We have many things to show them of which we can be justly proud. Our federal, state, municipal and other official health organizations, however, leave much to be desired, and it behooves us, in the few months still at our disposal, to prepare to show the visiting nations our methods and successes.

We need many other things, but due recognition and coordination of our federal health mechanisms is the first step, which, if we have taken it before the meeting of this international congress, will best enable us to profit by the experience of the world's experts there assembled.

Nature has been prodigal in her gifts to our nation. In no respect has she been kinder than in opportunities for health and efficiency. Her very prodigality has rendered us careless and extravagant.

It is high time that Americans do as well for themselves in health protection at home as they have done for themselves and others in Cuba, the Canal Zone, Porto Rico and the Philippines.

This demands the creation and maintenance of official organizations to amplify, extend and ultimately replace the work of our voluntary organizations whose lack of authority prevents complete success and whose continuance beyond the demonstrational stage or for other purposes than as a stimulus is an admission of American official incompetence which amounts almost to a repudiation of our belief in our own form of government.

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PICRIC ACID AND ITS SURGICAL APPLICATIONS *

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HISTORICAL REVIEW

Hausmann, in 1788, treating indigo with nitric acid, happened on a bitter yellow substance. Welter (1799) found a similar substance produced by the action of nitric acid on silk. Fourcroy and Vauquelin (1806) concluded that the two were identical, and Liebig (1827) and Wöhler (1828) established them as a definite chemical, calling it *Kohlenstickstoffsäure* (in French *acide carbazotique*). Laurent (1841) demonstrated it to be a derivative of phenol (carbolic acid).

The toxic properties of this chemical, later called "picric acid" from the Greek adjective "bitter," were investigated by Rapp and Föhr on dogs (1827). Bracnot (1830) introduced it into therapeutics in the treatment of intermittent fever. Dr. Bell of Manchester reintroduced it for the same purpose twenty years later, and it had for a time wide acceptance as a substitute for quinin, based on the clinical observations of Aspland. It came into general use in France, as well as in Germany, where it was also used and recommended as an anthelmintic. In America it was extolled by certain of the homeopathic school.

Its surgical application was suggested to Chéron (1876) by its power of coagulating albumin. Curie and Vigier (1877) recommended it for the treatment of wounds, but the drug was never properly appreciated

until Thiéry, ten years later, worked out by a protracted series of observations, the advantages of the saturated aqueous solution. He had many followers, who have spread its fame to other countries, and into other branches of medicine. His critics insisted on the danger of poisoning from absorption, but to this he had the answer that if properly used there was no danger of toxic symptoms developing, and that it had never been known to cause death even when taken internally, although five attempts at suicide by its use have been recorded.

CHEMICAL PROPERTIES

Picric acid ($C_6H_2(NO_2)_3O H$) is a trinitrophenol, and may be made by dissolving phenol crystals in strong sulphuric acid and adding nitric acid. Its crystals are small scales or elongated plates or needles, pale yellow, odorless, intensely bitter. They melt and sublime if warmed gradually, but if heated rapidly or rubbed briskly they detonate. The potassium and sodium salts are explosive.

It is soluble in alcohol (10 per cent.) and ether (20 per cent.), but only slightly in water (1.2 per cent. at room temperature). It may be purified by precipitation from a boiling solution. Its watery solution is deep yellow, having a marked affinity for animal tissues and fabrics, which gives origin to its use as a dye. Stained surgical dressings may be burned without danger of explosion. It is cheap.

Absorbed in sufficient quantity, it causes a yellow discoloration of the skin, simulating icterus, as well as of the internal organs. Large doses (dogs) cause destruction of the red corpuscles, and hemorrhage and inflammation of the kidneys and gastric and intestinal mucous membrane. It is excreted chiefly in the urine as picramic acid. About 15 grains internally will induce a yellow coloration of skin, conjunctivæ and urine in man. If it is continued the urine becomes black and there is headache, vomiting and epigastric distress. Aspland gave 1 to 4 grains three times daily for as long as nine weeks, without distressing symptoms. The discoloration disappears in two weeks after the dose is discontinued.

