planation unlikely. Also Yourga, Esselen and Fellers[2] have reported that *d*-isoascorbic acid may act as an antioxidant even for ascorbic acid, yet *d*-isoascorbic acid does not cause any potentiation of alloxan activity when administered just before the alloxan. Another possible explanation is that ascorbic acid decreases the available SH groups in the blood and thus permits more of the alloxan to reach the pancreas. Lazarow[3] has shown that administration of compounds containing the sulfhydryl group, as cysteine, reduced glutathione, and thioglycolic acid, prevent the diabetogenic action of alloxan. Prunty and Vass[4] have shown that feeding human subjects large doses of ascorbic acid decreases the amount of reduced glutathione in the red blood cells. Sulfhydryl groups are known to reduce alloxan to dialuric acid, a substance which has been reported not to possess diabetogenic action.[5]

An attempt was made in one series of animals to bind the SH groups by injecting the animals with mapharsen one minute before they received the alloxan. The animals appeared listless after the injections and almost on the verge of coma. When they moved they dragged their bodies around the cage, rubbing their bellies on the floor of the cage. This effect lasted about 3 hours. In no case did hyperglycemia develop in these animals. The dose of mapharsen given was low, but the MLD_{50} for this substance is only 16 mg per kg of body weight.

It appears most probable from these studies that the potentiation of the diabetogenic action of alloxan by ascorbic acid is due to the oxidation of SH groups in the animal and as such allows more alloxan to reach the pancreas.

Summary. Administration of ascorbic acid to rats which are given low doses of alloxan increases the diabetogenic action of the alloxan. To obtain this effect the alloxan must be given within a minute after the administration of the ascorbic acid. *d*-Isoascorbic acid, on the other hand, does not produce the potentiation of the alloxan diabetes.

2 Yourga, F. J., Esselen, W. B., and Fellers, C. R., *Ford Research*, 1944, **2**, 188.

3 Lazarow, A., PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 441.

4 Prunty, F. T. G., and Vass, C. C. N., *Biochem. J.*, 1943, **37**, 506.

5 Goldner, M. G., and Gomori, G., *Endocrinology*, 1944, **35**, 241.

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Primary Herpetic Vulvovaginitis.

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The varied pattern of clinical disease that may be produced by the agent of the common fever blister is gradually becoming apparent. There have been identified, due to herpes simplex virus, stomatitis and pharyngitis,[1-3] a varicelliform eruption,[4-7] encephalomyelitis,[8-10] and keratitis.[11,12] In

1 Youmans, J. B., *South. Med. J.*, 1932, **25**, 228.

2 Long, P. H., *J. Clin. Invest.*, 1933, **12**, 1119.

3 Dodd, K., Johnston, L. M., and Buddingh, G. J., *J. Pediat.*, 1938, **12**, 95.

4 King, A. D., *Arch. Dermat. and Syph.*, 1939, **39**, 1035.

5 Wenner, H. A., *Am. J. Dis. Child.*, 1944, **67**, 247.

6 Barton, R. L., and Brunsting, L. A., *Arch. Dermat. and Syph.*, 1944, **50**, 99.

7 Lynch, F. W., Evans, C. A., Bolin, V. S., and Steves, R. J., *Arch. Dermat. and Syph.*, 1945, **51**, 129.

8 Smith, M. G., Lennette, E. H., and Reames, H. R., *Am. J. Path.*, 1941, **17**, 55.

9 Armstrong, C., *Pub. Health Rep.*, 1943, **58**, 16.

10 Zarafonetis, C. J. D., Smadel, J. E., Adams, J. W., and Haymaker, W., *Am. J. Path.*, 1944, **20**, 429.

11 Grüter, W., *Munchen. med. Wchnschr.*, 1924, **71**, 1058.

12 Gallardo, E., *Arch. Ophth.*, 1943, **30**, 217.

TABLE I.
Isolation and Passage of Herpes Simplex Virus from 3 Cases of Primary Vulvovaginitis.

Patient	Source of virus	First rabbit passage. Corneal inoculation	Second rabbit passage Corneal inoculation*	No. passages intracerebrally in mice
B.H.	Vagina	Keratoconjunctivitis Death from encephalitis Herpetic inclusion bodies in brain	Numerous herpetic inclusion bodies in corneal epithelium	20
L.H.	"	"	"	20
F.E.	"	Keratoconjunctivitis No further illness Survived	"	19
	Pharynx	"	"	1

* Each animal killed 30 hr after inoculation and cornea examined for inclusion bodies.

TABLE II.
Development of Antibodies for Homologous and HF Strains of Virus Following Primary Herpetic Vulvovaginitis.

