to take down everything I said and everything the man said.* Using the same technique as before, I induced a hypnoidal state in which he recapitulated the whole episode with minute detail and appropriate actions but little emotion. The verbatim account occupies 1¾ foolscap pages, and I only spoke 41 words after he began. He reproduced the conversation over the telephone, and, by an extraordinary piece of luck, Dr. Phillips had been at the other end of the telephone during the actual dive and was able to affirm the verbal accuracy of the reproduction. I think that makes the experiment unique.

" So far, then, we could assure the authorities that the manifestations were not due to any defect in their physiological theory or practice—an important matter to them. That physiologists welcomed the psychological explanation is perhaps also unique.

" It was obvious, moreover, that the presence of a minor psychosis could have been recognized beforehand in these two men. This was being wise after the event, but in the following year Dr. Phillips was still in medical charge of men selected for training in deep-diving, and decided to put his psychological experience into practice. He ' vetted ' five men and asked me to vet them independently. We both agreed that one of them might readily fall a victim to the occupational neurosis, but for various reasons decided to let him carry on. His most important symptom in my view was a phobia of horses. The result of the dive to 300 ft. is described by Dr. Phillips in a paper given to the United Services Section [18]. The man demanded to be brought up, and emerged from the chamber in a state of collapse. Dr. Phillips decided to make the man abreact the experience and the dramatic result is described in his account:

" ' With sweat like a stream of water running down a face the colour of chalk, dilated pupils and rolling eyes, he went through all the emotions of the dive, sobbing and tearing at his clothes under the impression that he was again in his diving-suit, and clawing at his face to pull off the imaginary face-glass. It was a picture of stark mad terror and the impression it left is very difficult to describe. No earthly power could then have got him near a diving-suit.

" ' The interview lasted until about 10.30 (from 9.0), and when he had " come to " again there was an immense improvement in his condition. The deep sigh which heralded in the return to external consciousness was indicative of the dam which had been loosened.'

" Such abreaction I regard as essential for the prevention of further symptoms after terrifying experiences. I have described a case [19] in which the effects of a fright during compressed-air work were ascribed to caisson disease and a severe psychoneurosis was allowed to develop which, I believe, a timely abreaction would have prevented."

The other record (Donald, 1947) tells us that " the investigations of oxygen poisoning described here were started in April, 1942, owing to the occurrence of several cases of unconsciousness in oxygen-breathing apparatus at depths and in times that were then considered to be safe." This was a restatement of the problem that had presented itself in 1930, the introduction of oxygen-breathing having made no difference to what happened. A painstaking study of the physical effects of oxygen under all sorts of conditions (time, pressure, exercise, and so on) was carried out. The symptoms, reported at length, included vertigo, nausea, and syncopal and convulsive attacks, a long paragraph being headed, "Toxic Effects of Oxygen on Brain Metabolism." No conclusion, however, was reached about why several cases of unconsciousness occurred at depths and in times then considered safe. I wrote (Culpin, 1947) suggesting that Dr. Kenneth Donald and I had been concerned in the same problem, but no discussion followed.

*Without a witness my account might have been discredited, for this procedure was then under a cloud. Now it is correct and praiseworthy, though as a propitiatory ritual the physician should put on a white coat and inject some thiopentone. Let me explain that the first diver reproduced a story I had heard so often from shell-shockers: " Then I became unconscious and I came to myself when I reached the dressing station "—or the C.C.S., or the base hospital, or wherever there was freedom from fear. This " unconsciousness " had been regarded as due to concussion and became the starting-point of the shell-shock theories, but was really the blotting out of a period of terror the memory of which could be revived by a simple technique. The diver said, " I had the feeling of closed in and went off. When I came to daylight I came to my senses." This gave me the diagnosis, which I confirmed by using the same technique as that used for the shell-shockers.

Conclusion

Common to these episodes is a particular kind of diagnostic failure. Their recurrence through the years suggests that this failure is a constant factor in medicine, and recent discussions about the prescribing of placebos show a lamentable acquiescence in it.

When I lectured to students about the psychoneuroses I found I could get them interested in psychological theory, but I assured them that, as a clinician, my aim was to enable them to elicit a patient's symptoms and recognize their significance. I had to warn them, however, that my stuff was no use for examination purposes and they had better leave it behind when they entered the examination-room.

