorchidism is not infrequent in the dog and pig. While working in the Experimental Laboratory of the Department of Physiology at the University of Illinois, the writer noted 7 instances of undescended testis (two bilateral) in 200 dogs. At Armour and Company, South St. Paul, Minnesota, during one of the morning "kills," four cases of retained testes were noted in approximately 2,000 pigs. The microscopic appearance of the retained testes of these animals is similar to that in man, and is comparable to that of experimental cryptorchidism. The testes are ordinarily smaller than normal, their tunics are usually thicker, and the cut sections more fibrous and darker in color. They contain seminiferous tubules in which only Sertoli cells may be seen; some cells of the germinal line are found but never a complete germinal epithelium if the testes have been entirely abdominal. Moore states that testes located in the inguinal canal or upper scrotum may occasionally contain spermatozoa although this is very rare in the adult.

In this study, spermatozoa have never been seen microscopically in the abdominal or inguinal testis of adult man, pig, or dog. Botschi has recently described the appearance of the undescended testes of the pig, horse, dog and cat. He found that the greater number of retained testes of these animals were aspermatic, even spermatocytes seldom being found. Wangensteen believes that the germinal epithelium of the undescended gonad is better maintained in the horse than in man, pig, dog, or bull.

In most animals the empty tubules are more widely separated in the undescended than in the scrotal testis. The amount of interstitial tissue in the former varies in different animals. The interstitial mass of the cryptorchid boar is so prominent that Bouin and Ancel called it the "interstitial gland." It is less evident in the ram. (Moore)

### 3. Internal Secretion of the Retained Testis

The existence of a male sex hormone has been recognized for a long time. The interstitial cells, first described by Leydig in 1850 were regarded as its source by Bouin and Ancel in 1903. The hormone is thought by most investigators to be unrelated to spermatogenesis. However, since some germinal epithelium usually persists in most forms of aspermata, as in the undescended or irradiated testis, Oslund states that it has not been determined whether the germinal epithelium, the interstitial cells, or both produce the hormone. Some workers regard the interstitial cells as secretory, while others believe that they are no more than modified connective tissue cells (Moore).

The effects of deprivation of sex hormone, as in castration, are well known. As the effects of its removal are immediate, none appears to be stored in the body. Deficiency during the development of the individual will affect the accessory and secondary organs of sex; deficiency after development will affect their normal activity (Moore). The effect of castration on the epididymis, vas, seminal vesicle, and prostate are so constant that Moore has used it as a "testis-hormone indicator." The high columnar epithelium of the rat's seminal vesicle changes considerably within 20 days after castration. The subcutaneous injection of the purified lipid extract of a bull's fresh testis restores the vesicles of a castrated rat to normal.

Guinea pigs lose within 3 months after castration the reflex of ejaculation on electrical stimulation of the brain, but it reappears within two weeks after beginning the subcutaneous injection of fat

soluble male hormone. Capons have also been used in tests for the presence of male hormone; in fact, the first testicular graft by Berthold (1849) was of this type. If hormone is present, castrated chickens, even females, will grow combs, wattles, and ear lobes. The urine of normal men contains a substance which promotes comb-growth in capons (see reviews of Moore, Koch, Hinman).

It has been proved by the capon-comb test that male hormone is present in the urine in single and bilateral testicular maldescent (Koch and Webster). Clinical evidence of the presence of this hormone in cryptorchids (normal development of the secondary sex characters) has been recognized for some time. Pratt, Moore, Hinman and Meyer state that most patients with undescended testes exhibit normal physical and mental development except for occasional psychic disturbances of the sexual power. All but one of the 20 adult bilateral cryptorchids seen at this clinic have had normal secondary sex characters. The exception had Froelich's syndrome.

Lipschutz states that one-sixteenth of the normal testis suffices to permit normal development of the secondary sex character in the rabbit and guinea pig; judging from the small size of the gonads occasionally seen in otherwise normal cryptorchids, very little testicular tissue seems to be needed to carry on this function in man.

Whether the undescended or the normal testis secretes more than one hormone is not definitely settled, but the fact that the undescended testis does not have an internal secretion has been a strong argument for its conservative treatment (orchiopexy) rather than removal (Meyer, Lotheissen).

#### 4. External Secretion of the Retained Testis

##### a. Spermatogenesis in the undescended testis

The imperfectly descended testis is often aspermatic. This is thought to be due to the influence of the

higher temperature of its abnormal surroundings upon the germinal epithelium (Piana, Crew, Moore, Fukui), and also to pressure atrophy. Most experimental evidence seems to show that the undescended testis will develop normally when replaced in the scrotum. If it is too degenerate, mature germinal epithelium will not be produced subsequent to fixation in the scrotum.

