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WEYL:

THE SANITARY RELATIONS OF THE COAL-TAR COLORS

LEFFMANN

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THE

COAL-TAR COLORS

WITH

ESPECIAL REFERENCE TO THEIR INJURIOUS QUALITIES
AND THE RESTRICTION OF THEIR USE

A SANITARY AND MEDICO-LEGAL INVESTIGATION

BY

THEODORE WEYL

WITH A PREFACE BY PROFESSOR SELL

TRANSLATED WITH PERMISSION OF THE AUTHOR

BY

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TRANSLATOR'S PREFACE.

Dr. Weyl's essay which I present in English dress, came into my possession a couple of years ago, and seemed to me to be of such practical value in an important department of hygiene, that I sought permission to translate it, a request which was kindly and promptly granted by the author. The widespread employment of artificial colors in articles of food and household use and the absence of any comprehensive or even positive information in English as to their actions on the human system, will make the publication opportune.

I undertook the translation over a year ago, but the close application to my college work and to my duties as Port Physician of the Port of Philadelphia, during the last fall and winter, has caused considerable delay.

The introductory articles by Professor Sell and Dr. Weyl render an elaborate preface unnecessary, but I may speak briefly of some of the features of the essay which will be more likely to suggest themselves to an American than to a European reader.

The treatise will be found decidedly more technical than is usual in articles addressed to medical and sanitary circles in this country. I foresee that the array of formulæ and reactions, especially the ring symbols of benzene and naphthalene, may deter many from perusal of the essay, yet the essential matter is so distinctly set forth that the chemical portion may be passed by those who are unable to comprehend it. I have deferred a little of the purely theoretical discussion to the appendix; but, of course, I have not felt at liberty to omit any appreciable portion of the text.

The original work contains numerous references by foot-note to original authorities. Since these are accessible to few readers in this country, I have not thought it necessary to repeat the references in detail.

For the more accurate and satisfactory representation, I have had engraved a hexagon matrix, types cast from which have been used in the ring symbols.

It will be a source of gratification to the practical sanitarian to note the comparatively small proportion of really injurious colors, for even with some of those which produce marked toxic symptoms such large doses are required as to make it unlikely that serious results could occur by accident. The coloring power of these bodies is so high, as a rule, that almost inappreciable proportions are required for coloring articles of food, so that acute effects, at least, are impossible. A manufacturing confectioner of this city, for whom I make examinations of colors used by him, informs me that a yellow color sold as auramine, has such high tinctorial power that one ounce will color two thousand pounds of candy to the highest yellow tint required in his business. It is obvious that the toxic dose of such a body would have to be very high to render it harmful in such use.

A very interesting feature of the present essay is the summary of the existing legislation on the topic in the more progressive countries in Europe. We have here presented almost every method of reaching the end in view, viz., the protection of the public health without interfering with legitimate trade interests, from the practically absolute law-making power of Germany based on imperial will, to the constitutional system of England, with its reliance on the merits of each individual case. It is certain that none of the plans is even approximately satisfactory, and the problem will be even more difficult of solution in the United States ; indeed, it seems to me to be unsolvable. Possibly the simplest and most satisfactory method would be to forbid absolutely the use of any artificial color in certain food articles with which such coloration is likely to deceive the user as to quality or condition, and to require in all other cases that the name and amount of color should be placed on the package.

Thus, the addition of color to milk, butter, cheese, bread, cake, noodles, and wine should be absolutely forbidden, since the object of such addition will be always to deceive the buyer as to the quality or composition of the material, but candies, confections and toys are known to be colored, and either the use of certain colors and none others should be permitted, or the color used should be required to be indicated on the package. In this connection it is well to note that the most serious reported cases of poisoning from colored foods have been those in which mineral colors were used.

The knowledge that irritative or pathogenic microbes are apt to be present in any material which has been exposed to air, leads us to regard as of doubtful value all those experiments in which endermic or hypodermic application of the colors was employed without antiseptic precautions, since the results are complicated by such infection. This is doubtless the case with the observation of Tardieu, on the poisonous nature of corallin. The preparation made from the stockings was more poisonous than the original dye, because it was infected, as would naturally be the case, with more virulent organisms.