	Neutralizing capacity of patient's serum					
	B.H.		L.H.		F.E.	
Strain of virus	A*	C†	A	C	A	C
Homologous	0	6,500	10	1,000	0	160
HF	0	3,000	ND‡	20	0	250

* A—Acute phase serum.
† C—Convalescent phase serum.
‡ ND—Test not performed.

some instances, sufficient evidence has been reported to permit designation of each of these diseases as primary herpetic infections. The evidence upon which rests the case for their primary nature consists of studies of specific antibodies. The finding that human serum sampled at random contains either no antibodies against herpes virus or a high titer[13] has been interpreted to mean that, once infection occurs, the virus persists indefinitely in the tissues. It follows that isolation of herpes virus from lesions of individuals who possess no antibodies against it but who, during convalescence, develop such antibodies, can be accepted as probable evidence of the primary nature of herpetic infection.

The present report describes 3 cases of vulvovaginitis due to herpes virus, proven by isolation of the virus and demonstration of a rising titer of circulating antibodies. These cases are believed to represent the first description of primary vulvovaginitis due to the virus of herpes simplex.

[13] Burnet, F. M., and Lush, D., *J. Path. and Bact.*, 1939, **48**, 275.

The clinical picture of the primary disease is distinctive. In each of the 3 patients, it consisted of superficial erosions involving considerable areas of the labia minora, adjacent labia majora, and vaginal mucous membrane. The ulcers were tender and usually covered by greyish-yellow membrane. Some of the lesions apparently were autoinoculated for, in every case, opposing surfaces of skin or mucous membrane showed ulcers that obviously had arisen as a result of contiguity. The patients suffered discomfort for a week or longer. The lesions healed without scarification. To date, there has been recurrence in one patient. The recurrent lesion did not resemble that seen initially, but took the form of a cluster of vesicles upon the skin of the labia minora and majora.

As may be seen in Table I, the strains of virus from 2 patients, B.H. and L.H., produced fatal encephalitis in rabbits on first passage. Membranous pharyngitis and vaginitis developed in patient F.E. within 24 hours. Both strains of virus, isolated on successive days, were not encephalitogenic

when inoculated upon the rabbit cornea and were immunologically identical. All the strains were productive of "Type A," intranuclear inclusion bodies within epithelial cells of the rabbit cornea (Table I). Cultures of the vaginal ulcers of each case, including attempts to isolate *Corynebacterium diphtheriae,* were not of significance. Dark-ground examinations of the scrapings from the lesions and repeated serological tests revealed no evidence of syphilis.

The neutralizing power of undiluted, acute and convalescent phase serums from each patient was determined against decimal dilutions of both the homologous virus and of the HF strain of herpes virus.[14] Each mixture of serum and virus was tested for neutralization in 3 mice, the test carried out with the acute phase serum serving as a control. A summary of the results is given in Table II. The neutralizing capacity of the serums was computed by subtracting the logarithm of LD_{50} of virus plus patient's serum from the logarithm of LD_{50} of virus plus normal rabbit serum. It is apparent that the results of investigation of the 3 cases fulfill the criteria for identification of a primary infection due to herpes virus, as set forth in the introduction to the present report. The similarity and clinically distinctive nature of the cases support this conclusion. It may also be seen in Table II that there is probably no significant difference in the degree to which convalescent serums of patients B.H. and F.E. neutralized both the homologous and HF viruses. However, as tested against convalescent serum of LH, the LH and HF strains appear to be significantly different. Further evidence bearing upon this dissimilarity is contained in an accompanying report.[15]

That herpes progenitalis is essentially a venereal disease[16-18] has attracted little attention in recent years. The husband of patient L.H. had an evanescent, penile sore a few days before his wife became ill. His serum, obtained during the early stages of his wife's illness and again several months later, displayed, on both occasions, a high titer of antibodies against the LH virus. This finding suggests that the husband's infection was of long standing and that conjugal transmission coincided with its recrudescence.

Summary. Primary, herpetic vulvovaginitis may be a clinically distinctive disease. Isolation of the virus from 3 cases and immunological data establishing the probable primary nature of the infection in each have been presented.

[14] Flexner, S., and Amoss, H. L., *J. Exp. Med.*, 1925, **41**, 233.

[15] Slavin, H. B., and Gavett, E., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 346.

[16] Unna, P. G., *J. Venereal and Cut. Dis.*, 1883, **1**, 321.

[17] Hruszek, H., *Dermat. Wchnschr.*, 1937, **105**, 1150.

[18] Sharlit, H., *Arch. Dermat. and Syph.*, 1940, **42**, 933.

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Antigenic Dissimilarity between Strains of Herpes Simplex Virus.

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In the course of experiments with the virus of herpes simplex, several strains were compared by means of neutralization tests. A significant antigenic difference between some of the strains was demonstrated.

The antiserum used in all the neutralization tests included in the present report represented a pool of single bleedings of each of 2 rabbits, previously infected with one of the strains under consideration. These ani-