In experimental procedures, a normal testis is brought up into the abdomen, allowed to degenerate, replaced in the scrotum, and then seen to regenerate. It may be questioned to what extent this regeneration will occur in the naturally cryptorchid gland after orchiopexy, since its potentialities may be entirely different from that of the normal gonad. Wangenstein has noted that restoration of the mature germinal epithelium does not occur to the same extent after orchiopexy as after returning to the scrotum a normal testis previously placid in the abdomen by operation.

##### b. Fertility of cryptorchids

Griffiths believes that the undescended testis is incapable of producing spermatozoa, and doubts the authenticity of reports of fertility in bilateral cases. From a review of the literature, however, it seems clear that spermatogenesis may occur in cryptorchids. Unfortunately, the details of most of the reported cases are so incomplete that one wonders whether their authors are not stating as facts impressions or prejudices.

Sir Astley Cooper taught that patients with bilateral failure of descent were like castrates. A medical student with bilateral cryptorchidism consulted him, and, hearing of the probable outcome of his anomaly, committed suicide. Cooper examined his testes and found spermatozoa in each. Uffreduzzi stated that 10 per cent of cryptorchids exhibit spermatozoa. Marechal found 50 cases of bilateral cryptorchidism in which examination of the testis or semen revealed spermatogenesis. Rawlings found little if any



impairment of spermatogenesis in 10 of 27 undescended testes; and stated that organs situated in the inguinal, pubic, and pubosacral regions exhibit spermatogenesis in 40 to 50 per cent of cases up to 30 to 40 years. Vidal and Burghard believed the majority of abdominally retained testes to be capable of spermatogenesis. Meyer in a review of the literature quoted 19 authors who believe the cryptorchid testis capable of producing spermatozoa, and 13 who hold the opposite view. In the majority of instances in which spermatozoa have been demonstrated in the undescended testis, the patient has been young.

Odiorne and Simmonds, Eccles, Levin and others have reported patients with bilateral abdominal cryptorchidism who apparently became fathers. Eccles states that there are but few instances of fertility in the presence of double inguinal arrest. Why inguinal retention should be more likely than abdominal to cause sterility is not clear.

Since Hobday stated that stud horses with abdominal testes are always sterile, the statement that abdominal retention is less inimical to spermatogenesis than the inguinal variety is probably untrue.

At the University of Minnesota Hospitals, ejaculation tests have been done upon 3 patients with bilateral inguinal testes, and upon 2 with abdominal gonads. These patients had never had any treatment. Their ages varies from 21 to 25 years. Spermatozoa were absent from the semen of 2 with inguinal and from 1 with abdominal testes; another with abdominal cryptorchidism had only occasional non-motile sperm in the semen on 1 occasion (1 - 3 per high-power field); he is married and is the reputed father of a child.

The third patient with bilateral inguinal testes has on 2 occasions produced motile sperm: At first there were only 4 - 5 per high power-field, but on the next examination there were 1,500,000 per cubic mm. He was married and claimed to be the father of 1 child; his wife was again pregnant at the time of his last examination. Paternity tests have not been performed in either of the above

cases.

Whether cryptorchids are potentially or absolutely fertile is an important question. Macomber and Saunders state that the semen of the normal male contains between 100,000,000 and 120,000,000 actively motile spermatozoa per cubic centimeter; Rubin estimates as high as 400 millions per cubic centimeter may be present. The normal count in the same person varies with illness, age, exercise, diet, mental and physical fatigue, alcoholism, endocrine imbalance, and the frequency of sexual intercourse. It has been estimated that the count does not normally go below 50,000,000. 25,000,000 spermatozoa per cubic centimeter have been considered, but not proved, to be the smallest number compatible with fertility, as that many are thought to be destroyed by the vaginal secretions (Macomber and Saunders, and Belding).

Fertility with counts lower than 25,000,000 has been reported by Macomber and Saunders. MacCollum reports his experience with 2 men in whom unilateral, undescended testes had been operated upon, and whose counts were 16,000,000 and 26,000,000 respectively. Both men had had children. While repeated tests might have revealed that higher counts were actually present to account for the paternity, it may be also that the figures cited as necessary for fertility are too high. Certainly, the number of spermatozoa is only one of the factors involved in successful conception. The nature of the associated secretions in the male and female is probably just as important. Our instance of paternity with a sperm count of 1,500,000 is the lowest recorded in the available literature. While it is impossible to prove or disprove paternity with finality, the fact that the counts supposed necessary for fertility are only estimates, and that only one spermatozoan is necessary for fertilization, make it probable that fertility may exist in patients with sperm counts below the present accepted standards. Moreover, studies of the head, neck, and tail of the sperm show that 8 - 10 per cent may show variations in size and shape. Fertility is thought to be greatly impaired if the

number of abnormal forms reach 25 per cent.

To draw valid conclusions as to the fertility of bilateral cryptorchids is impossible because too few observations have been made. However, it seems permissible to conclude that some bilateral cryptorchids are fertile. All these patients have been young; whether fertility exists in older patients is unknown.