In the preparation of this translation I have endeavored to be strictly accurate, and yet to avoid the employment of forms of expression not recognized as good English. Some slips will, however, certainly occur, and further, I cannot hope to escape some errors in transcription or composition. For all such I express my regrets in advance.

I again express my thanks to Dr. Weyl for the permission to translate the essay, and hope that it may assist in diffusing accurate information on a topic of much practical sanitary moment.

H. L.

715 Walnut St., Philadelphia, August, 1892.

PREFACE.

Most civilized communities have considered it advisable to regulate the use of colors in food preparations and other household articles. It appeared to me, however, after much investigation, that the experimental basis for such enactments, notably as concerns coal-tar colors, is insufficient, indeed, in some respects, wholly wanting. The present contribution is intended to include a synopsis of such information as was already attainable, but more particularly to present new material which may have valuable bearing on the framing of restrictive laws. Practical application, therefore, is the especial purpose of this research. The method of presentation must be adapted to the fact that the essay is addressed to both physicians and chemists. Physicians will desire some general views of the chemistry of the colors, since this part of the subject is as much neglected by them as the principles of experimental pathology and toxicology are neglected by chemists. I trust I have done justice to each class, in that I have not been too medical for the chemist, nor too chemical for the physician. In exploring along the contiguous territory of two sciences it is not easy to escape such mistakes. The collection of enactments and regulations, as far as accessible to me, will be found useful. The names and properties of the colors are given in some detail, while the method of preparation is but briefly outlined. That such investigations as the present are rather a source of satisfaction than of anxiety to the color-making industry does not need argument.

I offer, therefore, to my professional brethren far and near, this first contribution, not without asking for myself some indulgent consideration of it, by reason of the difficulties attending the task.

My thanks are due to C. Liebermann, E. Salkowsky, and N. Zuntz, for affording me the facilities of the laboratories under their charge.

W.

CONTENTS.

INTRODUCTION.

Thanks to the co-operation of theory and practice, the coal-tar-color industry of Germany has conquered the world, and inasmuch as new and improved methods are continually being devised, will be able to maintain its pre-eminent position. As a result of this steady work, we find the list of colors constantly increased by new products which enter into competition with those already in the market.

Consumption must stand in some relation to production if satisfactory results are to be obtained, and trade interests stimulate endeavors to secure new uses for the growing supply. It is not surprising, therefore, that the applicability of these colors to food preparations has suggested itself. Whether these bodies are adapted to such uses, and whether they may be constantly taken into the system, even in small doses, without disturbing the organism, are questions of great moment in public hygiene; questions which hitherto could not be answered, for want of satisfactory information. For this reason the present essay of Dr. Weyl is especially welcome.

The author has made a valuable contribution toward determining the physiological relations of those colors applicable to foods, and his work does him much credit, even though, as he points out, experiments on animals cannot be unreservedly applied to human beings.

An especial recommendation of the work is that the author has sought to discover the relation between chemical composition and physiological action, an undertaking which, carried out fully, may make it possible that the expert will be enabled to indicate the action of each group instead of that of individual colors.

Assured that the author himself will further pursue the path he has opened, a hope must also be expressed that others may soon find it opportune to assist in the difficult work of this investigation.

Our thanks are due to Dr. Weyl, not only for presenting to us a conspectus of the most interesting features of each group, but also, for a summary of the existing legislation of these matters, in the principal civilized States of Europe.

It is to be hoped that the work will find favorable reception in all circles which are interested in these questions. S.

Berlin, October, 1888.

THE COAL-TAR COLORS.

GENERAL PART.

HISTORY AND GENERAL APPLICATIONS.

Preparation.—When coal-tar, the source of the coal-tar colors, is subjected to fractional distillation, products, technically known as raw materials, are obtained, among which are benzene, toluene, xylene, naphthalene, anthracene, phenol and cresol. The color-maker transforms these into intermediate products, and then into colors. For example, from benzene and toluene, are obtained by the action of nitric acid (nitration) the intermediate products, nitrobenzene and nitrotoluene. By reduction, aniline (amidobenzene) and toluidine are formed. By oxidation of a mixture of aniline and toluidine, a dye-stuff, rosaniline, is produced, which belongs to the aniline colors proper, or triphenylmethane derivatives. So also, naphthalene—raw material—yields naphthol—intermediate product—which united with diazobenzene chloride—the latter obtained from aniline by the action of nitrous acid—gives rise to an azo-color. Phthalic acid (intermediate product) united with another intermediate product, resorcinol, forms the dye called fluoresceïn, which belongs to the phthaleïns. The best known of these is eosin—tetrabromfluoresceïn. The highly important dye known as alizarin is derived from anthraquinone, the latter being obtained from anthracene. Other classes of colors have also been recognized, such as safranins, indamines, indophenols, etc.