ANTISEPTIC PROPERTIES

Concerning its antiseptic properties I have been able to find in the literature no definite information. It has been generally recognized as a mild antiseptic; it has been recommended internally for the purpose of arresting decomposition of urine in cystitis, and it has been advocated as a disinfectant of fecal and putrid albuminous matter; being without odor, it does not mask the odors of decomposition. In order to determine at first hand its bactericidal power, the following experiments were undertaken.¹

EXPERIMENTS

The so-called rod-method was selected as being the best means of estimating the antiseptic strength of solutions used in surgical dressing. In this method the solution is tested out on bacteria which have been dried in air, in contradistinction to the drop-method, which tests the solution against bacteria in thin fluid suspension. The rod-method gives, therefore, an estimate of the power of penetration possessed by the solution, and as between the two methods it gives the slower reading.

1. The experiments were carried out at the bacteriologic laboratory of the Boston Board of Health, to the director of which I hereby express my extreme obligations. The experiments were performed with the aid and under the supervision of Dr. C. L. Overlander, instructor in theory and practice, Harvard Medical School, assistant in clinical pathology, Boston City Hospital, to whom I wish here to give grateful recognition.

* A bibliography of the subject, omitted here for lack of space, is given in the author's reprints.

A sterile saturated solution of picric acid at room temperature was employed. To serve as a control, as well as to give a basis of comparison with a commonly used antiseptic of known value, a solution of phenol in sterile water of analogous strength, namely, 1 per cent., was also employed.

As objects of the experimentation, fresh virulent cultures of *Staphylococcus aureus* and of *Bacillus pyocyaneus* were used, the staphylococcus representing the most resistant of the pus-producing organisms which the surgeon has to meet, and the pyocyaneus representing the milder secondary and saprophytic wound-infecting agents. The culture of *Staphylococcus aureus* was taken from a freshly opened breast abscess, and in order to increase its virulence was passed successively through three guinea-pigs, the last of which it killed in forty-eight hours. The pyocyaneus was taken in pure culture from an abscess in a horse, and was passed through two guinea-pigs, the second of which it killed in thirty-six hours.

The mode of procedure was as follows: Long glass rods were sterilized in test-tubes. To a twenty-four-hour growth of each of the cultures on agar a half dram of sterile water was added, and into this the growth was rubbed by a sterile platinum loop. Into these bacterial suspensions a sufficient number of the rods were dipped and placed in a frame to dry in the air at room temperature. After drying one hour, the rods were inserted into the tubes already prepared containing each about 10 c.c. of one of the sterile antiseptic solutions. After being immersed for the measured length of time, each rod was removed, rinsed off in a tube of sterile broth to wash away the excess of antiseptic, and planted on an agar slant. The broth and agar were both incubated ten days, when the final reading was taken. In case of doubt as to the identity of the growth, transfers were made to study cultural characteristics, as in this method there is considerable opportunity for contaminating organisms to enter. To guard further against error, the experiments were performed twice under identical conditions.

The accompanying table shows graphically the result of the experimentation. From it we conclude that a saturated aqueous solution of picric acid (1.2 per cent.) kills bacteria from a fresh virulent culture of *B. pyocyaneus* which have been exposed to the air for one hour, in a half minute, and bacteria from a fresh virulent culture of *Staphylococcus pyogenes aureus* in about two minutes, whereas a 1 per cent. solution of phenol under the same conditions takes about twenty minutes to kill *B. pyocyaneus*, and ninety or one hundred minutes to kill *Staphylococcus aureus*. That is to say, the picric solution may be considered about fifty times more active as an antiseptic than the 1 per cent. phenol.

CLINICAL

My first surgical application of picric acid was made five years ago as house officer in the Boston City Hospital, at the suggestion of Dr. Frederic J. Cotton. Since that time I have employed it on about 300 patients, ambulatory and bed cases, and in private practice. Never, either in infants or in adults, have I seen sufficient absorption to show in coloration of the skin or urine. I have used it with satisfaction in first, second and third-degree burns, and in fresh lacerated and granulating wounds and ulcers. It is my purpose here to describe the technic of its use, and the results of my observation of its effect, particularly in burns.

I have used practically throughout a saturated aqueous solution of the C. P. crystallized picric acid. The stronger solutions sometimes recommended in alcohol and water are momentarily extremely painful on large raw surfaces, and are of course more liable to be followed by symptoms of absorption. They have a place only in limited areas of first-degree burns and in dermatologic affections in which the skin is not broken.

The surgical employment of the acid in the form of an ointment is illogical, in so much as its so-called keratoplastic properties are interfered with by the fatty base, and the powdered crystals also should not be used because of the grave danger of absorption, and because the characteristic action is produced only by the solution.

