TABLE III.—*Analysis of Series C (Infected, Non-penicillin)*

Type of Case	No. of Cases	Average Time Wounding to Limb-fitting	Average Time Operation to Limb-fitting
Open wounds still present at operation	Healed .. 5 Unhealed .. 2	41 weeks	20½ weeks
Infected cases*	Healed .. 5 Unhealed .. 6	32 "	21 "
Other factors present†	Healed .. 3 Unhealed .. 0	35 "	21 "
All cases ..	Healed .. 13 Unhealed .. 8	35 "	21 "

* Those with a history of severe infection of the wound.

† One case had a Charcot ankle, one had foreign bodies in the stump, and the third had had an ulcerated leg for years before amputation was undertaken.

Table IV gives details of the 90 cases operated on during a 6-months period, with comparisons between cases receiving

TABLE IV.—*Comparison of Results at Various Amputation Sites (in 90 Cases during 6-months Period)*

Site of Amputation or Re-amputation	Penicillin Series		Control Series		All Cases Combined	
	No. of Cases	Average Time Operation to Limb-fitting	No. of Cases	Average Time Operation to Limb-fitting	No. of Cases	Average Time Operation to Limb-fitting
Above elbow	2	10½ weeks	6	9 weeks	8	9½ weeks
Below elbow ..	2	11 "	10	5½ "	12	6½ "
Above knee ..	19	9 "	11	7½ "	30	8½ "
Below knee ..	11	12 "	29	12 "	40	12 "

and those not receiving post-operative penicillin. The results are given for the various amputation sites. It should be noted that the most difficult site to obtain a good result is below the knee, all but 2 of the 12 cases of delayed healing being below-knee amputations.

Conclusions

The best indications of the success of an amputation or re-amputation are: first, the shortness of time between operation and readiness of the stump for limb-fitting; secondly, the subsequent behaviour of the stump under the strain of wearing an artificial limb. Time alone can show the latter, but the former can be worked out quite easily and gives a reasonable index of the degree of success. It may be added that a rapidly healing stump is usually sounder than a slowly healing one.

Broadly speaking, these series give us the results in 3 types of case. First, potentially or actually infected cases receiving post-operative penicillin; secondly, uninfected cases not receiving penicillin; and, thirdly, potentially or actually infected cases not receiving post-operative penicillin. It is evident that in the uninfected cases the results were best, but they were only slightly better than in the infected cases receiving post-operative penicillin; the relevant average times of healing were 7 and 10 weeks respectively. It should be remembered that many of these infected cases had been grossly infected, and could not have undergone re-amputation for weeks or months later had it not been possible to administer post-operative penicillin; yet there were no failures in this series and only 3 cases of delayed healing. In the third series, even with 8 failures not included, it is found that the average healing-time was 21 weeks—more than twice the period in similar cases which had received penicillin after operation.

From these results it can be claimed that the use of penicillin not only shortens the time between operation and limb-fitting, but makes it possible to operate on doubtful cases considerably earlier than would otherwise be feasible. Convalescence is shortened and a far better prospect of success is assured.

Summary

A report is given of 102 amputations and re-amputations. Of these 55 were infected or potentially so at the time of operation; 34 of them received post-operative penicillin and 21 did not. The results show that, in selected cases, it is possible to operate on infected cases much earlier with than without penicillin, and with good prospects of success. In this way convalescence can be considerably shortened, and the patient can start earning his living earlier.

It is pointed out that there were no failures in the penicillin series, and in only 8.8% of this series was there delay in healing of

stumps. Emphasis should be laid on the necessity for penicillin-sensitivity tests before operation.

Careful attention should be paid to operative technique, and operation should not be undertaken in the presence of active inflammation or profuse discharge from a granulating wound.

My thanks are due to the Director-General, Medical Services, Ministry of Pensions, and the Medical Superintendent at Chapel Allerton for permission to publish these series; also to my colleagues—especially Mr. A. Lawson Light, who performed some of the operations—for helpful criticism, and to the pathological department and office staff for their assistance.

DESCENT OF THE TESTIS IN RELATION TO TEMPERATURE

BY

ALEC W. BADENOCH, M.D., Ch.M., F.R.C.S.

Wing Commander, R.A.F.V.R.; Surgeon, Metropolitan Hospital, London

The abdominal position of the foetal testis was known to Galen (Frankl, 1895), but Baron Haller (Hunter, 1837) and John Hunter (1837) really first focused attention on this point and began the stream of literature, which has flowed on in such quantity from observers, on all aspects of development and descent. The facts are few and not greatly in dispute; the fancies prolific and constantly recurring.

