him, he noticed that the rims of the spectacles were beginning to tarnish and a week later the eruption appeared on his face. This disappeared completely in three or four weeks after he discontinued the use of the white gold frames. When seen a year later, the eruption had not recurred.

The patient had also worn a nickel-plated wrist watch for the first time in his life during the past ten months. At the

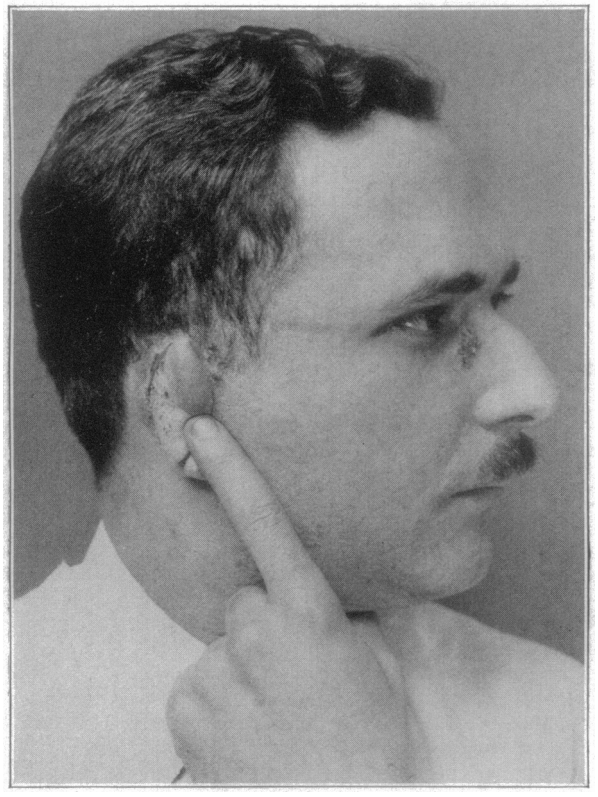


Fig. 1.—Dermatitis due to spectacle frames of "white gold."

end of four or five months an eruption appeared on the back of the right wrist, and the patient noticed that a good deal of the nickel plate had become worn. He discontinued wearing the watch and the eruption promptly disappeared. One month later he again wore the watch on the back of the wrist and for the second time an eruption appeared in this locality. He

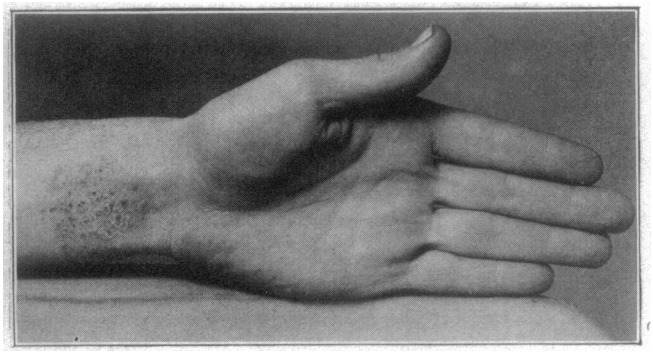


Fig. 2.—Dermatitis due to nickel-plated wrist watch.

changed the watch to the front of the wrist and this was also followed by an eruption confined to the area where the watch had been in contact with the skin. He stopped wearing the watch entirely, but since that time (three months) the eruption had persisted on both the back and the front of the wrist. He was given three fractional doses of unfiltered x-rays at weekly intervals with moderate improvement. He then disappeared from observation but when seen a year later (April 12, 1933) he stated that the eruption on the left wrist had disappeared one week or so after the last x-ray treatment and had not recurred.

It is well known that certain individuals are sensitive to nickel and after sufficient contact with this metal develop a dermatitis. This case is plainly one of contact dermatitis in such a person, as the eruption appeared at points of contact, disappeared on removal of the causative agent, and reappeared on subsequent contact. The persistence of the patches on the wrist simply indicated the high degree of sensitivity which repeated contact had produced.

140 East Fifty-Fourth Street.

RESORCIN ANAL DERMATITIS DUE TO RESORCIN IN ANUSOL SUPPOSITORIES

JAMES H. MITCHELL, M.D., CHICAGO

Resorcin sensitization is encountered from time to time in dermatologic practice. What the percentage of sensitized individuals may be is unknown at present. Urbach [1] says that only one person in several thousand will be found sensitized, and Nathan and Stern [2] state that cases of resorcin sensitization are rare.