A convenient method of preparing a sterile saturated solution is as follows:

Boil water in a flask sufficiently long to insure the sterility of the water and of the interior of the flask. While still boiling add the estimated quantity of pure picric acid crystals (12 gm. to the liter, or 1½ drams to the pint), stopper with absorbent cotton and allow to cool. Any excess of the acid will settle as a precipitate on the bottom of the flask. The contents can be kept sterile indefinitely.

MINUTES EXPOSURE	FIRST EXPERIMENT 10 DAYS INCUBATION								SECOND EXPERIMENT 10 DAYS INCUBATION							
	PICRIC 1.2%				CARBOLIC 1%				PICRIC 1.2%				CARBOLIC 1%			
	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.	PYO.	STAPH.
	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR	BROTH	AGAR
½			+	+	+	+	+	+			+	+	+	+	+	+
1			+	+	+	+	+	+			+	+	+	+	+	+
1½			+	+	+	+	+	+			+	+	+	+	+	+
2			+	+	+	+	+	+			+	+	+	+	+	+
2½			+	+	+	+	+	+			+	+	+	+	+	+
5					+	+	+	+			+	+	+	+	+	+
7½					+	+	+	+			+	+	+	+	+	+
10					+	+	+	+			+	+	+	+	+	+
12½					+	+	+	+			+	+	+	+	+	+
15					+	+	+	+			+	+	+	+	+	+
17½					+	+	+	+			+	+	+	+	+	+
20					+	+	+	+			+	+	+	+	+	+
22½					+	+	+	+			+	+	+	+	+	+
25					+	+	+	+			+	+	+	+	+	+
27½					+	+	+	+			+	+	+	+	+	+
30							+	+							+	+
35							+	+							+	+
40							+	+							+	+
45							+	+							+	+
50							+	+							+	+
55							+	+							+	+
60							+	+							+	+
70							+	+							+	+
80								+								
90															+	+
100								+							+	+

Table showing comparative antiseptic strength of a saturated aqueous solution of picric acid and of a solution of phenol of analogous dilution. The picric acid solution kills *B. pyocyaneus* and *Staphylococcus aureus* in approximately one-fiftieth the time required by the phenol.

The solution should be applied on gauze. In case of a superficial burn of hand or foot, the part may be completely immersed in the solution for some minutes and the gauze dressing then applied, covered with sheet wadding and bandaged. Waxed paper or other material to prevent evaporation and render the dressing occlusive is of no advantage except to prevent the solution from soaking through and discoloring the bandage. To avoid staining the fingers, the wet gauze may be handled with forceps, or the hands may be protected by

rubber gloves or petrolatum. Sometimes it is cleaner to apply the gauze about the part and then to moisten it by pouring the solution on the gauze directly from the bottle. Ordinarily, scrubbing the hands in soap and water immediately after contact, with or without a preceding soak in alcohol or ammonia water, readily removes all but the faintest traces of yellow discoloration.

In fresh burns of the first and second degree, or superficial lacerated wounds, no preparation is necessary if the parts are tolerably clean. If the skin is dirty it should be gently washed clean with a gauze sponge dipped in soap and water, and then rinsed off with sterile water or a weak antiseptic solution. Any blebs which have formed may be opened aseptically at their most dependent point, and the contents expressed. One dressing usually suffices in these cases, unless the lesion is extensive. If a burn has received previous treatment with ointments, or a carron oil or other emergency application, this should be carefully wiped away, so as not to interfere with the action of the picric acid.

In burns of mixed degree the same principles are to be followed, except that wherever the subcutaneous tissue is exposed, more particular care should be exercised in rendering the lesion aseptic. If a small area of third-degree burn is well cleaned up at the start and is dressed aseptically, it will granulate without pus formation and dermatize rapidly. Third-degree burns covering an extensive area should not be treated by picric acid. Ordinarily one or two dressings will suffice to heal the first and second degree elements of a mixed burn, and after that the granulating areas can receive attention.

The treatment of granulating areas, whether fresh or chronic, by picric acid is successful only in proportion as the exudation of pus can be controlled. Areas of third-degree burn may be made to heal aseptically under picric acid with an even granulating surface without exuberance or purulent discharge, which dermatizes rapidly with a smooth and supple cicatrix and very slight scar contraction, and forms an ideal base for a Reverdin graft.