The Position in Mammals

The descent of the testis is peculiar to mammals. In all animals, up to and including reptiles and birds, the testis lies high up in the abdomen, and in some of the more primitive mammals, such as the Monotremata (duck-billed platypus and spiny ant-eater), this position persists. In the higher groups the testis lies in the false pelvis. Most of the Edentata (sloth, ant-eater, and armadillo), some of the Insectivora (shrew), the Cetacea (whale and porpoise), and the Sirenia (seacows) have primary abdominal testis with no inguinal fold. In marsupials (kangaroo and wallaby) the testis lies in the suprapubic region, in a well-developed pouch with a closed processus vaginalis. According to Andrews and Bissell (1934) this is really inguinal and represents the earliest extra-abdominal position. In rodents, some of the Insectivora (mole and hedgehog), and Cheiroptera (bats) the testis is intra-abdominal in the resting phase of the sexual cycle. During the rutting season it is extruded by unstriated and retracted by striated muscle; there is no true vaginal process. In the Ungulata, Carnivora, and Primates there is a true vaginal process, and the testis is extra-abdominal. The elephant is an exception, the testis being inside the abdomen; and in some—e.g., the stag—the testis is retracted at other than the rutting season. It has been said that the processus vaginalis is occluded only in man and some of the higher monkeys, but occlusion must sometimes occur in other animals, since hydrocele has been reported in dogs and bulls.

Cause of Migration

There is no physiological reason why the testis should not leave its primitive position in the abdomen. Certainly as regards its spermatogenic function it plays no part in the general economy of the body, and, as Crew says, it belongs to the race rather than to the individual. When discussing the problem of its extra-abdominal position Herbert Spencer (1866) wrote: "We cannot consider it an adaptive change, since there seems no way in which the production of sperm cells, internally carried on in a bird, is made external by adjustment to the changed requirements of mammalian life. Nor can we ascribe it to the survival of the fittest, for it is incredible that any mammal was over-advantaged, in the struggle for life, by this changed position of the organ." I think all would be in agreement with the last sentence, but the previous one is now known to be incorrect.

Influence of the Scrotum on Spermatogenesis

In any animal in which the testis normally descends, in order that it may attain full development and function, it must reach and occupy the terminal part of its destined course. Griffiths (1895) showed that if the testis of a dog was replaced in the

abdomen it diminished in size and lost its spermatogenic function. In 1924 Moore performed a series of experiments at the Hull Zoological Department, Chicago, using guinea-pigs, rabbits, and rats. In these animals there is a wide-open connexion between the scrotum and the peritoneal cavity, and the testis can be kept in the peritoneal cavity without in any way interfering with its nerve or blood supply. Moore found that in testes retained in the abdomen for as short a time as seven days there was total disorganization of the germinal epithelium of the seminiferous tubules. The usually well-defined tubular lumen was practically filled with a mass of cells thrown out from the epithelium. Some of the cells could be seen in outline only. Others showed fragmentation of the nucleus, and protoplasmic masses were localized in a granular debris. After 14 days' peritoneal retention most of the debris resulting from degeneration had been removed from the tubules, although a few cells could still be seen. At the end of 21 days little remained of the tubules except the reticulum, with the cells of Sertoli lying against the inner border of the basement membrane. A typical cryptorchid had therefore been produced in three weeks. Subsequent examination of testes showed that there was a progressive diminution in the size of the tubules so that they had shrunk to about one-third of their former diameter. Concomitantly, the interstitial cells had become more prominent and were arranged in masses between the now more widely separated tubules. Certain testes were then replaced in the scrotum, and in a few months the tubules in these had returned to normal. These experiments were confirmed by Wangenstein (1927), who used immature and young dogs for the purpose.

It follows, therefore, that the scrotum exerts a peculiar and striking influence on the testes—an influence that is necessary not only for the differentiation of the germ cells but also for the retention of cells already differentiated.

Influence of Temperature on Spermatogenesis

Meek (1920) noted that the length and periodicity of the spawning of certain fish varied with the temperature of the water. Crew (1921-2) first drew attention to the efficiency of the scrotum as a temperature-regulating organ. It is a pouch of very thin skin well supplied with sebaceous glands. The dartos is firmly attached to the skin, is of non-striated muscle, and quickly responds to changes of temperature. In warmth the scrotum becomes lax, flaccid, and pendulous, while in cold it is corrugated, short, closely invests the testis, and draws it against the body wall. Further, there is no fat in a normal scrotum. When the scrotal skin becomes thickened by a pathological condition, such as elephantiasis, atrophy of the testis occurs. Fukui, in 1923, applied heat to the testis in various forms such as hot air, arc light, and sunlight, and found that exposure to excessive heat was followed by degeneration of the seminiferous tubules. He then elevated both testes of an animal into the peritoneal cavity and artificially cooled the external area in the region of the testes on one side. On examination of the testes after a few days he found that the cooled one was normal while the other showed degeneration of the tubules.