Resorcin (metadihydroxybenzene) is an ingredient of many hair lotions sold in the shops and used by hair dressers and barbers. Examination of the prescription files of a pharmacy doing a large prescription business discloses that many prescriptions for resorcin are filled daily and that resorcin is prescribed

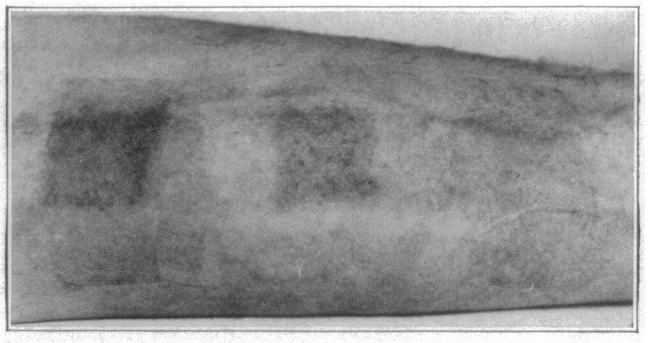
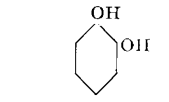
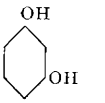


Fig. 1 (case 1).—Positive patch tests, from left to right: 1. Pyrocatechin (orthodihydroxybenzene) (twenty-four hour patch test). 2. Anusol suppository—resorcin (metadihydroxybenzene) (two weeks after twenty-four hour patch test). 3. Hexylresorcinol (alkyl resorcin).



Orthodihydroxybenzene



Metadihydroxybenzene

about four times more frequently than is monoresorcinol acetate (introduced as Euresol).

An informal inquiry of some of the druggists doing a large volume of business in the Chicago loop district indicates that the sale of Anusol suppositories is heavy. No one interviewed, however, had had any complaint of irritation set up by the use of these suppositories. A report of two cases of severe dermatitis occurring in resorcin sensitized individuals as the result of the use of these suppositories, therefore, may be of interest. One of these cases was demonstrated at the April meeting of the Chicago Dermatological Society, and photographs of the patch tests in both cases were shown at this session of the society.

CASE 1.—A physician developed a mild hemorrhoid in September, 1932. Never before having had occasion to use or prescribe anal suppositories, he had an ample accumulation of Anusol samples in the office. Curiosity as to the possible effect of anal suppositories on hemorrhoids led him to test the efficacy of the generous supply of samples. The suppositories were

1. Urbach, E.: Arch. f. Dermat. u. Syph. **148:** 146, 1924.
2. Nathan, E., and Stern, F.: Dermat. Wchnschr. **91:** 1471 (Oct. 4) 1930.

used as directed for three days. At the end of that time the itching and burning had become almost intolerable, but the hemorrhoid remained unchanged. The suppositories were discontinued, petrolatum was applied freely and, in the course of two weeks, the discomfort gradually disappeared.

A twenty-four hour patch test of the suppository on the arm resulted in a severe reaction, which lasted for three weeks.

Fig. 2 (case 2).—Positive patch test with Anusol suppository after twenty-four hours (metadihydroxybenzene).

When a medical student, the patient had discovered, as a result of application of resorcin to the scalp, that he was highly sensitized to this drug. A patch test with hydroquinone (paradihydroxybenzene) gave a slightly less sharp reaction. A patch test with pyrocatechin (orthodihydroxybenzene) gave a sharp reaction but was perhaps slightly less than that of hydroquinone. A test with monoresorcinol acetate was about equal to that of hydroquinone. A patch test with hexylresorcinol gave a very slight but definitely positive reaction. A patch test with plain cacao butter was completely negative.

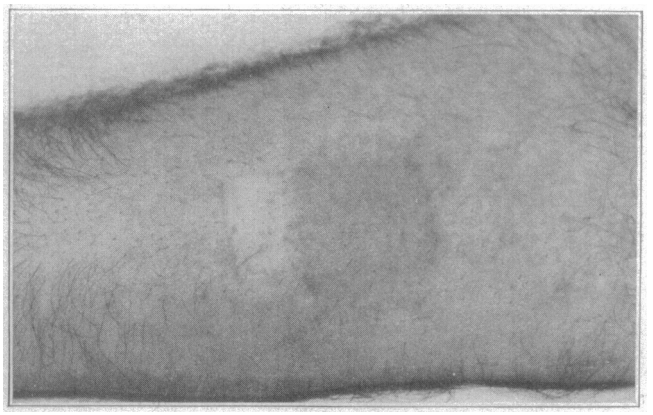


Fig. 3 (case 2).—Positive patch test with 0.4 per cent solution of resorcin after twenty-four hours (metadihydroxybenzene).