Classification.—The various colors were at first merely designated as red, green, yellow, etc., coal-tar colors. Later they were named according to source, as aniline, phenol, and naphthol colors. Subsequent research has elucidated the atomic structure, and rendered possible a classification in natural groups based on the chemical constitution. The following are some of the most important groups, with examples of each:

I. Nitroso-colors. Naphthol green B, solid green.
II. Nitro-colors. Picric acid, Martius' yellow, naphthol yellow S, aurantia.
III. Azo-colors. Aniline yellow, Bismarck brown, Biebrich scarlet, fast yellow, fast red, tropæolin.
IV. Triphenylmethane colors (anilines, properly so called), fuchsin, malachite green, Victoria green.
V. Rosolic acid colors. Corallin, rosolic acid.
VI. Phthaleïn colors. Eosin, erythrosin.
VII. Anthracene colors. Alizarin, alizarin orange.
VIII. Indigo colors. Indigo.
IX. Quinoline colors. Quinoline yellow, cyanine, chrysaniline.
X. Indophenol colors. Methylene blue.
XI. Azine colors. Safranin, magdala red.
XII. Aniline black.

The characteristics of these groups will be given in the Special Part. These dyes deport themselves in part as acids (acid dyes), partly as bases (basic dyes), and in part as indifferent bodies (neutral dyes). Indigo belongs to the last group. Among the acid colors are the nitrated and sulphonated bodies, such as picric acid, oranges, ponceaux, and all nitro-colors. Basic colors are salt-like combinations of color bases with acids, *e. g.*, fuchsin and methylene blue, and are precipitated by tannin or picric acid in the presence of sodium acetate. Acid colors are mostly insoluble in water, but dissolve in alkalies.

Nomenclature.—The trade names of the coal-tar colors are mostly fanciful, since the scientific titles are cumbersome and difficult to remember. Thus, tetramethylthionine hydrochloride is called methylene blue; aurantia is hexanitrodiphenylamine; wool-black is the sodium salt of sulphazosulphobenzeneparazotolyl-β-amidonaphthalene. A color may have various names: croceïn orange, ponceaux 4 GB, and brilliant orange, are identical. The terms Bismarck brown, phenylene brown, Manchester brown, and canelle, refer to the same color. Different colors are often designated by the same name, especially with a view of substituting a cheap for a costly product. In this way, according to Kertész, the low-priced Martius' yellow is called naphthol yellow S, although the latter name belongs to a more expensive preparation. Finally, mixtures of familiar colors necessary to produce peculiar tints are frequently sold under new names, with deceptive intent. Cardinal, for example, is a mixture of chrysoidin and fuchsin.

Commercial Forms.—Coal-tar colors are offered by dealers either in the form of paste or powder. They may be soluble in water or alcohol, or both. Insoluble colors find obviously but limited application, but it has become possible by special treatment to render them soluble. This takes place, for instance, by the action of sulphuric acid (sulphonation), or when azo-colors are converted into bisulphites. The commercial colors are often mixed with dextrin, sodium sulphate, sodium carbonate, or ammonium chloride. This so-called *coupage* (reduction) is rarely done with fraudulent intent, but generally for one of the following reasons:—

The method of preparing a color does not always yield the same tint; the product may be now lighter, now darker, perhaps due to slight differences in the temperature during the process, or in the subsequent drying. Since, however, the dyer requires that a certain color shall yield a definite shade when a given proportion is employed on the fabric, the manufacturer must reduce the strength of the more highly-colored product. Furthermore, the dyer is accustomed to employ considerable weight of the materials, since it involves less variation from loss or error when, for example, 2000 to 2050 grams are employed, than when only from 100 to 110 are to be weighed out. Hence the manufacturer reduces considerably the strength of the dyes of high coloring power. Finally, the prices may be made lower for the more extensively diluted articles. In general, the coal-tar color-maker strives to furnish pure articles, and we must not forget that small admixtures of foreign substances are unavoidable. The traces of salt, lime, etc., are without significance. Injurious impurities, such as arsenicum, lead, etc., are scarcely found at the present time in coal-tar colors of German manufacture.