In 1924 Moore and Oslund insulated the scrotum of a ram against heat loss by loosely encasing it in a woollen garment, with a waterproof cover sewed to fit the contour of the scrotum and suspended by artificial supports to prevent abnormal pressure. After 80 days the testes were found to be devoid of spermatozoa; many tubules were in an advanced stage of degeneration, and in others the germinal epithelium had disappeared. As Moore says, "the animal had sterilized itself with its own body heat."

Subsequently Moore and Quick (1924) performed a series of experiments on rats, rabbits, and guinea-pigs and found the scrotal temperature was appreciably lower than that of the peritoneal cavity in each case. They applied hot-water pads to the external surface of a guinea-pig's scrotum, raising the temperature approximately 7 to 8° C. above normal, and on examining the testes in 10 days' time found severe tubular degeneration.

Hill (1937) has made the interesting observation that when the ovaries of mice are grafted on to the ears of castrated

male mice the atrophied vesicles and prostate are restored to almost normal. Abdominal transplants have no effect. The inference is that the lower temperature of the ear (similar to that of the scrotum) has stimulated the ovary to produce androgen. Hill suggests that the environment may well condition the production of the specific compounds of the gonad.

Temperature in the Human Scrotum

Harrenstein (1928) performed experiments on 16 children, between the ages of 1 and 11 years, on whom an operation for inguinal hernia or retained testis was being done. He found a considerable difference between the intraperitoneal and scrotal temperatures in each case, the average being 4.9° C. and 3.5° C., depending on whether a short- or long-bulbed thermometer was used.

I have recently carried out temperature recordings in 30 male adults operated on for inguinal hernia. Two long-bulbed laboratory thermometers registering degrees centigrade in tenths were employed. The hernial sac was dissected clear from the cord and opened. A finger was passed downwards into the scrotum, along the cord, until the tip was in approximation with the body of the testis. Both thermometers were introduced through the opening in the sac into the peritoneal cavity, until each bulb was lying on the floor of the iliac fossa. In two to three minutes the temperature on each thermometer

TABLE I.—*The Intrascrotal and Peritoneal Temperature Recordings in 25 Adults*

Age	Initial Peritoneal Temperature	Scrotal Temperature			Final Peritoneal Temperature		Theatre Temperature	Maximum Variation	Anaesthetic
		1 Minute	2 Minutes	3 Minutes	P. Ther.	S. Ther.			
21	37.5°	35.0°	34.5°	34.1°	37.8°	37.6°	74°	3.7°	L
27	37.0°	35.8°	35.5°	35.5°	37.3°	37.3°	78°	1.8°	L
22	37.0°	35.5°	35.2°	35.0°	37.0°	37.0°	78°	2.0°	L
24	37.5°	36.0°	35.5°	35.5°	37.5°	37.5°	78°	2.0°	G
38	37.5°	36.0°	35.5°	35.5°	37.5°	37.5°	78°	2.0°	G
20	36.5°	34.8°	34.9°	34.9°	36.8°	36.8°	72°	2.0°	L
18	37.0°	34.0°	33.8°	33.8°	37.0°	37.0°	72°	1.6°	L
19	37.0°	35.4°	35.6°	35.6°	37.0°	37.0°	72°	1.6°	L
26	38.1°	35.8°	35.6°	35.5°	38.2°	38.1°	76°	2.0°	L
40	36.5°	35.2°	34.8°	34.9°	36.9°	36.9°	70°	1.1°	L
26	36.8°	34.4°	34.2°	34.2°	36.8°	36.8°	70°	1.9°	L
33	37.0°	34.5°	34.5°	34.6°	36.4°	36.3°	73°	1.6°	L
19	37.0°	35.2°	35.2°	35.3°	37.2°	37.1°	72°	2.0°	L
37	36.5°	33.3°	33.2°	33.4°	36.2°	36.1°	72°	2.3°	L
31	36.4°	34.1°	34.1°	34.2°	36.7°	36.6°	75°	2.6°	L
19	37.0°	35.0°	35.1°	35.1°	37.2°	37.3°	75°	2.1°	L
40	36.7°	34.7°	34.7°	34.7°	36.8°	36.8°	74°	2.1°	S
31	36.8°	35.0°	35.1°	35.1°	36.8°	36.8°	74°	1.7°	L + P
40	36.5°	35.2°	35.2°	35.2°	36.8°	36.7°	74°	1.4°	L
42	36.5°	35.6°	35.7°	35.6°	36.6°	36.7°	72°	1.0°	L
39	37.2°	34.6°	34.5°	34.5°	37.2°	37.2°	70°	2.8°	L + P
18	36.9°	34.3°	34.3°	34.4°	37.1°	37.0°	74°	2.8°	L + P
19	36.8°	34.6°	34.7°	34.7°	37.0°	36.9°	72°	2.4°	L + P
30	37.0°	36.3°	36.4°	36.2°	37.0°	37.1°	78°	0.8°	L + G
27	35.2°	33.5°	33.0°	32.9°	35.4°	35.5°	72°	2.5°	S