CASE 2.—A man, a cosmetic manufacturer, was first seen in January, 1927, with a severe dermatitis about the anal region. He had consulted his family physician for a hemorrhoid. There had been no itching. He was referred to a dermatologist who instructed him to break an Anusol suppository into two parts, one of which was to be inserted and the other to be rubbed about the anal region. A severe pruritus developed. He deserted the dermatologist and consulted a proctologist, who discontinued the suppositories but added other irritants. At the height of the dermatitis the patient was seen by me. A treatment dermatitis was obvious but sensitization to the resorcin in Anusol suppositories was not suspected. The patient was given radiotherapy and soothing application, with complete recovery.

In April, 1927, the patient was again seen with a mild dermatitis as a result of the appearance of a hemorrhoid and the use of one Anusol suppository. The suppository was still not incriminated, but never having prescribed suppositories I discontinued them. The patient was not seen again until April 1, 1933, when he appeared with an area of dermatitis the size of his palm about the anal region. He stated that another hemorrhoid had developed and that he had applied and inserted the Anusol suppository as directed by the dermatologist in 1927. A patch test with an Anusol suppository gave a violent reaction. A patch test with resorcin gave a similar reaction. Patch tests with hydroquinone (paradihydroxybenzene) and with pyrocatechin (orthodihydroxybenzene) were exactly similar to those in case 1. The anal dermatitis subsided with soothing applications and discontinuance of the suppository.

Presence of resorcin in Anusol suppositories was readily determined by applying the United States Pharmacopeial tests as follows: Two suppositories were dropped in 10 cc. of boiling distilled water. The fat was filtered out through paper; the resulting clear liquid was tested as follows: a few cubic centimeters were mixed in a test tube with 10 cc. of sodium

Fig. 4 (case 2).—Positive forty hour patch test with pyrocatechin (orthodihydroxybenzene).

hydroxide test solution and a drop of chloroform added. Heating the solution resulted in an intense crimson solution. The same test carried out with a 1 per cent solution of resorcin gave a similar result. Tests carried out with solution of hydroquinone and pyrocatechin were entirely dissimilar. A few cubic centimeters were mixed with ferric chloride test solution. A violet color resulted. Adding ammonia test solution resulted in a deep brownish yellow solution. These positive chemical tests, together with the sharply positive patch tests, occurring in a known resorcin sensitized individual and in another individual who also gave a positive resorcin test, would seem to

Fig. 5 (case 2).—Positive forty hour patch test with hydroquinone (paradihydroxybenzene). The relic of the resorcin patch test is seen higher up on the forearm.

leave little doubt as to the presence of resorcin in the suppositories.

These two cases are of interest because of the lack of agreement in the observations of Urbach and those of Nathan and Stern. Urbach found that his patient also reacted to hydroquinone and to pyrocatechin. In other words, there was a group reaction to the isomers of resorcin. Moreover, internal administration of the drug caused a violent generalized erup-

tion. Gradually increasing doses of the drug, however, resulted in desensitization. Nathan and Stern, on the contrary, state that their patient did not react to hydroquinone and to pyrocatechin. Their patient, however, did react to the monomethylether of resorcin but not to the dimethylether. Their patient, therefore, did not react to the isomers but did react to some of the derivatives of resorcin.

CONCLUSIONS

1. Two cases of severe resorcin anal dermatitis resulted from the use of Anusol suppositories.

2. The rarity of such cases seems to be indicated by the few references in the literature to resorcin dermatitis and to the absence of reference to cases of dermatitis due to this drug when used in suppositories.

3. My observations agree with those of Urbach and are contrary to those of Nathan and Stern as regards the reaction of resorcin sensitized individuals to the isomers of resorcin.

