symptoms of cortical insufficiency was rapid, and similar to that seen in cats treated with cortico-adrenal extract. The blood chemistry at this time was found to be essentially normal. The injection of progesterone was stopped 21 days after operation when both animals were in excellent condition. They subsequently succumbed, with typical symptoms of adrenal insufficiency and careful examination failed to reveal any trace of adrenal tissue.

Non-pregnant female cats, on the other hand, showed no favorable reaction to progesterone injection. All succumbed, indeed, within the usual life-span of untreated animals and with typical symptoms of adrenal insufficiency, despite increased progesterone dosage. The blood and tissues showed the usual abnormal chemical values characteristic of untreated adrenalectomized animals.

Gaunt[8] has shown that in the ferret the symptoms of adrenal insufficiency are accentuated by the injection of estrone. The possibility that the cats used in the present experiments, adrenalectomized in the spring, possessed a sufficiently high estrone content in their blood to vitiate the progesterone therapy should be considered as an explanation of the apparent sex-specificity noted herein.

One pregnant animal, restored from symptoms of adrenal insufficiency, survived 17 days during progesterone treatment. It then succumbed, however, with typical symptoms, although the dosage of progesterone was increased from 10 to 12 mg per day. The abnormally extended survival period of this animal may be accounted for on the basis of additional progesterone secretion from the corpora lutea present in its ovaries, as well as the absence of estrone. These probably favorable conditions, however, failed to maintain life indefinitely.

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Relation of Spermatogenesis to the Factor in the Testis Which Increases Tissue Permeability.

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The ability of aqueous extracts of the mammalian testis to increase the dermal spread of particulate matter has been demonstrated by

Duran-Reynals[1] and others.[2] Claude and Duran-Reynals[3] showed that extracts of other organs in the normal adult mammal also possess this ability, although to a much lesser extent, indicating that possibly this spreading capacity is primarily a property of the testis. On the other hand, a number of actively growing mammalian tumors as well as placental tissue and mammalian embryos have been found to be high in spreading factor content.[4, 5] A consideration of these facts has led Boyland and McClean[5] to suggest the possibility that the spreading factor in a property of any rapidly proliferating tissue, of which the testis is but one example.

In the hope of throwing light on this interesting question we have determined the diffusing activity of extracts of testis in which spermatogenesis was inactive. In such an experiment one is, of course, employing testis tissue, but testis tissue in which the rate of cell proliferation is quite low or absent. For our purpose the immature testis and the cryptorchid testis were chosen.

The immature testes were obtained from 18 rabbits weighing about 800 g. These testes, which weighed between 170 and 900 mg were

TABLE I.

Spread of India Ink by Aqueous Extracts of the Testes of Immature and Mature Rabbits.

Rabbit No.	Immediate cm²	1 hr cm²	4 hr cm²	24 hr cm²
	1:1 Dilution.			
1, 2, 3	3.22	9.35	15.30	18.51
4, 5, 6	3.21	6.39	8.99	12.96
7, 8, 9	3.06	7.13	9.34	13.59
10, 11, 12	3.02	6.04	8.24	11.68
Mean	3.11	6.81	8.73	13.18
Mean of controls	3.44	6.08	6.28	7.64
Mean of 20 adult testes, 1:1 dilution	*	19.27	31.39	27.68
	1:5 Dilution.			
13	3.33	6.13	9.58	4.51
14	3.27	5.72	9.53	6.37
15	3.18	6.24	8.46	4.32
16	3.09	5.68	6.65	2.84
17	2.90	6.25	6.90	3.55
18	2.58	4.97	7.61	3.87
Mean	3.16	5.92	8.65	4.65
Mean of controls	3.01	5.70	6.93	3.57
Mean of 20 adult testes, 1:5 dilution	6.13	9.34	11.89	10.68

* Spread too fast to obtain reading.

[1] Duran-Reynals, F., *Compt. rend. Soc. biol.*, 1928, **99**, 6; *J. Exp. Med.*, 1929, **50**, 327.

[2] McClean, D., *J. Path. and Bact.*, 1930, **33**, 1045; 1931, **34**, 459.

[3] Claude, A., and Duran-Reynals, F., *J. Exp. Med.*, 1934, **60**, 457.

[4] Duran-Reynals, F., and Stewart, F. W., *Am. J. Cancer*, 1931, **15**, 2790.

[5] Bayland, E., and McClean, D., *J. Path. and Bact.*, 1935, **41**, 553.

triturated separately with an abrasive. Six testes were mixed with 5 times their weight of Locke's solution and the remainder were grouped into 4 lots and mixed with an equal weight of Locke's solution. After centrifugation the supernatant fluids were mixed with equal volumes of India ink in a 1 :2 dilution with Locke's solution. The resulting mixtures were injected in 0.5 cc amounts intradermally in adult rabbits. As a control the same rabbits were also injected with India ink diluted 1 :5 with Locke's solution. For comparison 20 adult rabbit testes were tested in 1 :1 and 1 :5 dilutions. Tracings were made of the spread of the ink in the injected rabbit and the area was determined with a planimeter.

The results are shown in Table I. The immature testes contained decidedly less of the spreading factor than did the adult testes; but it is interesting that the spread obtained from the immature testes was related inversely to the weight of the testes.

Although their small size precluded histological study of the immature testes, sections of testes of rabbits of similar size revealed that the tubules were immature. Some of the cells were undergoing mitotic division but no mature sperm were being formed.