We shall have made some progress towards remedying our failure when at a qualifying examination it becomes possible for an examiner to expect from a candidate an intelligent response to the request, " Will you please find out what neurotic symptoms that man has and tell me what you make of them ? "

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SIGNIFICANCE OF TESTICULAR EXFOLIATION IN MALE INFECUNDITY

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Infecund semen often contains numerous exfoliated testicular cells (Lane-Roberts *et al.*, 1939, 1948 ; Baker, 1939 ; Moench, 1940 ; Joël, 1942 ; Staemmler, 1942–3 ; Belonoschkin, 1949 ; and others). Incidental observations had suggested to us that exfoliation was of diagnostic significance, and special attention was therefore paid during the past six years to such cases. The present communication reviews some data and conclusions which require but simple methods for their verification and which may be of interest to the clinician.

Recognition of Exfoliated Cells

By comparing the cells in semen with biopsy and post-mortem sections most testicular cells can be readily recognized as such, provided stained semen films are examined—for example, wet films stained by the osmic-acid–Giemsa method (Lane-Roberts *et al.*, 1948). The most common cells have a single unfragmented nucleus but differ greatly in size. One type has a cell diameter of 10–15 μ, with a nuclear diameter of 8–12 μ ; the chromatin may be concentrated in a skein, the cell having preserved the appearance of the spermatocytes familiar from cross-sections through the seminiferous tubules (see Figs. 4 and 5). Other cells of this group are less well preserved and may show pyknosis and distortion of the nucleus (Fig. 3). Usually such cells can be identified as exfoliated spermatocytes. The second type of cell, which corresponds to a spermatid, is much smaller (diameter 5–10 μ) and shows less variation except with respect to the position of the nucleus, which is not infrequently found in process of being extruded.

These cells correspond essentially to normal stages in spermatogenesis, though their presence in large numbers indicates that spermatogenesis is abortive, at least in some areas of the epithelium. Of greater biological interest are other types of exfoliated testicular cells—namely, the binuclear and multinuclear cells. The binuclear cells vary greatly in size (6–25 μ) (see Fig. 1, also Lane-Roberts *et al.*, 1939, Fig. 20). In some binuclear cells the nuclei are connected by an isthmus of chromatin as if an "amitotic" division had been arrested. In others the nuclei are separated from each other while the cell body seems to have been arrested in the process of division. Also, small binucleated cells may show partial differentiation, and a series of transitional forms links them with certain duplex forms of spermatozoa—for example, double-headed sperms.

FIG. 1.*—Exfoliated testicular cells in semen. Note (*a*) large binuclear cell (near lower margin), (*b*) small binuclear cell (near left-hand margin), (*c*) large mononuclear cells (near right-hand margin), (*d*) spermatozoa, (*e*) extruded nuclei and nuclear remnants. (Dry film. ×320.)

The multinuclear cells are of varying shape and size (largest diameter 9–28 μ). The number of nuclei varies from three to nine (Figs. 2, 4, and 5). The nuclei may be well preserved, and are distinct from the fragmented nuclei seen in some degenerating epithelial cells. They clearly correspond to the giant cells found in human post-mortem testes (see Oberndorfer, 1931, and other references marked with asterisk) and also in testicular biopsies. Though sometimes mistaken for polymorphs, these cells differ from the latter in being much larger, apart from other distinguishing cytological characteristics.

The presence of binuclear cells indicates that exfoliation may not be limited to the interception of a normal process, but may involve the production of abnormal cells. Their structure reflects a disturbance which besets the cell at varying stages of division and arrests the latter. Such "antimitotic" effects probably also account for the occurrence of multinuclear cells; the alternative explanation, invoking fusion of spermatids or spermatozoa (cf. Maximow, 1899; Morgenstern, 1923; Kraus, 1928; Stieve, 1930), does not equally well account for the presence of multinuclear cells in biopsy specimens where spermatogenesis ceases at spermatocyte level.

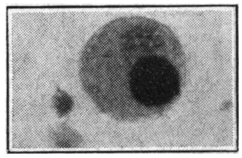

FIG. 3. — Exfoliated testicular cell in semen (large mononuclear cell with pyknotic nucleus). The adjacent spermatozoon (duplex form) lies in a different optical plane. (Wet film. ×920.)

