ment of various kinds, was tested by homoplastic grafting into the subcutaneous space of the flank in newly castrated adult rats. The tissue was grafted (a) without further treatment, (b) after soaking in 15% glycerol-saline, and (c) after soaking and cooling slowly in saline or 15% glycerol-saline to -79°C . (the temperature of dry ice) or -190°C . (the temperature of liquid air) for various periods, and thawing quickly at $+40^{\circ}\text{C}$., according to the technique described by Parkes and Smith (1953) for ovarian tissue. Groups of 10 animals were used for each experiment. One or more animals in each group were killed at early stages, but the majority were allowed to live for three to four months after grafting, during which time a number of mating experiments were carried out. At necropsy the graft was removed for sectioning and the seminal vesicles were fixed and weighed. The gametogenic activity of the graft was assessed by its histological appearance, and its androgenic activity by the previous mating behaviour of the animal and the size of the seminal vesicles.

The histological development of these and other grafts of frozen testis tissue, especially in relation to spermatogenesis, will be dealt with in a paper by Dr. Deanesly. All that need be said here is that the endocrinologically active grafts recovered during the present series of experiments, whether derived from frozen or unfrozen tissue, resembled those usually obtained when testis tissue is grafted subcutaneously. The tubules were small and the interstitial and other intertubular tissue was prominent. The later stages of spermatogenesis were absent, but some tubules contained spermatocytes in active division. No regular difference was detected between established grafts derived from unfrozen tissue and those from tissue frozen in glycerol-saline.

Results

The experiments recorded here are summarized in the Table, in which the number of animals showing evidence of substantial androgenic activity on the part of the graft

Results of Grafting Rat Testicular Tissue Soaked and Frozen in Saline or 15% Glycerol-saline

Treatment	Time Tissue Frozen	No. of Animals Receiving Grafts	No. Developing Androgenic Grafts
Untreated	—	8	5
Soaked in glycerol-saline	Not frozen	8	5
Soaked in saline and frozen to -79°C .	One hour	6	0
	One hour	8	7
	One week	8	6
Frozen to and stored at -79°C .	8 weeks	5	2
	22 "	9	4
	One hour	16	14
Frozen to and stored at -190°C .	One week	10	8
	7 weeks	6	3
	22 "	9	7

Animals killed 12 to 16 weeks after receiving grafts.

is given in relation to the conditions and duration of freezing. It will be seen that tissue which had been frozen in 15% glycerol-saline and thawed formed an androgenic graft as readily as did unfrozen tissue, and that its viability did not obviously decrease on prolonged storage at low temperature. It appears that the difference between preservation in liquid air and in dry ice is not so marked as with rat ovarian tissue (Parkes and Smith, 1953). In considering the percentage of takes, it must be remembered that grafts showing only slight activity were not included in the right-hand column of the table, and that in all cases the grafts were homoplastic ones of some months' standing. In these circumstances the results with the tissue frozen in glycerol-saline must be regarded as promising.

The entry in the table for the grafting of tissue frozen in saline only should be amplified by recording that of the six rats kept for more than 12 weeks after implantation four developed small grafts, histologically recognizable as rudimentary testis tissue. The seminal vesicles, however, were completely atrophic macroscopically, and histological examination of the vesicular epithelium failed to provide

evidence that the grafts had been even slightly active androgenically. The results were thus in strong contrast to those obtained with testes frozen in 15% glycerol-saline.

It seems, therefore, that the endocrine cells of the testis can be added to the list of tissues the prolonged storage of which at low temperatures is made possible, or greatly facilitated, by the use of media containing glycerol. It remains to be seen to what extent this technique may promote the use of viable transplants of endocrine and other tissue in man. Discussion of this problem will be found in the forthcoming volume of the Proceedings of the recent Ciba Symposium on the Preservation of Normal Tissues for Transplantation.

The operations and day-to-day observations were carried out by Miss J. Masson and Miss M. Mansi.