### III. Treatment of Undescended Testis

Undescended testis is one of the more common genitourinary anomalies with which the surgeon must deal. It occurs in from 0.1 per cent (Marshall) to 0.12 per cent (Monod and Terrilon) of males. The statistics of the Austrian Army show that 2.2 cases of undescended testis occurred in every 1000 men drafted for military service (Ziebert). According to our War Department's medical records for the World War, there were 3.1 cases of ectopy for every 1000 men examined. Eccles found 2 per cent of undescended testes in 48,000 hernias. Bevan, Coley and Wangenstein put the incidence of retained gonad at 1 in 500.

Incomplete descent is more common on the right than on the left side. From the statistics of Berger, Hofstatter, and others, the incidence of right-sided maldescent is equal to that of double and left-sided retention combined. In 20 per cent of undescended testes, the deformity is bilateral (Wangensteen).

Pain, torsion, hernia, and malignancy are the most common complications of undescended testis. However, except for hernia, most patients with undescended testis do not present themselves for treatment because of complications. Some are conscious of the aberrant position of the ectopic gland. Others are concerned about the fertility of the undescended testis. Not a few, wishing to avoid a surgical operation, ask about the chance of spontaneous descent or the results of "injection" therapy.

The surgeon is confronted with the problem of selecting the best treatment

for these patients. If the treatment is to be surgical, should the retained testis be removed, because of the danger of malignancy or because of its questionable function, or should it be scrotally fixed? If the testis is anchored in the scrotum is the result to be considered purely cosmetic or will the function of the testis be improved? Although orchiopexy has been performed for more than a century, it is surprising how few investigators have inquired if the undescended testis had any function, or if such a function existed, whether it could be maintained or improved by scrotal fixation. From a review of the literature it seems established that in most cases, the undescended testis may have an internal secretion and occasionally may possess an external secretion sufficient for potential if not absolute fertility. It is estimated that 10 per cent of untreated human cryptorchids remain fertile (Uffreduzzi). It has been proved clinically that as high as 82 per cent of those patients treated by orchiopexy have active spermatozoa in the semen (MacCollum). Placing the slightly atrophic or immature retained testis of man and the pig in the scrotum has been shown experimentally to allow a mature germinal epithelium to be produced. The degree of maturity after scrotal fixation is never as great as that seen in the case of the experimentally produced cryptorchid testis so treated. However, clinically and experimentally the value of scrotal fixation for testicular development has been proven beyond doubt.

There is a diversity of opinion among surgeons as to the best treatment for the undescended testis. Some believe that the cryptorchid testis is potentially malignant and should be removed. Others believe that if left alone, most of these retained gonads will descend spontaneously. Recently the reports of some investigators indicate that the results from hormonal therapy are equally as good as, if not superior, to those obtained by surgical treatment (orchiopecy). In formulating a rational plan of treatment of the undescended testis, one is influenced by the number and type of cases he has seen, his surgical ex-

perience and that of his associates, and the type of case that receives hormonal therapy.

The following are impressions gained in the treatment of the undescended testis during the past years at the University of Minnesota Hospitals.

### 1. Malignancy of the undescended testis

There has been much discussion about the incidence of malignancy of the undescended testis. Hinman reviewed 649 cases of cancer of the gonads and found 12.2 per cent in undescended testes. Coley, Cunningham, Odiorne and Simmonds, Schischko, Lipschutz and Dean reported altogether 1371 cases of malignancy in the male sex gland. The undescended organ was the seat of malignancy in 136 or 9.9 per cent. Since but 0.12 to 0.2 per cent of testes are undescended, the ectopic testis appears to be involved 50 times more often than its incidence would justify. Rubaschow reviewed the cases of undescended testis reported by 21 observers and found that in 11 per cent of the whole group tumors were present, a figure in striking contrast to the 0.05 to 0.06 per cent incidence of neoplasm in the testis. (Rea)

It is evident that the ectopic testis is definitely more liable to neoplasia than is the normal gland. However, the actual percentage of undescended testes that undergo malignant degeneration is another question and is the phase most commonly overlooked in the discussion of this subject. Eccles reported 859 cases of undescended testes without finding malignancy in any of them. Coley did not have a single case of malignancy in 1357 cases of undescended testes. Kocher found only one case of neoplasm in 1000 cases of maldescent up to 1931. MacKenzie and Ratner had never seen a case of malignancy in a series of 105 cases of undescended testis. However, in 1934, they reported 3 cases occurring in retained glands. Pace found 3 adenocarcinomata in 24 undescended testes. It should be stated, however, that the series was small, the diagnosis questionable in one case, and the degrees of malignancy low (grade I). Hinman and

Benteen state that 3 of 155 cryptorchids had a testicular tumor--about one in every 50, or 2 per cent. If one checks the records of the Divisions of Vital Statistics, Washington, D. C., one finds that possibly 3.2 per cent of undescended testes become malignant. Haberland claims that 0.75 per cent of undescended testes in animals become malignant. Clinically, the incidence of malignancy in the retained testis does not seem to be higher than in the normal breast or uterus (2 per cent), which speaks against the indiscriminate castration of cryptorchids for fear of malignancy.