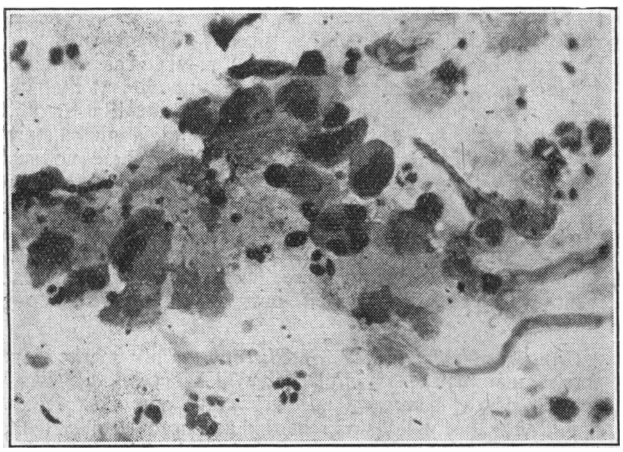

FIG. 2.—Exfoliated testicular cells in semen. Note (*a*) small binuclear cells—for example, upper left corner and near centre of upper margin; (*b*) large cell with nucleus in arrested division (near left-hand margin); (*c*) multinuclear cell (centre); (*d*) various types of large mononuclear cells; (*e*) fully differentiated spermatozoa. (Dry film. ×320.)

*Figs. 1, 2, 3, and 4 were made from a slide of a semen specimen obtained by Dr. H. G. Close. The degree and variety of exfoliation in this specimen rendered it particularly suitable for demonstration.

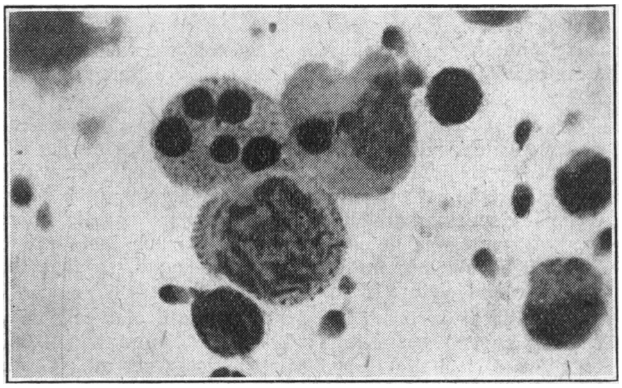

FIG. 4.—Exfoliated testicular cells. Note (*a*) partial preservation of skein in large mononuclear cell; (*b*) large binuclear cell with one pyknotic nucleus; (*c*) multinuclear cell; (*d*) differentiated spermatozoa. (Dry film. ×920.)

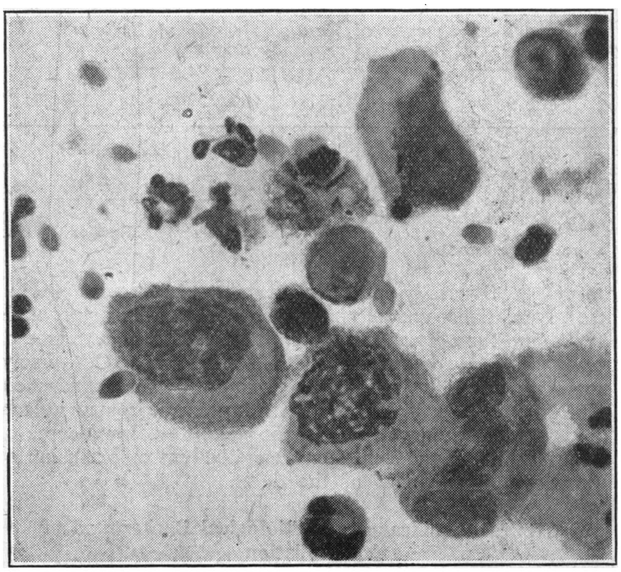

FIG. 5.—Exfoliated testicular cells in semen. Note large mononuclear cells and multinuclear cell (cf. with polymorph near lower margin). (Dry film. ×920.)