Uses.—The natural colors formerly employed by the dyer, have gradually given way, in great part, to the more convenient and cheaper artificial products. There are hardly any dyed materials now in the market in which coal-tar colors are not used. Of course, their prime use is in dyeing the textiles, silk, wool, cotton, hemp, etc., but they are largely used to color various other animal and vegetable products, among which may be mentioned, hair, feathers, leather, bone, ivory, wood, straw, leaves, flowers, paper, soap, and ink. Finally, foods, such as butter, cheese, noodles, confectionery, wines and liquors, are colored by these bodies. The staining of microscopical preparations by means of coal-tar colors has been of great value in scientific investigations.

Dyes that are absorbed directly by the fibre are called *substantive* dyes; among these are fuchsin, safranin, and Bismarck brown. Those that require the fibre to be impregnated with some substance are known as *adjective* dyes. The material used is called the mordant, and its action is due to the formation of an insoluble compound between the fabric and the color. When a metallic salt is used as a mordant, the insoluble compound is called a lake. Among the familiar mordants are lead, copper, and chromic acetates, alum, zinc chloride, and tartar emetic. Turkey-red oil—produced by the action of sulphuric acid on castor oil—tannin, starch, and white of egg are frequently used. Mordants are important in the dyeing of vegetable fibres, notably cotton. Recently, however, some azo-colors belonging to the Congo-red group have been obtained, which give fast colors on cotton without mordanting.

Dyeing, Mordanting, Printing.—The dyeing of textiles depends, as is generally known, upon the production of a chemical combination between the color and the fibre. A given color does not necessarily color all fibres. Cotton is not dyed by alkali blue, naphthol yellow, or acid magenta, while silk is easily colored by them. Picric acid dyes animal fibres readily, but can be attached to vegetable fibres only by the aid of a mordant. Textiles can be dyed either in the yarn or in the piece. For printed goods the procedure is as follows: The color is mixed with starch paste, tragacanth, or some other suitable thickening material, the mordant being often incorporated at the same time. The mixture is imprinted on the goods by means of rollers, and the tissue subsequently steamed, by which the insoluble compound between the fabric and dye is formed; this then will remain after rinsing and soaping. Patterns can be produced upon cloth in two ways. Either the proper portions of the tissue are protected by the imprinting of materials which prevent the dye from adhering, which method is known as *reservage*, or the entire cloth is dyed, and then certain portions are removed by the application of some decolorizing material, this latter method being known as *enlevage*. These methods are especially applicable in calico printing.

Fastness.—A color is said to be "fast" when it is unaffected by various external influences. Obviously, this quality concerns especially the dyed colors. The dyer recognizes colors as fast to light, to washing, to moisture, to scouring, to the action of soap, acids, and alkalies. Nearly every organic color is more or less rapidly bleached by light. Wool, for instance, dyed with picric acid acquires, after a few days' exposure to light, a brownish tint, while alizarin is one of the fastest of colors. Alizarin blue and Congo red are almost perfectly fast to washing, when on cotton, while eosin is easily removed by the same means. Fastness to scouring concerns such articles as require treatment with alkaline solution, *e. g.*, stale urine mixed with ammonium carbonate. By such treatment, oil and gelatin are removed, and a felting of the fibres brought about. Acid green is tolerably fast to scouring; still better are alizarin blue and rosaniline blue.

Detection.—The recognition of the coal-tar colors on fabrics and in food offers so many difficulties, in many cases at least, that even expert chemists are not always able to get satisfactory results. The difficulty originates partly in the fact that there are a great number of these colors, partly because the amount of color used is, as a rule, owing to the high tinctorial power, very small. It is, therefore, best in such investigations to employ considerable amounts of the material to be tested.

For methods of recognizing the various colors, see the Special Part of this work and the authorities cited.

POISONOUS COLORS.