When one considers the low incidence of malignant degeneration in the undescended testis, the fact that 20 per cent of retained testes are bilateral, and the generally poor results in the treatment of testicular neoplasms, the procedure of choice in the treatment of the ectopic gland is orchiopexy. That orchiopexy per se does not protect against malignancy has been mentioned in the reviews of Wangenstein and Rea, as there are instances where malignancy later has developed in such testes. However, this and the other evidence cited above tend to show that it is not so much the position as it is "the biophysical and chemical factors involved in the growth of tissue" which plays the important role in neoplasia of the undescended gland (Hinman).

### 2. Spontaneous Descent

Hofstatter states that in 600 male newborn children, 96 per cent of the testes were in the scrotum. In 8 - 10 days nearly all the testes were in the scrotum or slipped out of the external ring easily. If the testis fails to reach the scrotum at the end of the first year, it is a rare event that it ever does so by its own initiative (Hofstatter). At the University of Minnesota Hospitals, no instance of spontaneous complete descent has been noted in a series of 100 imperfectly descended testes (ages 2 to 79 years). To be true, there are several reports of late descent in the literature (Buehlman, Mayor, Harris, Drake). Most interesting of these studies is that of Drake. He

found that 11 boys, ages 9 to 19 years, out of 260 had undescended testes (incidence 4.2%). Four of these retained gonads were on the right side, six on the left, and one was bilateral. As Drake watched these cases over a period of years, 10 of the 12 testes descended spontaneously. If most undescended testes descend on their own accord, as Drake infers, it is difficult to explain the incidence of 3.1 cases of ectopy per 1000 men according to the Draft Statistics. Also, since the incidence is about twenty times the normal incidence (0.2 per cent), it is possible that a number of his cases could be classified as physiological ectopy.

By physiological ectopy is meant the condition in which one finds a normally descended testis with a very short or active cremasteric muscle which pulls the gonad into a high scrotal or inguinal position. This condition, also known as ectopy en retour, has been little appreciated by most investigators. From the point of view of therapy, it is as important to differentiate it from a true undescended testis as it is to differentiate testicular maldescent from hernia, benign and malignant tumors in this region, adenitis, etc. MacCollum noted instances of physiologic ectopy in 336 cases of cryptorchidism of 16 patients referred to Hamilton and Hubert, only 6 were actually cryptorchid and 10 were pseudocryptorchids. Stefko in 1924 reported a high incidence (27 per cent) of inguinal testes in starving children. This he attributed to too short a cremaster occasioned by starvation in which an unequal growth of muscles of the abdominal wall occurred. Hofstatter has described a group of 8 to 10 year old boys who could not replace a testicle which he had pushed above the penis, and only with difficulty could it be replaced by a physician. Bevan states that one-fourth of the cases of retained testes referred to him are not true cases of undescended testes at all, for when the examiner runs his finger down the inguinal region of these patients, the testicle can be pushed into the scrotum.

To differentiate physiologic ectopy from true testicular retention, the

following criteria may be helpful: (1) In physiologic ectopy the extremely short or active cremaster may be seen to contract. (2) The patient may give the history that at one time the testis has been in the scrotum. (3) It is not associated with hernia as frequently as undescended testis. (4) In physiologic ectopy the testicle can be brought into the scrotum by manual traction, but on releasing the traction, the testicle again recedes to its original position. (5) The scrotum in these cases is better developed than in cryptorchids. (6) Fraser believes that in children with strong cremasteric reflexes the testis does not usually enter the inguinal canal, but lies under cover of the loose fatty tissue which covers the front of the pubes. If the examiner palpates in the region immediately below the external ring, the cord can be picked up by the fingers. On tracing it, the testis will be found. (7) Hamilton and Hubert state that if relaxation of the cremasteric and other muscles is obtained by a general method of approach and by direct application of heat to the groin, scrotum and perineum (the patient lying with his legs apart), a differentiation between pseudocryptorchidism and true cryptorchidism can be made.

To be certain, a sharp distinction cannot always be made between these two entities, but the history and multiple observations by different examiners will aid in the diagnosis. At the University of Minnesota Hospitals, at least 3 examiners pass on every case of undescended testis. Physiologic ectopy may be considered to vary only in degree from true maldescent, but certainly differentiation should be made in tabulating any results of treatment.