Summary

The androgenic tissue of the testis of the young rat can be preserved in viable condition for long periods by freezing in media containing glycerol, as previously described for the ovary of the rat (Smith and Parkes, 1951).

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Medical Memoranda

Intolerance to "Veriloid"

"Veriloid," a preparation of the alkaloids of *Veratrum viride* or green hellebore, is a potent hypotensive agent. Alarming symptoms from its use in moderate dosage occurred in the following case.

CASE REPORT

A married woman aged 59, living alone, was admitted to Whittington Hospital at 9 p.m. on August 14, 1952, complaining of severe dull epigastric pain radiating upwards into the neck and down both arms; it had come on at 5 p.m. the same day. At the onset she had felt choked, vomited, and had some blurring of vision. She had been unable to get to her doctor for some time.

On examination she looked ill and her extremities were cold. The pulse rate was 40, regular, and the blood pressure was 80/60. The apex beat was displaced a little to the left; the heart sounds were normal. The fundi showed only slight arterial changes. There was no excessive salivation, and the pupils were of normal size. No abnormality was found in the lungs, abdomen, or central nervous system.

A provisional diagnosis of myocardial infarction was made, and she was given morphine $\frac{1}{2}$ gr. (11 mg.). The pulse rate did not rise above 60, and the blood pressure remained at 100/60 or less. The symptomatology was then reconsidered, and veriloid overdosage was thought more likely to have been the cause. She was therefore given atropine, 1/150 gr. (0.43 mg.). Her pulse increased slightly to 64, her blood pressure rose only to 115/80, but her pain ceased in the next hour and a half. At this point ephedrine, $\frac{1}{2}$ gr. (32 mg.) was given by intramuscular injection. One hour later her pulse rate was 74 and her blood pressure 165/100. Electrocardiograms on August 15, 19, and 26 showed no abnormality. The white-cell count was 7,700 with a normal differential count, and the sedimentation rate was 8 mm. in one hour.

She remained well, up and about in the ward, with no return of pain or distress, from August 16 to 30, when she was discharged. Her resting blood pressure was then 200/110.

COMMENT

The patient had been taking two tablets of "veriloid-VP" three times daily after meals for six weeks before admission. The drug had been prescribed for hypertension, first diagnosed five years previously. Each tablet contains 2 mg. of veriloid and 15 mg. of phenobarbitone. On the day of admission she had had her last dose after lunch, and symptoms had occurred when she began her tea.

According to Kauntze and Trounce (1951), some patients taking 12 mg. of veriloid daily had toxic symptoms, including a substernal burning sensation (sometimes amounting to pain), salivation, globus or choking sensation, vomiting, coldness and tingling in the finger-tips, hiccup, and collapse. They stated that toxic symptoms are minimized by combining the veriloid with phenobarbitone and administering the tablets immediately after meals. In our patient the symptoms were so severe as to simulate myocardial infarction, and continued for several hours, but appeared to be controlled partially by atropine and, more effectively, by ephedrine. In a search of the literature we can find no reference to toxic symptoms so severe and protracted as these with moderate dosage of the drug.

Several authors comment on the narrow margin between therapeutic and toxic levels in some patients (Freis *et al.*, 1949; Kauntze and Trounce, 1951), but it is said that the emetic property of the drug precludes serious overdosage. Our patient vomited, but continued to have severe toxic symptoms for several hours. It is therefore clear that vomiting does not always occur in time to prevent very undesirable effects.

We would like to thank Dr. A. L. Jacobs, consultant physician, for permission to submit this case report.

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A Case of Meigs's Syndrome with an Ovarian Carcinoma

The association of hydrothorax, usually on the right side, with ascites and fibroma of the ovary was described in 1937 by Meigs and Cass, and since this time Meigs's name has become attached to this syndrome. This is not to say that he was the first to note such an association of clinical findings, for he quotes at length in a later article (Meigs *et al.*, 1943) a report by Lawson Tait (1892) of a typical example successfully operated on. Following Meigs's original article there has been a much more general recognition of the syndrome. Soon it became apparent that hydrothorax, usually on the right side, might occasionally be present in association with any marked ascites, whether caused by an ovarian tumour or cirrhosis of the liver, though the former was most commonly responsible.