Non-poisonous coal-tar colors may be rendered injurious by admixture with poisonous substances. Medical literature furnishes us with an imposing array of cases of poisoning by "aniline colors," in most of which fuchsin or similar colors are concerned. When the manufacture of aniline colors was first introduced, toward the close of the sixth decade of this century, the poisonous quality of these bodies was unquestioned, in view of their derivation from so poisonous a body as aniline. It was natural to assume that the deleterious properties of the parent substance should be transmitted to the derivatives. The first aniline color manufactured on the large scale was mauveïn, which Perkins prepared in 1858. Fuchsin, discovered by A. W. Hofmann in 1858, was the second color, and was first made on a commercial scale by Verguin, in Lyons, in 1859. At that date a kilo of the color was worth about 1200 marks; in 1866, 50 marks. The first investigations into the effect of fuchsin and its congeners upon the animal organism seem to have been made by Sonnenkalb. The colors examined, aniline red and aniline blue on silk, and fuchsin, were found to be non-poisonous. Sonnenkalb, however, pointed out that they might become poisonous by reason of impurities such as arsenicum and mercury, which were employed in the process of manufacture. To such impurity he ascribed the case first reported by Friedrich and subsequently so frequently quoted, of apparent poisoning in a young man who was for two months engaged in packing aniline colors, Lyons blue, light blue, and fuchsin Nos. 1 and 2. I doubt if this case was due at all to the work in which the patient was engaged.

Sonnenkalb confirmed the correctness of the general opinion as to the poisonous nature of arsenical fuchsin. In this category belongs also the case of poisoning by arsenical fuchsin observed by Clemens, in which a girl engaged in embroidery work permitted the red silk thread to glide constantly over the same point on the finger until a narrow incised wound in the skin was developed, from which arose phlegmonous inflammation, which spread over the hand and forearm.

In consequence of the fact that, about the year 1860, it became known that many French wines were being extensively colored with fuchsin, the French investigators were especially active in studying the effects of this dye on the animal organism. In the experiments of Clouet and Bergeron, dogs were found to bear without injury daily doses of 20 grams of fuchsin, and a man took in the course of a week a total of 3.5 grams without noting any inconvenience. Clouet and Bergeron therefore regarded fuchsin as harmless. It is uncertain whether the fuchsin employed by Feltz and Ritter,* which gave rise to diarrhœa and albuminuria, was pure.

As is known, Coupier † discovered a method of making fuchsin without the use of arsenic acid or mercuric oxide, by employing nitrobenzene, which, although very poisonous, is volatile and can be easily driven off. Grandhomme fed two rabbits for several weeks with fuschin prepared by the Coupier-Brüning method, administering daily 0.5 gram with 50 grams of barley. The animals remained in good health and the urine contained no

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* In Cazeneuve's work, p. 43, is a review of what seems to be rather an inexpert research by Poincaré on the effect of various coal-tar colors on the animal organism.

† The Coupier-Brüning fuchsin was for some time called "nitrobenzene fuchsin."

albumin. After an interval, 15 grams of fuchsin and 15 grams of barley were mixed and fed during two weeks. No disturbance in the condition of the animals was noted. Subcutaneous injection of a one per cent. solution once or twice daily had also no effect. Similarly, a hen, which had eaten for three weeks oats colored with fuchsin, was in good health. In entire accord with all information concerning the harmlessness of pure fuschin are Grandhomme's interesting observations among the workmen of the Höchst Color Works. In the fuchsin department, 52 workmen were employed, of whom—

6 had been working there from 3 to 4 years.
6 " " " 4 " 6 "
11 " " " 6 " 10 "
5 " " " 11 " 18 "

None of these men suffered either from diarrhœa, colic, or disturbance of the urinary secretion, although daily breathing the fuchsin dust. Tests of the urine, made on Saturday evening after the entire week's work, showed absence of albumin. Further, investigations as to the effect of pure fuschin in cases of heart and kidney disease showed the entire harmlessness when taken into the stomach.

Finally, it is now and then asserted that skin diseases have been brought about by garments dyed with fuchsin and similar colors. In the notice of Bruce's case—cutaneous eruption following the wearing of a red-dyed chest-protector—no account is given of any chemical examination of the color. The case of skin disease reported by Viand-Grand-Marais, of Nantes, which appeared during the wearing of an amaranthine and violet-colored woolen shirt, was ascribed to a dye which, according to the authority, showed by Marsh's test only small amounts of arsenic.