What the ultimate fate of these cases of physiologic ectopy is, has not been definitely ascertained. MacCollum gives one to believe that if such testes can be brought into the scrotum at all, they all will eventually descend of their own accord. Bevan also believes that at puberty with enlargement of the testes, they descend into the scrotum and develop normally. Wangenstein has brought to this writer's attention

several cases which he has followed personally. Nearly all had been referred for orchiopexy, but were not operated upon when the real condition was appreciated. Of 3 boys in one family, 2 had physiologically ectopic testes which descended into the scrotum at puberty and have remained there. At a recent examination the testes of both boys were normal in size, shape, and position. The other boy in this family, age 11 years, has a left inguinally retained testis. Another case with physiologic ectopy has been followed: at the age of 12 years, the right testis descended into the scrotum and has remained there, but is about half the size of its scrotal fellow.

### 3. Surgical Treatment

The surgical treatment of the undescended testis consists either of removal, abdominal reposition, or scrotal fixation (orchiopexy). Castration is justified only in certain cases of unilateral undescended testis: if the patient is old and has a very atrophic testis, or a large inguinal hernia; if the testis is painful or if one suspects malignancy. Too often castration is performed because it is an easier procedure than scrotal fixation. However, it is surprising how much the cord can be lengthened by patiently separating the testis from the vaginal process, freeing the vessels and vas deferens in the retroperitoneal space even as far as the renal pedicle, and separating the fascial coverings of the cord. Cutting the blood vessels of the cord to give length is to be condemned as MacCollum found that every patient so treated showed complete atrophy of the testes when observed 10 to 20 years later. If an inguinal testis cannot be made to reach the scrotum, abdominal reposition is preferable to castration and may be the only elective procedure in the young bilateral cryptorchid.

In orchiopexy one combines the freeing of the cord with fixation of the testicle in the scrotum. Since Rosenmerkel's orchiopexy of more than 100 years ago, numerous procedures to anchor the testis in the scrotum have been de-

vised (see Hofstatter's outline). Over 40 operations have been described (Wolfson and Turkeltaub). The most recent ones are of the Keetley-Torek type. From the reports of Burdick and Coley, McKenna and Ewert, Ada, Gobell, Cabot and Nesbit, Tyrell, Meyer, Eisenstasdt, Goetsch, Wangensteen, Newell, Wolfson and Turkeltaub, and others, it is to be inferred that good anatomical results (size, position, cosmetic results) are obtained in most cases, even with various techniques. For the past few years at the University of Minnesota Hospitals, Wangensteen's modification of the Keetley-Torek operation has been used with uniformly good results.

In the Keetley-Torek operation, the testicle is freed until it is of sufficient length to reach the bottom of the scrotum. The skin of the thigh is sutured to the skin of the scrotum; the testicle itself is sutured to the fascia lata of the thigh, and the wound in the scrotum closed over the testicle. The testis is thus kept at enough stretch so that it will remain low in the scrotum after the second stage is performed. It is important that there be no undue tension. At the second stage, the scrotum is separated from the thigh, the testicle from the fascia lata, and the scrotum closed again over the testis. In Wangensteen's operation, a cutaneous juncture between the thigh and scrotum is made, and the testis anchored by means of sutures which are placed in the tunica albuginea, brought down through the tunica vaginalis communis, and fastened to the fascia of the thigh. The important difference in this operation is that while fastened to the thigh, the testicle is still in the scrotum. The first stage is not only more physiologic, but at the second stage, the scrotal-crural detachment is performed more easily and simply than in the Keetley-Torek operation.

From an anatomic and physiologic point of view, orchiopexy is the procedure of choice in the surgical treatment of the undescended testis. It is important that the testis after orchiopexy lie free in the bottom of the scrotum and be movable. If one cannot

get the testicle to the lowest portion of the scrotum, a high scrotal position is better than an inguinal one. If necessary, the testicle may be brought from its ectopic position to the scrotum in stages. Whether inguinal or abdominal reposition is better is questionable except that one can observe a testis better in the inguinal region. If the inguinally retained testis is painful and conservative measures give no relief, orchidectomy may be indicated, as such testes will probably be just as painful if placed in the abdomen. In older men, orchiopexy may be performed more for the cosmetic result than for the functional potentialities.

#### 4. Hormonal Therapy

The researches of Evans, Engle, Ascheim and Zondek, Allen and Doisy and others are largely responsible for our ideas regarding the hypophyseal-gonadal relationship, as well as the rationale of hormonal therapy in cryptorchidism. Time and space does not permit a review of the literature. The work of Engle and Aberle and Jenkins who found that the immature testes of monkeys could be brought into the scrotum by means of anterior pituitary-like substances suggested that this material might be of value in treating human cases of undescended testis.

Shapiro in 1930 reported genital growth and testicular descent by treatment with anterior pituitary like substance in boys and young men with hypogenitalism and cryptorchidism. Since then there have been several reputed series in the literature of undescended testes in man treated by this material. Thompson et al and Cramer have recently summarized the results of most investigators; in over 70% of cases, descent of the retained testis has occurred. How critically some of the cases were observed may be questioned when in some instances the testis was reported to have descended within 3 hours after treatment. Some of the cases showed signs of hypopituitarism or adipogenitodystrophies and received other therapy besides pituitary extract (thyroid extracts, diet, etc.).