There has been some discussion on the way hydrothorax is produced. The following case is reported as there seemed to be a fairly wide channel through which fluid passed readily from peritoneal to pleural cavity.

CASE REPORT

A married woman aged 52 was admitted to hospital on July 26, 1951, with marked ascites. Her haemoglobin being only 58%, 4 pints (2.3 litres) of blood was transfused over the course of the next few days. On July 31 she became dyspnoeic. I first saw her on the following day. Examination then showed a gross ascites, though no tumour could be detected on abdominal or vaginal examination. The right chest was dull to percussion, and an x-ray examination confirmed the presence of a pleural effusion. No underlying lung disease could be detected. A malignant ovarian tumour was suspected and laparotomy advised.

Before the operation repeated aspiration of the right chest was carried out. On August 1 36 oz. (1,020 ml.) of clear

straw-coloured fluid was aspirated, followed by 38 oz. (1,080 ml.) two days later and 40 oz. (1,140 ml.) on August 11.

On August 13 the patient was anaesthetized and placed on the operating-table. Inspection then showed an obvious bilobar swelling lying more to the right side of the abdomen, while the ascitic distension had apparently disappeared. Laparotomy confirmed these findings except for a little ascites, which was cleared with sucker and mops. The upper pole of the tumour was then delivered through the incision. The lower pole was fixed by infiltration of the right ovario-pelvic ligament and adhesions to the rectum. By finger dissection enough mobilization of the tumour was obtained to allow the remaining pedicle to be clamped, and the tumour was removed. There was fairly profuse bleeding from the infiltrated area, and several clamps had to be applied to open gushing veins. Haemostasis was finally obtained, and, as the left ovary and uterus appeared normal and the complete removal of malignant tissue in the region of the pedicle was impossible, the abdomen was closed. There were no obvious secondaries in the omentum or on the peritoneum.

Blood transfusion was given post-operatively as there was some degree of shock, but there were no other complications, and the patient was discharged from hospital on August 29. She was referred for deep x-ray therapy, and received a full course of treatment. When last seen on November 15, 1951, she was well, there being no sign of recurrence, and no evidence of ascites or hydrothorax. An x-ray film of the chest showed no sign of pleural effusion or of metastasis.

Pathological Report.—"The specimen consists of a right ovarian cyst measuring 23 by 15 cm. Microscopically the appearances are those of a papillary adenocarcinoma."

COMMENT

The point of particular interest in this case is the considerable reduction in the amount of the ascites after aspiration of fluid from the chest. This seemed to indicate that there must be a fairly wide communication between these two cavities to allow so rapid a passage of such a large quantity of fluid. The presence of a persistent pleuro-peritoneal canal seemed to explain the features of this case most satisfactorily.

Meigs rejected his original suggestion that the right hydrothorax was due to lack of drainage by the azygos vein. He believed that a persistent pleuro-peritoneal canal was usually incompatible with life, and finally concluded that the fluid found its way through a lymphatic pathway in the diaphragm. This latter theory, however, would not account for the relative rarity of the occurrence of hydrothorax with ascites. Nor would it explain why the right side is favoured. It would, indeed, be reasonable to expect that a bilateral hydrothorax of some degree would occur in all cases of marked ascites.

A congenital opening, then, seemed to us to explain this syndrome most satisfactorily, and especially an opening resulting in a direct communication between the two cavities such as the persistent pleuro-peritoneal canal. Why, however, is the gap usually on the right side, while a diaphragmatic hernia through a persistent pleuro-peritoneal canal is usually on the left side? It is recognized that this type of hernia is uncommon on the right side, as the liver tends to occlude the right-sided openings. As herniation is then prevented, and as an opening on the left side usually results in a herniation incompatible with life, it is suggested that the more frequent occurrence of right-sided hydrothorax is due to lack of survival of those individuals whose persistent canal happens to be left-sided.

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