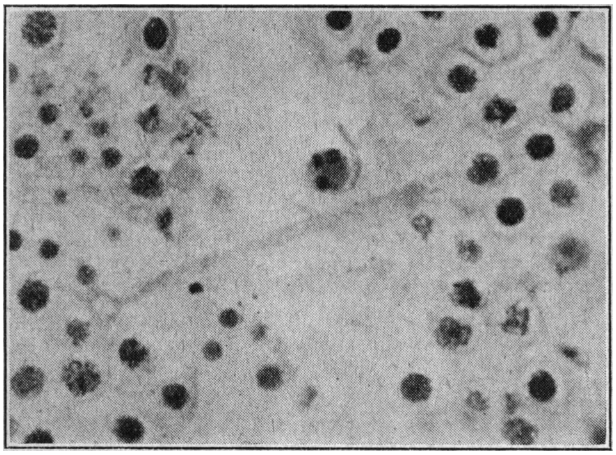

FIG. 6.—Exfoliated multinuclear cell in seminiferous tubule. (Biopsy specimen. ×560.)

Density of Exfoliated Cells

All types of cells may be present in a single specimen of semen ; more commonly one or the other type predominates. Small cells with a single nucleus and small binuclear cells are the most common forms. Their density may be estimated directly in a haemocytometer using stained semen, or, more simply, by an indirect count ; in the latter the density of spermatozoa is established first by the usual count and then the cells and spermatozoa are counted in a stained film, using a number of fields in which the cells are well separated from each other. In many cases the cells are scarce or occur in groups, and no precise count is possible.

Some testicular cells are present in virtually all specimens of semen with a density of 1,000,000 or more sperms per ml. They are sometimes present in azoospermic semen, in which they may represent the only evidence of patency of the ducts. Generally speaking, testicular cells are numerous only where spermatogenesis is in evidence ; and in such cases up to 20,000,000 cells per millilitre may be found, so that the microscopical picture is dominated by them.

For clinical purposes the density of testicular cells may be roughly graded as follows: Grade I, not more than 10,000 cells per ml. ; Grade II, 10,000–50.000 cells per ml. ; Grade III, 50,000–300,000 cells per ml. ; Grade IV, more than 300,000 cells per ml.

The relationship between testicular exfoliation and fecundity has been emphasized by Joël (1942) and others. It is further illustrated in Table I, which relates to some random

TABLE I.—*Frequency of Various Degrees of Exfoliation in Relation to Fecundity*

Character of Semen	No. of Cases	Grade I	Grade II	Grade III	Grade IV
Fecund ..	50	72%	10%	8%	10%
Subfecund* ..	37	51·4%	5·4%	24·5%	18·8%
Azoospermic ..	41	90·2%†	4·8%	4·8%	0

* For criteria of subfecundity, see text.
† In the majority of these cases no testicular cells were identified (" acytospermia ") (see text).

samples. Generally speaking, pronounced testicular exfoliation is relatively uncommon in semen of proved or probable fecundity, though we have found that even a high degree of exfoliation is compatible with fertilization. Conversely, intensive exfoliation is fairly common in subfecund men. The rarity of testicular cells in azoospermic semen reflects the most common causes of azoospermia—a low degree of proliferation of the seminiferous epithelium or occlusion or functional impairment of the ducts.

Clinical Significance and Biological Background of Exfoliation

It seemed likely that the causes of testicular exfoliation were also responsible for the associated infecundity. In considering possible endocrine causes we took into account the fact that a considerable number of subjects had received endocrine treatment—for example, serum-gonadotropin, testosterone—before the present study was undertaken, without showing significant diminution of exfoliation. It was also noted that exfoliation may be associated with the formation of numerous normal motile spermatozoa and with the production of apparently normal seminal fluid, either of which depends upon adequate secretion of testosterone. Nor is there any other evidence that exfoliation reflects specific endocrine deficiencies. Thus hypophysectomy in animals results in inactivity of the seminiferous epithelium, but not in the epithelial disorganization combined with proliferation reflected by exfoliation.

A more likely explanation suggested itself from experimental and other findings. Numerous authors have described testicular changes in animals resembling those seen in human cases of exfoliation and caused by widely different unspecific factors. Such derangement of spermatogenesis occurs in man and animals after pyrexia or experimental increase of scrotal temperature, under the influence of emotional strain, and in certain nutritional deficiencies. Again, infections, whether genital or not, ingestion of certain organic compounds, exposure to *x* rays, and severe physical trauma may produce the same condition (see references marked with a dagger). Experimental data also suggested that the damage resulting in excessive exfoliation need not be permanent and that recovery of the epithelium with increased fecundity may occur when the noxa has been eliminated.