Kunstadter, Robins, Schapiro and Goldman, and Stein believe that the administration of extract of pregnancy urine is indicated in hypopituitarism of the male characterized by genital underdevelopment. However, the clinical diagnosis of pituitary or other endocrine dyscrasia is always subject to considerable variation in interpretation. Hess, Kunstadter and Saphir believe that if their cases of cryptorchidism could be studied with more objective criteria, a more rational therapy could be instituted. It is known that whenever gonadal function is diminished or absent, as in adult hypogonadism, the menopause or castration (Evans, Engle and Smith), there is an excessive excretion of the gonadotropic hormone, presumably of pituitary origin. Katzman and Doisy have shown that the urine of normal children contains little or no gonadotropic hormone. Hess and co-workers reasoned that since in the castrated person or in cryptorchid boys the gonadotropic hormone is presumably of pituitary origin, it seemed logical to conclude that the presence of gonadotropic substance in the urine of cryptorchids indicates an active anterior pituitary gland as to gonadotropic function. The appearance of the hormone in the urine may be due to insufficient activity of the gonad which failed to modify the hormone or remove it from the blood. On the other hand, the occurrence of cryptorchidism with an absence of gonadotropic hormone from the urine may be interpreted to mean either the presence of a primary pituitary dysfunction or the presence of a functionally active bilateral undescended testis, or at least one functionally active testis.

Accordingly Hess et al determined in a semiquantitative manner the excretion of gonadotropic substance in the urine of cryptorchid boys before and after treatment with gonadotropic substance. Nine of thirteen of their cases of cryptorchidism responded to the use of anterior pituitary-like factor by descent of the testis and disappearance of the hormone from the urine. They believe that in the absence of mechanical obstruction, the best results after using

anterior pituitary-like substance are obtained in those cases of undescended testis which have gonadotropic hormone in the urine which disappears after treatment.

Hardy, Bigler and Scott have reported one of the largest series, to date, of cryptorchid testes treated by hormonal therapy. In one group, 32 boys with 40 undescended testes were treated with gonadotropic principle of the anterior pituitary gland. In 26 cases the testicles remained unchanged in location, in 4 there was partial descent, and in 10, or 25%, there was complete descent. After discontinuing treatment, however, only 7, or 18%, remained descended. In another group, Antuitrin-S was used in the treatment of 23 patients with 31 undescended testicles. No change was observed in 12 testicles, 4 partially descended, and 15 or 48% remained descended. However, only 14, or 45%, remained descended upon further observation. Both extracts were used in the treatment of 16 boys with 20 undescended testicles. In 9 cases, there was no change, 2 descended, and in 9, or 45%, there was complete descent, which was permanent in 5, or 25%, of the cases. They found that descent of the testicle usually begins to take place before 4000 rat units of gonadotropic substance have been given.

Rubenstein has summarized the current concept regarding hormonal therapy in the treatment of undescended testis in the following statement: The water-soluble fraction of pregnancy urine seems to produce testicular descent only if the pituitary gland is sexually underdeveloped. It then leads predominately to a stimulation of the intestinal cells of the testicle and may result in descent when mechanical obstruction does not exist.

Undoubtedly in the literature, more prominence has been given to the successes than the failures. Few contra-indications to therapy with hormones are recognized and the method is too recent to permit investigation into the possibility of late complications. Thompson, Bevan, et al, obtained descent in 4 inguinally retained testes in 21 instances

of cryptorchidism (197). Mimpres, who obtained descent in only 6 of 20 cases of undescended testis so treated, believes that anterior pituitary-like substance should be used chiefly in bilateral cryptorchids with subnormal genital development. Cabot has referred to the possibility of late atrophy of the testes and Cole has produced atrophy of the tubules of the testes by high doses. Goldman and Stein have commented on the possible development of precocious sexual maturity, and for this reason consider 9 years as the earliest age at which treatment with gonadotropic hormones should be started. In this clinic also there is some hesitancy in using Antuitrin-S in very young children, but Dorff and Aberle and Jenkins have used this hormone in children about 3 years of age with no untoward results. Geschickter et al found that extracts of the urine of pregnancy in young male monkeys produced hypertrophy of the prostate and enlargement of the breasts. From a survey of the available literature, however, the danger of most of the above complications is more theoretical than real.

The results at the University of Minnesota Hospitals using anterior pituitary-like substances in the treatment of retained testes are summarized below. Three products have been tried: Antuitrin-S (Parke-Davis), Follutein (Squibb), and Prephysin (Chappell). The last 2 products have been used in only a few cases.

#### a. Antuitrin-S

It is our practice to inject 1 cubic centimeter (100 rat units) of Antuitrin-S daily into the subcutaneous tissue of the thighs for 30 days (3000 units). If no results are obtained before this time, the patient is then observed every month for 3 months and then every 3 months. Some of the cases in which no results were obtained have been followed for 2 years.