The above facts justify the view that pure fuchsin is non-poisonous: the poisonous action of the commercial color is due to arsenical compounds. According to Grandhomme, aniline blue, aniline violet (dahlia), and malachite green are also non-poisonous.

A similar statement seems to apply to corallin. Tardieu regarded this as poisonous. It is produced by heating phenol with oxalic and sulphuric acids "to 120–130° C." The crude melt, which presents itself as a dark red resinous mass with metallic lustre, is known as yellow corallin. The pure color obtained from yellow corallin is called aurin. On account of their fugitive character, red and yellow corallins are not much used in dyeing, but are employed in the printing of calicoes and woolens. Red corallin, also known as pæonin, is produced by treatment with ammonium hydroxide under pressure. Tardieu, has reported eight cases in which the wearing of stockings dyed with corallin was attended by the development of a vesicular eruption. He undertook, in conjunction with Roussin, two series of experiments. In the first, red corallin obtained from Persioz, was injected into the stomach. The majority of the animals died. In the second series, Tardieu used the extract from the suspected stockings. The animals died more quickly than in the first series. Weickert pointed out that the corallin was administered in alcoholic solution. The post-mortem indicated alcoholic poisoning, but it does not appear why the extract from the stockings was the more poisonous. Moreover, Weickert's trustworthy researches have proved the entire harmlessness of the red corallin made by Würtz of Liebenau, whether administered endemically, hypodermically, or by the stomach. The men engaged in preparing and putting up the corallin in the Würtz factory were in good health, although the skin of the hands was intensely colored. From these facts it appears that pure corallin is non-poisonous. In all probability, the eruption that attended the wearing of the stockings was due to an arsenical mordant. The German law, relating to the use of injurious colors, etc., restricts the use of arsenical mordants to such proportions as will give not more than 0.002 gram to 100 sq. cm. of the finished goods. It is known that the workmen in color-printing departments are most likely to be affected. I may note some observations made in the extensive cotton-spinning and printing establishment at Zawiercie, formerly operated by A. & B. Ginsberg, for the report of which I am indebted to Mr. Ginsberg, of Berlin. Workmen dealing with sodium arsenate and other arsenical preparations, especially in the damp rooms of the dye-house, in which they worked all day in wet clothes, suffered from swelling of the hands, feet, and testicles. Dermatitis and a pock-like eruption occurred which necessitated removal of the patients to the hospital. In consequence, the use of arsenical mordants was discontinued and without disadvantage to the operation of the establishment. Landrin, Babaut, Bourgongnon, Chevreul, and P. Guyot agree with Weickert. However, it seems, as Sell has pointed out, commercial corallin occasionally contains phenol. For this reason, the German law of July 5th, 1887, places corallin among the prohibited colors. According to Zulkowsky, rosolic acid (methyl-aurin) is obtained by the oxidation of cresol (methyl-phenol) by arsenic acid, in the presence of sulphuric acid. If this method should be actually used, as to which I have no knowledge, commercial rosolic acid might contain arsenicum.

In this connection, the remarkable case of hyperidrosis, reported by Grandhomme, should be mentioned. In the Höchst dye-works, at various times from 1874 to 1882, many workmen, in all 47, most of whom worked in the eosin department, were affected as follows: After a varying period, the men were seized with pain in the finger tips and ball of the thumb, and in three cases abscesses were formed. In every case the perspiration was so abundant that drops fell from the depending hands. The general health did not seem to be disturbed and the perspiration showed no abnormality either in odor or appearance. Recovery took place in about sixteen days. The cause of the affection is not definitely known. Possibly, it arises from some, as yet unknown, admixture in the material, possibly, from the use of strong chlorated lime solution for cleansing the hands. At any rate, the cases have become less frequent since the use of such strong solutions has been interdicted. The eosin itself cannot be the cause, since those engaged in packing it are in no wise affected. Dr. P. Seidler has kindly communicated to me the note of a case of hyperidrosis which affected a chemist of his acquaintance. The patient had been in the dye-works of Bayer & Co., in Elberfeld, and had used very strong chlorated lime solution for cleaning his hands. Grandhomme's view as to the cause of the malady is, according to this, confirmed. I am now investigating this subject.