Clinical observations also suggested a corresponding approach to the problem of exfoliation in human subjects. Several highly fecund subjects submitted specimens of semen at intervals during the last eight years. In these, exfoliation was normally limited to a few cells or was virtually in abeyance. But in three of these subjects pronounced exfoliation occurred during transitory illness, only to disappear spontaneously within two to three months. The role of unspecific noxae in the causation of exfoliation was further borne out by observations in infecund men in whom infective or toxic conditions were present.

In the past six years nearly 200 cases of infecundity combined with exfoliation were investigated and where possible treated. The primary investigation involved the usual semen, post-coital, and invasion tests. The following characteristics, occurring singly or in conjunction, were regarded as signs of lowered fecundity: (*a*) oligozoospermia (fewer than 15,000,000 per ml. seminal fluid) ; (*b*) asthenozoospermia ; (*c*) gravely impaired invasive capacity as shown with ovulatory invadable mucus ; and (*d*) pyospermia or severe and rapid agglutination of spermatozoa. High frequency of abnormal head forms was not by itself regarded as a criterion for inclusion in the group. Where routine clinical examination suggested possible sources of toxic absorption or other potential testicular noxae—for example, metabolic disturbances—treatment for these was advised. Where no such likely cause presented itself the patient was referred for more specific investigation, and treatment was advised in the light of the results. Where extended search failed to reveal any definite abnormality, treatment was either abandoned or some purely tentative measures were undertaken. Treatment was generally carried out by the patient's own doctor.

Criteria of Effectiveness of Therapy.—Only marked and persistent reduction of exfoliation which necessitated classification of the semen in a lower grade was regarded as significant. Fecundity was regarded as improved only if the stigmata mentioned above were eliminated. The occurrence of conception alone was not regarded as evidence of adequate response, since even severe infecundity occasionally permits of fertilization. Many subjects display a comprehensible but annoying disinclination towards further investigation once conception has occurred.

The results of treatment varied widely, as illustrated by abstracts from case histories.

Case 1, Showing Response to Treatment

Subject aged 32, married seven years; wife aged 30. No contraceptives used. No conception. Effective duration of marriage reduced to about two years through war service. Patient was prisoner of war for three years.

First specimen of semen: volume 2.5 ml.; density, 3,000,000 spermatozoa per ml.; about 27% severely abnormal head forms, including 7% duplex forms; initial motility, 35% (paraffin film); viability, 2% survival six hours after emission, room temperature. Exfoliation of testicular cells marked (Grade III); mostly small mononuclear, with some binuclear cells. No polymorphs. In the following three months second and third specimens showed similar findings, with invasive capacity gravely impaired. Sims post-coital test: cervical invasion virtually absent.

Clinical findings: tall, asthenic man with history of furunculosis (generalized boils) of three years' duration. No other abnormalities. Bacteriological findings (semen, urine, throat): no pathogens recovered.

Advised to have (as a first step) treatment for furunculosis. Responded well to treatment.

Two months later, before other measures could even be considered, the wife's menstrual period was overdue, the temperature level luteal, and the pregnancy test positive. The semen then showed a volume of 1.8 ml.; approximately 4,000,000 per ml., with high initial motility. Viability: about 20% motile six hours after emission. Exfoliated cells virtually absent. Considerable gain in weight. No skin complaint.

The pregnancy went to term. No relapse occurred in the subject's condition during the next two years. The child is healthy and a second pregnancy has now gone to term.

Case 2, Illustrating Absence of Response

An accountant aged 49, married 13½ years, wife aged 38. No conception. A semen test two years previously by another investigator showed 29% abnormal head forms and poor motility, many testicular cells and pyospermia, and 17,000,000 spermatozoa per ml. He was then given testosterone, also by another physician. A repeat test by the same investigator ten months later showed no definite changes. He was then given a course of penicillin (no cultures taken), again without seminal response. He was then seen by one of us (M. B.) and the semen was found to be subfecund—21,000,000 spermatozoa per ml. Motility after three hours, 21%. There was unusually heavy exfoliation of testicular cells (Grade IV), with predominance of spermatocytes in arrested division, also some prostatic cells and pus cells in large numbers (pyospermia). A semen inoculum on blood agar showed a moderate growth of *Bact. coli.*