Thirty patients with 36 undescended testes have been treated to date with Antuitrin-S (Parke-Davis) in this clinic

The ages of the patients varied from 4 to 24 years. The testes were bilaterally retained in 6 instances. Two of the bilateral cryptorchids also had hypospadias and there was a suggestion of Frolich's syndrome in one bilateral and one inguinally retained case. Five patients responded to the treatment by degrees of descent of the testis into the scrotum. While descent of the retained gonad was complete in 3 cases, it was only to a high scrotal position in the other 2 cases. Both of these patients were older and later submitted to orchiopexy. One of these patients received a total of 6000 units over a period of 2 months. It is interesting that no spermatozoa were seen in either the biopsy or smear of the testis when the patient later submitted to orchiopexy. Also the microscopic section of the testis showed the usual atrophic appearance.

No untoward results have ever been observed over a period of 2 years following the use of Antuitrin-S in this clinic. There was suprapubic edema in three cases which disappeared after treatment and one patient complained of swelling in the left breast which clinically was thought to be a fibrous mastitis. In none of the cases was there a demonstrable increase in the size of the penis. The testes of the successfully treated cases often enlarged; we could not be sure that there was any change in size of the testis in the unsuccessfully treated cases. The scrotum of one boy became red and slightly edematous after 2000 units Antuitrin-S had been administered. In none of the cases were there premature appearance or increase in the amount of pubic, axillary or facial hair. Five patients noticed increased frequency of erections.

#### b. Follutein

Two patients, ages 21 and 23 years, were treated by Follutein (Squibb) for undescended testes. The testes were bilaterally retained (inguinal) in one case and right inguinally arrested in the other. One cubic centimeter of Follutein (125 cc.) was injected daily for 10 days into the subcutaneous tissue of the thigh (1250 u.) No

improvement was noted following this therapy on observing these patients for a period of one year.

#### c. Prephysin

Three patients, ages 2, 7, and 11 years, were treated with Prephysin (Chappell). The undescended testes were unilateral and inguinally retained in all 3 cases. The 2 younger boys were brothers. Prephysin contains the follicle stimulating principle of the pituitary gland, including small amounts of luteinizing factor. It differs from Antuitrin-S and Follutein in that it is extracted from the pituitary gland itself and not from pregnancy urine as the latter 2 are. One-half of 1 cubic centimeter of Prephysin was injected daily for 4 days into the subcutaneous tissue of the thighs of these 3 boys. No descent of the testis was observed in any of these 3 cases over a period of 9 months.

Thus, of 35 patients with the undescended testes treated by anterior pituitary-like substances, degrees of descent were noted in 5. In only 3 was descent complete. The doses used and the interval of observation in this study are comparable to those reported in the literature.

In the cases of cryptorchidism which have been operated upon at the University of Minnesota Hospitals, nearly all have shown evidence of mechanical causes for arrest of descent. The testis was often lodged in pockets or bound down by adhesions to such extent that it was with great difficulty that they were freed or the cord lengthened by loosening adhesions. MacCollum thinks that it is incongruous to suppose that at some time this fibrous tissue will disappear and allow the testicle "to drop like a plummet" into the scrotum. In our series, 5 patients with undescended testes who had been treated with Antuitrin-S (total 3,000 units in each except 1 case that received 6,000 units), submitted to operation 3 to 6 months later. The same degree of fibrous adhesions and mechanical arrest was noted in these as in cases which had not been treated by hormonal therapy previous to operation.



These observations, particularly, raise doubt concerning the efficacy of hormonal therapy even in selected cases of bona-fide instances of testicular failure of descent. One wonders if many of the successful results reported in the literature were not obtained in cases of physiologic ectopy and not true undescended testes. It may be that anterior pituitary-like substance is valuable in the treatment of physiologic ectopy but it should be remembered that such cases often descend spontaneously.

It is not to be inferred that the writer believes that all the reported cases of retained testes that have descended after a course of hormonal therapy are cases of physiologic ectopy. However, because of the poor results obtained with this therapy at this clinic, and because of the existence of mechanical causes for testicular arrest in most of the operated cases, it is believed that endocrine imbalance alone does not fully explain the cause or give a rational basis for treatment in all cases of true testicular maldescent.

#### A Suggested Plan of Treatment of Undescended Testis

It is known from the experiments of Moore and Wangenstein that the testis must be in the scrotum before spermatogenesis occurs or degenerative changes will set in. Puberty in the male lies between the ages of 13 and 15 years, without regard to race, climate, or individual differences (Spangero), the extremes being 9 years (Scammon) and 18 years (Crampton). Therefore, treatment of the congenitally retained gland may be deferred until the patient is 9 to 11 years old. If surgery is contemplated, there is no objection to operating upon a patient with uncomplicated retained testis at any earlier age, but it is unnecessary. The presence of a large associated hernia may necessitate earlier surgical intervention.