Peritoneal and scrotal recordings are in centigrade, theatre recordings are in Fahrenheit. L = Local; G = General; P = Pentothal; S = Spinal.

TABLE II.—*The Intrascrotal, Pubo-inguinal, and Intraperitoneal Temperature Readings in 5 Adults*

Age	Initial Peritoneal Temperature	Scrotal Temperature	Pubo-inguinal T.		Final Peritoneal T.		Pubo-inguinal Variation	Scrotal Variation	Theatre Temperature	Anaesthetic
			1 Minute	2 Minutes	P. Ther.	S. Ther.				
40	36.7°	34.6°	35.6°	36.0°	37.2°	37.0°	1.6°	2.1°	74°	S
33	37.3°	35.5°	36.5°	36.5°	37.5°	37.5°	1.0°	2.0°	78°	L + G
19	37.1°	34.6°	35.8°	35.8°	37.1°	37.2°	1.3°	2.6°	70°	L + P
27	37.1°	34.5°	37.7°	35.7°	37.2°	37.1°	1.5°	2.6°	74°	L + P
35	37.3°	34.8°	35.6°	35.6°	37.4°	37.4°	1.8°	2.5°	74°	L

Peritoneal and scrotal recordings are in centigrade, theatre recordings are in Fahrenheit. L = Local; G = General; P = Pentothal; S = Spinal.

appeared stabilized, and a reading was taken. One thermometer was now withdrawn and passed into the scrotum. Readings were recorded at one-, two-, and three-minute intervals. The thermometer was then removed and again introduced into the peritoneal cavity, a further reading being taken at the end of

a minute. The majority of cases were operated on under block local analgesia, occasionally supplemented with 0.5 g. of pentothal intravenously. In no case was any deleterious effect produced. Table I shows the results in 25 cases with a three-minute record of scrotal temperature. Table II shows the results in 5 cases when the thermometer was withdrawn from the scrotum after one-minute and two-minute interval recordings of the temperature in the pubo-inguinal region were taken.

From these two tables the following facts are deduced. In each case the temperature is lower in the scrotum than in the iliac fossa. This varies from 0.8°C . to 3.7°C ., with an average difference in 30 cases of 2.2°C . The temperature in the pubo-inguinal region in each of 5 cases is higher than that in the scrotum but an average of 1.4°C . lower than that in the iliac fossa.

Discussion

Is this thermal influence a cause or an adaptation of migration? Many observers (Hart, 1908-9; Crew, 1921-2; Keith, 1933) have taken the view that the cause of migration is mechanical. With changing methods of progression, the dense, compact, suspended testis was gradually compelled to pass from the primitive position towards the inguinal region of the abdominal cavity. It then came to lie in the lymph spaces described by Sabin. With increasing impulsiveness of movement and with the increase in abdominal pressure following the development of the diaphragm, the testis was forced along the lymph tracts until it came to lie in the subintegumental position in the groin. Further impulsive activity produced a hernia of the testis into the scrotum. I do not consider this theory at all satisfactory. It is only in the male of the species that the reproductive gland normally "herniates"; and why should this comparatively small organ be the only one to do so on mechanical grounds? The large group of rodents and the stag, which undoubtedly are as active and impulsive in their movements as any other mammal, have intra-abdominal testes except in the rutting season. I believe that the migration is a search for a lower temperature. In the Monotremata and certain lower orders with abdominal testes, body temperature is much more variable than in the higher mammals. In the whale the amount of subcutaneous blubber would insulate the testis, and the thick skin of the elephant would preclude heat loss. Andrews and Bissell have put forward the view that these two groups are secondary testiconda. We know that eels migrate to breed in the depths of the Saragossa Sea, that salmon and other fish migrate to the upper reaches of mountain streams for their breeding, and that birds migrate to a colder area during their nesting season. It is not unreasonable, therefore, to suggest that in mammals the reproductive gland, instead of the whole animal, migrates for the same specific purpose.