Clinical findings: normal build; very pallid complexion. No abnormalities found. No relevant history. He received a course of sulphadiazine, and simultaneously his wife was treated for an infected cervix with impaired invadability. There was no significant change in the semen after the course of sulphadiazine; but conception took place, with spontaneous miscarriage in the seventh week of gestation. Without further treatment a second conception occurred during the first cycle following upon abortion. However, abortion took place again at six weeks. The semen at that time still showed excessive exfoliation (Grade IV). The cells were mostly well-preserved spermatocytes and other mononuclear cells, including spermatids with abortive differentiation. Several million spermatozoa were found, but no precise count could be made because of aggregated testicular cells. A few polymorphs only were present. A semen inoculum (blood agar) remained sterile.

The patient was now given a course of cacodylate, advised on dietary measures, and seen again after a holiday abroad. A semen test two months later showed about 10,000,000 spermatozoa per ml., high viability, approximately 6,000,000 cells per ml. (50% large mononuclears, 12% small mononuclears, 20% large and small binuclear cells, the remainder intermediate forms); 30% of the heads of the differentiated spermatozoa were abnormal. In view of this persistent exfoliation the patient was referred to hospital for full examination (by Dr. P. E. Thompson Hancock). Exhaustive search failed to reveal any abnormality except severe bacilluria (*Bact. coli*). No symptoms. A course of mandelamine was given. Two months later a repeat urine culture remained sterile and the urine was normal. A semen test after a further four weeks showed about 7,000,000 spermatozoa per ml. with high initial motility and high viability, few abnormal forms, but persisting exfoliation of Grade IV with predominance of mononuclear cells. No further tests could be made until four months later, the wife having had further treatment in the meantime. On this occasion the high viability combined with oligozoospermia was noted again, but there were about 20,000,000 cells per ml., including numerous polymorphs (about 38% large mononuclear cells, 11% small mononuclears, 7% large binuclears, 11% small binuclears, 19% multinuclears, and 15% polymorphs). At this time the wife suffered a relapse of cervical infection and had a further course of antibiotics, but in view of the husband's seminal condition and the likelihood of repeated abortion the couple were advised to discontinue specific treatment to procure conception. Eighteen months later no further conception was reported.

Summary of Results

In about three-quarters of our cases definite pathological conditions were detected, though they were not always reflected by subjective complaints and were often of the "subclinical" type. Most commonly they were seemingly localized infective conditions such as bacilluria or chronic sinusitis.

Effective attention to such conditions resulted in reduced exfoliation and improved fecundity in about one-third of the cases.

On the other hand no potential noxa was discovered during the period of investigation in about one-quarter of the cases. In some of the latter purely empirical and tentative measures such as dietary correction were followed by response, possibly reflecting an improvement in general health.

We satisfied ourselves that specific hormone therapy should always be postponed until exfoliation has at least begun to decrease and that premature efforts to increase invasive power and viability of spermatozoa by such means are likely to fail.

The results are illustrated in greater detail in Tables II and III, which relate to 50 successive cases.

TABLE II.—*Clinical Rating of Cases in Relation to Effect of Treatment*

	Total No.	Exfoliation after Treatment		
		Significantly Reduced	Not Significantly Affected	Increased
Systemic abnormalities detected (Group A):				
Group A as a whole ..	38 (76%)	21 (42%)	14 (28%)	3 (6%)
Group A, fecundity improved .	15	12 (24%)	3 (6%)	0 (0%)
Group A, fecundity not improved	23	9 (18%)	11 (22%)	3 (6%)
Systemic abnormalities not detected (Group B):				
Group B as a whole ..	12 (24%)	3 (6%)	8 (16%)	1 (2%)
Group B, fecundity improved	3	2 (4%)	1 (2%)	0 (0%)
Group B, fecundity not improved	9	1 (2%)	7 (14%)	1 (2%)

TABLE III.—*Summary of Table II*

	Exfoliation Significantly Reduced	Exfoliation Not Reduced
Fecundity improved ..	14	4
,, not improved ..	10	22

Control Data.—Exfoliation, though occasionally of a temporary nature, usually persists in untreated cases. Twelve of the subjects included in the present series had been infecund for fairly long periods before the present study began; during this period semen tests were carried out, and in some instances endocrine treatment was given; yet the condition of the semen remained virtually unchanged, exfoliation persisting. Positive responses were observed in seven of these men.