Since in the literature competent observers have reported descent of the "retained" testis into the scrotum after therapy with hormones in over 70% of cases, it is our practice at the Univer-

sity of Minnesota Hospitals to suggest first a trial of anterior pituitary-like substance in all uncomplicated cases of undescended testes before surgical procedures. Probably the determination of the gonadotropic hormone in the urine before treatment (Hess et al) will aid in the selection of these patients. It would be of practical value to know before treatment if there existed mechanical causes for the testicular maldescent, but unfortunately no such diagnostic means is known to date.

There are various methods of administering hormonal therapy. If Antuitrin-S (Parke-Davis) is used, it is the practice at this clinic to inject 100 rat units (1 cc.) daily into the subcutaneous tissues of the thigh for one month (total 3000 units). If after 3 to 6 months of observation, no results have been obtained, surgical treatment of the undescended testis is advised if the patient is 9 to 11 years or older. Only on rare occasions has the patient been advised to continue hormonal therapy if no results are apparent at 3 months.

It is possible that the dosage and period of injections of anterior pituitary-like substances in the cases treated at this clinic were not adequate but the factors are comparable to those reported in the successful cases in the literature. The mechanical obstruction to spontaneous or hormonal induced testicular descent as revealed by subsequent operation seems adequate exploration of the failure of hormonal therapy. In comparing the results of hormonal and surgical therapy in the treatment of testicular maldescent at this clinic, orchiopexy has given the surest and most satisfactory results to date. However, a method that gives the patient any chance of avoiding a surgical operation certainly merits trial; hence, even granting that some of the successful results reported in the literature were obtained in not true cases of undescended testis, the use of hormonal therapy at least as a preliminary form of treatment is worthwhile.

#### IV. Conclusions

Cryptorchidism is not an unusual anomaly, as it occurs once in every 500 males. Differentiation must be made between true testicular maldescent and physiologic ectopy. At the University of Minnesota clinics no instance of spontaneous complete descent has been noted in a series of 100 consecutive cases of retained testes. The suggestion is offered that some of the instances of spontaneous descent and successful results caused by hormonal therapy were obtained in cases of physiologic ectopy and not true undescended testis.

The undescended testis should not be considered a precancerous lesion.

Treatment of the retained gonad may be deferred until the patient is 9 to 11 years old. Reports in the literature of the larger series of cryptorchids treated by hormones reveal that in about 70% cases treated there is descent of the testis into the scrotum. With the hope that the case may be a favorable one, a course of treatment with anterior pituitary-like substance may be tried first in cryptorchids before surgical procedures. However, this form of therapy has been very disappointing in the cases treated at this clinic, degrees of descent being obtained in only 5 of 35 cases so treated. No untoward effects resulting from hormonal therapy have been observed in these cases.

For reasons mentioned elsewhere, it is believed that endocrine imbalance alone does not fully explain the cause or give a rational basis for treatment in all cases of true testicular maldescent. However, anterior pituitary-like substance should be given at least a preliminary trial in the treatment of undescended testis, and if no results are obtained, an orchiopexy should be performed.

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#### Case Report

White male, 23, admitted to the University of Minnesota Hospitals

11-12-34 with history of right lower quadrant pain for about 1 week. Had similar pain in left lower quadrant for 5 years. Physical examination revealed right indirect inguinal hernia and right inguinally retained testis. Left testis was in scrotum. There was a large left indirect inguinal hernia. Patient was treated by means of Antuitrin-S, 1 cc. of which was injected subcutaneously into the thighs for one month until a total of 3000 units were injected. The right testis descended to a high scrotal position but could not be pushed any farther into the scrotum. Because of this orchiopexy and hernioplasty were done on the right side. The left hernia was treated by means of truss and hernial injections. Before operation the left testicle measured  $4\frac{1}{2} \times 4\frac{1}{2} \times 3\frac{1}{2}$  cm. while the right undescended testis measured  $4\frac{1}{2} \times 3\frac{1}{2} \times 3\frac{1}{2}$  cm.: 11 months after orchiopexy both testes were about the same size and measured  $4 \times 4 \times 3\frac{1}{2}$  cm. The cosmetic result of the orchiopexy was excellent. Ejaculation test showed 40,000,000 sperm per cubic centimeter.

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#### Case Report

White male, 9, admitted to Pediatrics Service for penoscrotal hypospadias and also bilateral inguinally retained testis. Had one operation to correct the ventral curvature of the penis with good result.

The testes were normal in size for a boy of his age but could not be pushed from their inguinal position into the scrotum. Was given Antuitrin-S, 1 cc., subcutaneously into the lateral aspect of the thighs every day for 1 month. After 3000 units of this material were given the right testis descended into the scrotum but even after a total of 4000 units had been injected, the left testis did not descend. The patient had noticed redness and edema of the scrotum after 2000 units had been administered and also noted frequent erections. There was no premature appearance of axillary pubic or facial hair.

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