A chronic ulcer may, under proper circumstances, be cleaned up and freshened so as to respond similarly to picric acid treatment. If the lack of healing depends on interference with circulation, as in varicose ulcers, the patient should be kept in bed with the part elevated. The limb and ulcer should be scrubbed with soap and water and washed off with ether and 60 per cent. alcohol; exuberant granulations should be trimmed down, and the marginal epithelium, if callous, should be lightly curetted and an aseptic picric acid dressing applied. The dressing should be changed daily, with a repetition of the cleansing, until the purulent discharge has ceased. After this, the ulcer will dermatize rapidly under dressings every three to six days.

For superficial lacerated and incised wounds and abrasions the solution acts well. Such lesions, if not too extensive, after being cleaned up with some antiseptic, may be expected to heal under one or two dressings in four to six days. Septic blebs, such as frequently occur on the hands, in paronychia, from pin-pricks, following burns and scalds which have not been attended to, and on the feet from chafing and bruising, respond readily to picric acid. If the tops are trimmed off, the pus wiped away with a cresol-soap solution and dried, one application of picric acid will usually suffice to form a new and substantial horny layer over the

denuded epithelium—unless the basal layer has been destroyed and the subcutaneous tissue exposed.

The local action of picric acid solution has been the subject of considerable speculation. Its essential action may be referred to its power of coagulating albumin. Over any clean denuded surface it forms a protective, aseptic scab, by coagulation of the secreted serum, which seals up ruptured lymph-spaces, protects exposed nerve-endings, and splints the wound in such fashion that epithelial proliferation may proceed rapidly beneath, simulating Nature's method. This artificial scab protects against infection from external sources and promotes rapid and painless epidermatization.

In burns of the first and second degree, and other superficial lesions, the original dressing may be removed after three or four days and the wound will be found healed into a flat, pliant scar. If the gauze adheres to the scab it should be moistened with picric acid to avoid pulling away the scab, which may be softened with boric ointment and removed, or allowed to remain until it comes off—unless there is suspicion that pus is imprisoned beneath. If there still remain unhealed portions the dressing should be renewed.

It is essential that the wound be clean and aseptic at the time of the first application. Pus may become confined beneath a scab, or, in a lesion of considerable size, the gauze may become adherent at the edges by inspissation of the secretion and the pus collect under tension. In either case the lesion is likely to become converted into an ulcer. In third-degree burns, when doubt exists as to the sepsis or asepsis of the lesion, it is wise to inspect the original dressing within forty-eight hours.

In comparison with other commonly used dressings for lesions of this nature, picric acid solution stands out in marked relief as the only agent actually encouraging epidermatization. Oils and greases usually employed in burns are ordinarily far from aseptic, and they tend to macerate the tissues with which they come in contact and prepare it as a suitable medium for the multiplication of the bacteria which they themselves supply. Other solutions employed for their antiseptic properties, such as phenol, corrosive sublimate and cresol-soap solution, oppose epithelial growth in proportion to their antiseptic power, by their chemical action. Picric acid, on the other hand, is distinctly keratoplastic—it is bland, unirritating, definitely antiseptic, if properly used is non-toxic, and at the same time it promotes so rapidly the formation of epidermis from the basal layers that it has been said "with it one can create epidermis at will."

Pain, which has been noted with the stronger alcoholic solutions, is rarely present when the watery solution is used. Sometimes over an area of a third-degree burn of considerable size, smarting is felt on the first application, but this is momentary and not severe, and is followed by a complete and permanent analgesia.

CONCLUSIONS

The saturated aqueous solution of picric acid is incontestably superior to any other antiseptic surgical dressing at our disposal for the treatment of superficial wounds and lesions in which the rete Malpighii of the skin is not completely destroyed—particularly in first and second degree burns. It is cheap and simple in application and induces rapid regeneration of the skin without pain or irritation. Deeper lesions may be made to heal by the formation of a smooth, level, non-secreting granu-

lating surface, over which dermatization will proceed rapidly, or which will serve as an ideal base for the reception of Reverdin or Thiersch grafts. The mild toxic symptoms which have been reported as occasionally occurring will never be seen if reasonable care is exercised.

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COLITIS *

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That there should be such a conflict of professional opinion regarding the nature and concept of colitis is perhaps not surprising when we consider its protean characteristics.

The more experience one has in dealing with these cases the more likely is he to be convinced of the futility of attributing to them either a common origin or a constant pathology. The term "colitis," as here used, is intended, therefore, to include both conditions associated with catarrhal inflammation and those in which the disturbance in colonic function is dependent on a secretory neurosis. I have excluded, however, cases of gastro-enteritis, enterocolitis, and all conditions in which the colonic involvement seemed of secondary importance, as also the acute forms of colitis.