Summary

The position of the testis in the various groups of mammals is discussed.

The influence of temperature on spermatogenesis is reviewed.

Recordings of the temperature in 30 young adults are given.

It is suggested that the extra-abdominal position of the testes is a migration in search of a temperature lower than that of the body.

BIBLIOGRAPHY

- Andrews, E., and Bissell, A. (1934). *J. Urol.*, **31**, 839.
Crew, F. A. E. (1921-2). *J. Anat.*, **56**, 98.
Frankl, O. (1895). *Arch. f. Anat. u. Ent. d. Organ.* 339.
Fukui, N. (1923). *Jap. med. World* (Tokio), **3**, 27, 160.
Griffiths, J. (1895). *Lancet*, **1**, 795.
Haller, Baron. Quoted by John Hunter (1837).
Harrenstein, R. J. (1928). *Zbl. Chir.*, **55**, 1734.
Hart, D. B. (1908-9). *Trans. Edin. Med. Soc.*, **34**, 101.
Hill, R. T. (1937). *Endocrinology*, **24**, 495, 633.
Hunter, John (1837). *Palmer's Edition of Hunter's Works*, Vol. 4, London.
Keith, Sir Arthur (1933). *Human Embryology and Morphology*, London.
Lydekker, R. (1922). *Royal Natural History*, London.
Meek, A. (1920). *Nature*, **106**, 532.
Moore, C. R. (1924). *Endocrinology*, **8**, 493.
— and Oslund, R. (1924). *Amer. J. Physiol.*, **67**, 595.
— and Quick, W. J. (1924). *Ibid.*, **68**, 70.
Spencer, Herbert (1866). *Principles of Biology*, **1**, 573, New York.
Wangensteen, O. H. (1927). *Arch. Surg.*, **14**, 663.

H. H. Rosenblum (*U.S. Nav. med. Bull.*, 1945, **44**, 375) states that Reiter's disease, which has been recognized only in young men, is characterized principally by acute purulent urethritis, acute conjunctivitis, and acute arthritis, often occurring in that order. The most helpful analgesic was acetylsalicylic acid and codeine in moderate doses.

"FASTNESS" OF STAPHYLOCOCCI, HAEMOLYTIC STREPTOCOCCI, AND PNEUMOCOCCI TO PENICILLIN

BY

E. W. TODD, M.D., D.P.H.

G. S. TURNER, A.I.M.L.T.

AND

L. G. W. DREW

(From the Serum Institute, Wellcome Foundation, Carshalton, Surrey)*

In a previous communication Todd, Turner, and Drew (1945) showed that two different strains of staphylococcus became highly resistant to penicillin when subcultured daily in penicillin broth. The resistance of the strain "Oxford H" was increased 3,000 times after 27 subcultures, and the resistance of strain "Staphylococcus A" was increased 250 times after 21 subcultures. This high degree of resistance to penicillin disappeared rapidly when the organisms were subcultured daily in plain broth.

The same methods of investigating (1) the time required to produce "fastness" to penicillin and (2) the temporary or permanent character of this acquired change have now been applied to haemolytic streptococci and pneumococci.

Staphylococcus

The cultivation of strains of "Oxford H" and "Staphylococcus A" in penicillin broth, described in a previous paper, was continued. After 75 subcultures in penicillin broth both the strains were 5,000 times more resistant to penicillin than the original cultures; they both grew in broth containing 400 units of penicillin per c.cm. On subcultivation in plain broth the resistance of both strains to penicillin was rapidly lost.

Haemolytic Streptococcus

Rake *et al.* (1944) subcultured *Str. pyogenes* (Strain C 203, Group A, Type 3) in penicillin broth. After 58 subcultures the dose of penicillin required for "bacteriostasis" had increased from 0.03 to 0.95 unit per c.cm., showing a 30-fold increase in resistance. They do not state whether this resistance was maintained or lost on subcultivation in plain broth.

Fig. 1 shows the results of subculturing Strain C 203 daily in broth containing falling dilutions of penicillin on a 20% range in a total volume of 1 c.cm. The daily variations in

FIG. 1.—Showing increasing resistance on subculture in penicillin, followed by diminishing resistance on subculture in broth. *Str. pyogenes*, Strain C 203, Group A, Type 3.

resistance were much greater than those obtained with staphylococci (Todd, Turner, and Drew, 1945). This was particularly noticeable at the beginning of the experiment, before any definite increase in resistance was observed. Resistance to penicillin was increased five times after 35 subcultures and four

* Seconded from the London County Council.