25 East Washington Street.

Special Article

LYMPHOGRANULOMA INGUINALE, THE FOURTH VENEREAL DISEASE

ITS RELATION TO STRICTURE OF THE RECTUM

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CLEVELAND

A disease known as climatic bubo has been, in part at least, recognized for the past seventy-five years. It was supposedly tropical in character, running a very chronic course with more or less suppuration of the affected inguinal lymph nodes. It was supposed to follow venereal exposure, especially to Negro women. The lymph node symptoms did not show up, as a rule, until an entrance for the infective agent was no more to be found. The cause was unknown. As long ago as 1865, the French clinician Trousseau [1] gave a very good description of it:

> I must not forget to say a few words about a lymph node infection which I have often observed in the young Creoles, and more particularly in the Creoles of Réunion and Maurice. . . . In adolescence, and more in the boys, we see the superficial and deep nodes in the groin swell up on one or both sides. Symptoms of the disease come on in cycles lasting one, two or three months, and separated by intervals, it may be, of several months. Then comes a violent paroxysm and several of the nodes suppurate. In certain of the cases the suppuration extends to several of the nodes or to the entire mass. The patient is thus bedridden for a long time and the suppuration may last for a year. . . . In most of the cases the disease comes in the virile years.

Scheube,[2] in 1867, while independently writing of this trouble as seen in Japan, gave it the name "climatic bubo." Jouet,[3] in 1882, in Indo-China, described a suppurating bubo not accompanied by a portal of entry. Peculiarly enough, H. G. Klotz,[2] in 1890, reported that in a period of ten years' hospital practice in New York he had seen 120 cases of "strumous bubo," most of them coming in the summertime. He felt that they had no relation to syphilis, though he had often noted the concomitant appearance of an erosion, of a small sore, or of herpetiform lesions of the genitalia. He found that the lymph nodes in the groin were filled with miliary pus foci, and he was astonished that so little was said about them in the literature.

Subsequent reports have been made on this disease by various writers, including Müller and Justi [4] who, in 1914, reviewed the entire condition. In the United States various naval medical officers have, from time to time, written on the subject of tropical bubo.[5] Hansmann [6] recently reported several cases, using the term "nontuberculous lymphadenitis." Later Barber and Coogle used the same term in reporting cases. It remained, however, for Nicolas, Favre and Durand [7] to describe fully and interpret correctly the clinical and histologic picture of this disease, which they termed "subacute inguinal lymphogranulomatosis" (lymphogranulomatose inguinale subaigue). They considered the origin venereal. They considered the small foci of suppuration disseminated throughout the parenchyma of the lymph node as very characteristic. They also noted the occasional presence of an evanescent primary lesion. These observations were amplified in 1922 by a pupil of theirs, Phylactos.[8] He pointed out that the disease was relatively common, was transferred by coitus, and had an incubation period of from ten to twenty-five days. He felt that it was an independent disease that should be differentiated from Hodgkin's disease, tuberculosis, syphilis, soft chancre and bubonic plague.

Pardo-Castello [9] in Havana, Destéfano and Vaccarezza [10] in Argentina and de Bellard [10] in Venezuela have observed cases of this syndrome. In 1925, Frei [11] reported a skin test for the disease. Since then, as the specificity of this test has been proved and as the scope of the disease has widened, interest in the whole problem has greatly increased. The result is that there has been an enormous increase in the number of reports on the condition, almost entirely from Europe and South America. The first complete report in the United States was made by DeWolf and Van Cleve [5] from our clinic in 1932. The reader is also referred to the complete monograph by Hellerström [12] and to recent complete reviews of the entire subject by Hellerström,[13] by Koch [14] and by Ravaut and Cachera.[15] A symposium on Nicolas, Durand and Favre's disease (lymphogranuloma inguinale) was held at the dermatologic clinic in Strasbourg in March, 1931, and reported in the bulletin of the French Dermatologic Society.[16]

As reports on the disease have increased, new names for the condition have multiplied. Nicolas, Durand and Favre suggested "subacute inguinal lymphogranulomatosis." Scheube named it "climatic bubo." It has also been given such names as "the fourth venereal disease,"

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Clinical lecture, read before the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 13, 1933.

The writer is indebted to the head of his staff, Dr. H. F. DeWolf, as well as to his residents, Drs. J. V. Van Cleve, Harris Connors, Bruce Palmer and Henry C. Shaw, for their enthusiastic help in the studying of these cases and in the preparation of this report.

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