Conclusions and Comments

1. The present findings support the view that the pathological process of excessive testicular exfoliation commonly reflects a systemic "load." This conclusion is not invalidated by the failure to identify the causative noxa in any one case, for clinical and biological investigation is necessarily limited by available methods and by circumstances. Furthermore, some testicular noxae—for example, vitamin-E deficiency (Mason, 1933)—produce irreversible changes and may no longer be discoverable at the time of investigation. The demonstration of systemic noxae does not exclude purely local factors—for example, local effect of heat.

2. Since there is little doubt that testicular "sloughing" is commonly associated with infecundity special attention should be paid to the presence of testicular cells in the semen. This applies even to specimens where other general features indicate fecundity; for it is our impression that exfoliation in such cases may presage decline in other respects—for example, fall in the spermatozoa count. But semen analysis cannot determine the line of treatment to be pursued, and the therapeutic advice which in recent years has often been expected from the "seminologist" properly belongs to the physician.

3. Most experiments with antimitotic agents have been concerned with the effect of *exogenous* mitotic poisons—for example, stilboestrol, benzoquinone, benzene—upon embryonic tissues, meristem, bone marrow, and other rapidly proliferating cell systems (cf. Toeppner, 1941; Lehmann, 1947). It is therefore of some interest that the seminiferous epithelium may also reflect the antimitotic action of *endogenous* factors. Its reaction resembles that of the bone marrow, which, under the influence of certain antimitotic agents and in disease, produces cells bearing a striking resemblance to binuclear and multinuclear testicular cells—cf. illustrations given by Leitner (1949) and by Schleip and Alder (1928).

4. Lastly the antimitotic nature of some testicular noxae suggests certain tentative conclusions which, though theoretical, deserve to be mentioned. The exposure of the testis of the mouse to *x* rays at certain antimitotic dosage levels has a twofold effect upon fertility. First, ova fertilized by males soon after irradiation—that is, by spermatozoa which were hit by *x* rays—show low viability and the number of young produced is abnormally small. Secondly, this infertility or "reduced prolificacy" (Tyler and Chapman, 1948) is transmitted to the surviving offspring, so that a hereditary and dominant form of infecundity is produced. Irradiated mice may regain full fertility, with normal prolificacy in their offspring, if allowed a period of recovery during which the seminiferous epithelium can regenerate from unaffected spermatogonia (Hertwig, 1938).

It is as yet uncertain whether other antimitotic agents, such as those which are involved in exfoliation in our cases, may produce a similar effect upon prolificacy. But the possibility must be borne in mind and requires further investigation, *particularly since the histological pictures in the testis of the mouse after irradiation and that in the human testis in severe exfoliation from other causes* are in some respects very similar. Furthermore, we have some evidence of the reduced viability of human zygotes produced from semen showing severe exfoliation (high incidence of miscarriage). Until further information is available it might be wise to advise against attempts to procure conception from men with signs of severe and unrelenting antimitotic effects.

Summary

Persistent exfoliation of testicular cells, including abnormal cell forms, is often associated with infecundity, though it is compatible with the occurrence of fertilization. It does not respond to specific endocrine measures, but does respond in a significant proportion of cases to the treatment of associated systemic conditions such as metabolic disturbances or infective states.

Reduction of exfoliation is often accompanied by an increase in fecundity.

Some exfoliated cells reflect disturbances of cell division, and it is concluded that endogenous as well as exogenous factors may act as antimitotic agents and possibly produce genetic changes.

It is suggested that in subjects in whom antimitotic effects are much in evidence attempts at reproduction might wisely be postponed in view of the possible danger of hereditary subfertility.

We wish to express our thanks to Mr. Kenneth Walker, who carried out most of the testicular biopsies referred to in this study; to Dr. R. Gottlieb for references to the haematological literature; and to Dr. H. G. Close, West Hill Hospital, Dartford, for lending the specimen used for Figs. 1, 2, 3, and 4. We are particularly indebted to Dr. R. C. Matson, Pathologist, Royal Surrey County Hospital, for carrying out numerous pathological investigations in many of the cases referred to in this communication.

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