In the study of the cryptorchid testis 14 adult white rats were used. Four of these animals were bilaterally cryptorchidized and 4 were unilaterally cryptorchidized by occlusion of the internal inguinal rings with black silk sutures after elevation of the testes into the abdomen and section of the gubernaculi. These animals were killed 45 days after the operation along with 6 normal rats. A section of each testis was made for histological study. The remainder of each testis was ground and extracted with an equal weight of Locke's solution. After centrifugation the supernatant fluid was mixed with equal parts of India ink in a 1 :2 dilution, and the resultant mixture was injected in 0.5 cc volumes intradermally in rabbits. The area of the spread of the ink was ascertained as before by planimeter measurement of tracings of the area.

As shown in Table II the difference in the spread of the ink by extracts of the scrotal and the abdominal testis was quite marked, with the abdominal testis possessing approximately one-half of the spreading power of a scrotal testis. The spread by the abdominal testis of the unilateral cryptorchids was possibly significantly less than by the testis of the bilateral cryptorchids, while the scrotal testis of the unilateral cryptorchids had about the same capacity of this nature as the testis of the normal rats.

Histologically the cryptorchid testes showed the usual atrophy and hyalinization of the tubules without alteration of the intertubular elements. In our animals the atrophy was more marked in the uni-

TABLE II.
Spread of India Ink by Extracts of the Testes of Cryptorchidized and Normal Rats.

Rat No.	Immediate cm²	1 hr cm²	4 hr cm²	24 hr. cm²
	Bilateral Cryptorchids.			
1	3.40	9.10	9.07	10.19
2	3.31	10.60	13.85	15.70
3	3.13	14.58	25.96	30.46
4	2.36	8.25	16.10	16.73
Mean	3.05	10.63	16.25	18.27
	Unilateral Cryptorchids. Scrotal Testis.			
5	3.20	24.52	38.76	34.72
6	3.37	25.94	33.86	34.02
7	2.99	20.61	26.31	30.96
8	3.00	12.48	19.65	*
Mean	3.14	20.89	29.65	33.23
	Unilateral Cryptorchids. Abdominal Testis.			
5	2.99	11.76	11.74	13.39
6	1.98	6.53	6.08	8.99
7	2.81	10.55	13.00	12.74
8	2.48	8.23	13.75	14.67
Mean	2.57	7.07	11.14	11.45
	Normal Animals.			
9	2.81	17.39	20.48	20.48
10	6.62	30.79	48.87	57.40
11	6.58	19.97	30.00	36.69
12	4.42	22.53	18.74	20.12
13	4.26	25.84	34.32	38.76
14	4.25	20.73	19.06	17.92
Mean	4.82	22.88	28.58	31.89

* The spread was too diffuse to measure.

lateral cryptorchids than when both testes were abdominal. The degree of atrophy in these cases corresponds with the extent of diminution of the spreading factor. In certain instances among the bilateral cryptorchids there was a slight persistence of spermatogenesis. In all the testes the extent and amount of spermatogenesis corresponded quite closely with the amount of spread of the ink by their extracts.

These experiments show that for a testis to possess the spreading factor in large quantity the testis must be undergoing active spermatogenesis, and it is possible that complete spermatogenesis is essential. This fact was indicated by Hoffman and Duran-Reynals[6] and McClean[2] who reported, without details, that in 4 experiments the cryptorchid testis contained less than normal testicular spreading capacity. They also reported that rabbit spermatozoa from the epididymis possessed the factor.

Thus it appears that the spreading factor is probably a characteristic of rapidly proliferating tissue and its high concentration in nor-

[6] Hoffman, D. C., and Duran-Reynals, F., *J. Exp. Med.*, 1931, **53**, 387.

mal adult testis is the result of this fact. Whether this is the only factor involved, however, seems unlikely as one of us[7] has shown elsewhere that India ink spreads over a large area in castrated male rabbits than in normal males.

Summary. A study of the amount of spreading factor present in the undescended testes of young rabbits and of the cryptorchidized testes of mature rats showed that this factor was greatly reduced. From this we concluded that the spreading factor was related to spermatogenesis.

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Influence of Diet on Intoxication with Phenol and Cyanide.

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The influence of diet on resistance to disease and to various intoxications has been recently reviewed.[1, 2] The rôle of the vitamins has been extensively studied, but relatively little attention has been paid to the proportions of protein, carbohydrate and fat in the diet. From available reports it would appear that in some conditions one of these foodstuffs possesses an advantage, and in other conditions another. Many of these studies are of doubtful value since the vitamin factor was inadequately controlled. The present work was undertaken to compare the effects of diets high in protein, carbohydrate or fat on certain intoxications for which a definite detoxication mechanism is known. This report deals with 2 such poisons—phenol, which is detoxicated in part as an ethereal sulfate and in part in combination with glycuronic acid, and cyanide, which is in part detoxicated by conversion into thiocyanate.

Plan of Study Young rats from a mixed albino and hooded Norwegian colony, weighing 60 to 70 g, were placed in separate cages and given diets varying in their content of protein, carbohydrate and fat. Littermates were divided equally in the various experimental groups. After an interval varying from 10 to 24 days on the test diet they were injected subcutaneously with a 5% aqueous solution of phenol or a 0.1% solution of NaCN freshly made. The mortality

7 Sprunt, D. H., and McDearman, S., in preparation.

1 Clausen, *Physiol. Rev.*, 1934, **14**, 309.

2 Robertson, *Medicine*, 1934, **13**, 123.