A critical review of the existing literature shows that trustworthy evidence of poisoning by pure aniline colors is not at hand.*

In all probability, the cases in which the color has been suspected, have arisen from admixture with arsenical compounds, or the use of arsenical mordants. The following additional consideration confirms the view as to the harmlessness of pure anilines.

The general condition of the health of those engaged in coal-tar color factories weighs against the harmfulness of these colors. If the aniline colors, and artificial colors in general, were as poisonous as is often gratuitously assumed, those engaged for long periods in the manufacturing or handling the same, or otherwise brought in close contact, ought to be frequently affected injuriously. Of course, the products and by-products of the processes bring about, frequently, both acute and chronic poisoning. It would, indeed, be surprising if those who are engaged in the manufacture of benzene, nitro-benzene and similar bodies, should not be more affected by them than those who may have but seldom, perhaps only once, even seen such materials as specimens in a cabinet. Nevertheless, Grandhomme states that in the extensive factory at Höchst-on-the-Main the proportion of sick among those who are concerned in manufacture of the

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* For a small number of cases of poisoning by picric acid, see the Special Part.

raw material, is insignificant. The following tables are from Grandhomme's work :—

Department of Factory.	No. of Men.	Illness Due to the Work.		Remarks.
		Number.	Per Cent.	
Nitrobenzene, . . .	96	5	5.2	No nitrobenzene poisoning.
Aniline, ...	116	18	15.5	Aniline poisoning.
Anthracene, . . .	2	0	0.0	

Still more favorable are the figures relating to those who work at the actual manufacture of the aniline colors :—

Department.	No. of Workmen.	No. of Years.	Illness Due to Work.		Remarks.
			No. of Cases.	Percentage.	
Rosaniline, .	2	2	0	. .	
Fuchsin, . .	396	9	31	7.8	Skin affections.
Blue, . . .	120	4	1	0.83	Aniline poisoning.
Dahlia, . .	88	4	0	0.0	
Green, . . .	84	4	0	0.0	
Eosin (principally),	112	4	27	24.1	Hyperidrosis.

Even this small percentage has been reduced materially by the introduction of hygienic measures, as the following table shows :—

Years.	No. of Workmen.	Illness.		Remarks.
		No. of Cases.	Percentage	
1879	325	13	4	Aniline poisoning.
1880	447	18	4	" "
1881	508	17	3.3	" "
1882	500	7	1.4	" "

The hygienic provision consisted in better ventilation of the work-rooms, and the regulation that the workmen should be allowed more frequently to go into the open air, also prohibition of the employment of chlorated lime solution.

If now we determine the percentage of sickness among the workmen in branches of industry in which actual poisons are used, we find that the statistics of the aniline industry compare very favorably.

The numbers for the workers in aniline have been determined from the following statistics given by Grandhomme :—

DISEASES.	WORKERS IN ALIZARINE.	WORKERS IN ANILINE.
Infectious diseases, ...	7	35
Diseases of nutrition, ...	77	172
" " circulatory system, ...	5	12
" " nervous "	16	56
" " special senses, ...	28	63
" " respiratory apparatus, ...	89	288
" " digestive "	103	339
" due to occupation, ...	. .	88
Not otherwise classified, ...	5	7
	330	1060

Therefore, a total of 330 plus 1060 equals 1390 internal affections. Of these 88 were cases of poisoning from occupation, which equals 6.3 per cent.

OCCUPATION.	PERCENTAGE OF CASES OF DISEASE.	FORM OF AFFECTION, ETC.
Gilders, ...	. . .	
Zinc white workers, . . .	. . .	
Phosphorus makers, . . .	2–3	Phosphorus poisoning.
Mercury miners, ...	3–4	Mercury "

OCCUPATION.	PERCENTAGE OF CASES OF DISEASE.	FORM OF AFFECTION, ETC.
Aniline makers, ...	6.3	Aniline poisoning and hyperidrosis, probably due to arsenicum.
Hat makers, ...	7.5	Mercury poisoning.
Glaziers, ...	10.0	Lead “
Blue color makers, . . .	12.5	Arsenical “
Artificial flower makers, .	15	“ “
Arsenicum miners, . . .	20	“ “
Sweinfurth green makers,	20	“ “
Sugar of lead makers, . .	21	Lead “
Potters, ...	25	“ “
Tin workers, ...	35	Lead and arsenical poisoning.
Type founders, ...	35	Lead poisoning.
Tobacco workers, ...	15 (male).	Nicotine poisoning.
“ “	45 (female).	“ “
Silver miners, ...	58	Lead “
White lead makers, . . .	68	“ “

Dr. Coster thus expresses himself in regard to the general health of the workmen in aniline works:—

“We are justified in saying that work in aniline-color factories, usually regarded as very injurious to health, does not, in any way, involve greater dangers than belong to working in factories in general, apart from such acute effects as result from sheer carelessness.”