The statistics given are based on a series of 625 cases observed during my four years' residence at French Lick Springs. All have one feature in common, *viz.*, an excess of mucus and, with few exceptions, pain and tenderness along the course of the colon. I have not attempted a further classification under the headings of colica mucosa and intestinal catarrh, for the reason that while I believe that a certain proportion of such cases, as clinically observed, may be readily recognized as belonging to one or the other of these forms, there still remains a considerable number which, either for the lack of sufficient data or because of the coexistence of certain features supposedly characteristic of each of these types, cannot be thus differentiated with certainty.

ETIOLOGY

From the standpoint of etiology, neurotic influences, both hereditary and acquired, undoubtedly play an important rôle, for, with few exceptions, the evidences of a neurosis are present, yet I am by no means convinced that such influences are necessarily primary. Not a few of these cases have apparently had their origin in an intestinal catarrh occurring in early childhood, although the symptoms present have exactly corresponded to the classic descriptions of colica-mucosa. On the other hand, I believe that there are many which in their inception are simple secretory neuroses, are at a later period complicated by a catarrhal inflammation, the result either of fecal retention or of measures employed for its relief.

Of the patients whose cases are included in this report, forty-four were under 20 years of age, the youngest 3. Fifty-six were over 50, the oldest 78. The greatest number were between the ages of 30 and 40 years. The duration of the disease has varied from three months to twenty years, usually from two to six years.

SYMPTOMS

In 87 per cent. the symptoms first observed were those of a disturbance of digestive function; in some it was attributed to the stomach, more often to the intestinal tract, particularly the colon. Fifty-four per cent. gave a history of constipation; in a majority of the cases, of the spastic variety. In 15 per cent. diarrhea was present more or less constantly, the number of stools varying, as a rule, from two to five daily. Frequently constipation alternated with diarrhea; in a few the stools were apparently normal.

Mucus, as has been stated, was present in all cases in appreciable amounts. In 36 per cent. it existed in the form of casts or tenacious inspissated shreds, showing evidences of pressure and retention. In the remainder, it was found in the form of small flakes more or less mixed with fecal deposit or in gelatinous masses sometimes passed alone. The appearance of the mucus was, however, most variable, not only in different cases, but in the same case at different times, so that very often it was without special diagnostic significance.

Colic was a prominent feature. In only 15 per cent. was this symptom entirely absent. In 35 per cent. it was described as slight or moderate in degree and in the remainder as at times severe. Neurotic tendencies, sometimes of the most manifold nature, were exceedingly common, as were also autotoxic symptoms.

Physical examination showed gastroptosis in 17 per cent. of the cases and enteroptosis in 24 per cent. The right kidney was palpable in eighty-four cases, the left alone in nine, and both kidneys in fourteen. Tenderness over the course of some portion of the colon was present in about 90 per cent. of the cases. Most commonly it was over the sigmoid flexure. Next in point of frequency was the cecum and then the transverse colon. Very often it included both the ascending and descending colon and in about 15 per cent. it was quite general.

Urinalysis showed indican in excess in 34 per cent. and urates in 27 per cent. Oxaluria was present in 19 per cent. and phosphaturia in 23. Other abnormalities of renal function were probably not more common than might be expected in a like number of cases of other diseases.

Among the other symptoms observed, that which was most frequently complained of was a disagreeable sensation in the abdomen, hardly amounting to actual pain and usually referred to the region of the descending colon or sigmoid. Gastric distention, eructations, burning, regurgitation, coated tongue, and a bad taste were common symptoms; nausea less so. Cardiac palpitation, arrhythmia, intermittence of the pulse and precordial distress were often a source of much anxiety to the patient, as were also vertigo, and unusual fatigue. Insomnia, migraine, and general neuralgic pains still further added to their discomfort. Mental depression of some degree was a very constant feature, in some instances amounting almost to hypochondriasis.

Many of these phenomena were probably merely the evidences of the underlying neurosis, but most of them, I believe, were the result of auto-intoxication, as they usually disappeared or were much mitigated as soon as the disturbance of digestion was relieved.

DIAGNOSIS

The diagnosis in typical cases of colitis is not difficult, although mistakes are common, and its significance is often overlooked, even when its existence is recognized. I am sure that this is true in a considerable number of

* Read before the American Gastro-Enterological Association, St. Louis, June, 1910.