From the above facts it follows that the poisonous qualities of the aniline colors are not manifested among those who manufacture them.

It remains to mention a few colors known to be poisonous. The injurious character of picric acid and its salts has long been known. Cazeneuve and Lépine pointed out the poisonous nature of Martius' yellow, safranin, and methylene blue :[*] and I have shown the same for dinitrocresol (saffron-substitute).[†]

NON-POISONOUS COLORS.

According to Cazeneuve and Lépine's experiments the following are not poisonous to human beings and dogs: Naphthol yellow S, and certain azo-colors employed for the coloring of wine: viz., orange, ponceau R, purple, and solid yellow.

According to Grandhomme, rabbits bear without injury, fuchsin free from arsenic, and other triphenylmethane derivatives (aniline colors) eosin, erythrosin and orange. Butter yellow (dimethylamidoazobenzene) produces no disturbance in rabbits. The toxic action of aurantia is in dispute, concerning which, see the Special Part.

LAWS REGULATING THE USE OF POISONOUS COLORS.

In spite of the facts recorded in the preceding pages, which show that the danger of poisoning from the aniline colors has been much overrated, at least as far as our present knowledge extends, most civilized countries have deemed it necessary to enact laws against the employment of the common colors in the preparation of food, drink and household articles generally. These regulations, as far as obtainable by me, are presented as an appendix to this chapter.[‡] All these various legal provisions have the same purpose: to prevent the adulteration of food,

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[*] Confirmed by P. Ehrlich, by information kindly communicated verbally. Compare also the exhaustive investigation on "Neurotropic" colors by the same authority, *Therap. Monatsh.*, March, 1887.

[†] See Zeit. f. angew. Chem. 1888, No. 12, for confirmation of my results by Gerlach.

[‡] I gladly avail myself of the opportunity to express my sincere thanks to Messrs. Carnelutti, of Milan, Otto Hehner, of England, and E. Ludwig, of Vienna, for furnishing me with the text of the laws concerning their respective countries.

drink, and household articles. The method by which this is reached is threefold.

Germany, France, and Austria, enumerate the harmful colors which are not allowed to be used. England places a penalty for the adulteration without stating what colors are to be considered injurious. Italy, coincides with England in the form of the law, but provides that the determination of the injurious articles shall rest on the judgment of experts appointed by the Secretary of the Interior. A justification for these laws, of course, cannot be denied. A little consideration will show that the practicability of the legal provisions is as unequal as the sense of equity and justice which finds expression in them.

The English law imposes a fine of fifty pounds sterling upon every one who mixes or colors food with any injurious ingredient. Subsequent offenses may be punished with imprisonment, up to six months. This law seems to give satisfaction in England. At least Mr. Otto Hehner writes me, under date of July 3d, of this year: "So far as I know, no case has come under this paragraph of the law of 1873, since its enactment. Aniline colors, as long as they are not strongly arsenical, are not regarded as injurious. Nor do any special provisions exist here (*i. e.* in England) concerning the use of poisonous colors in the carpet-weaving or calico-printing industries. The force of public opinion and publicity is so great that no one would dare to employ poisonous colors."

Unfortunately, here in Germany, we cannot rely upon the force of public opinion, nor on publicity, in matters concerning the adulteration of food. We cannot regard a law as either correct or practical which punishes the adulteration of food without enumerating those ingredients which are to be regarded as harmful. The Austrian law seems to be the simplest: The various provisions enumerate those colors which may be used in food, and punish every dealer who has in his factory or store any other colors, no matter what name these bear. The regulation of May, 1866, (see Appendix) is indeed difficult of execution. How can a confectioner be held responsible for the employment of a color, the harmfulness of which was not known at the time of its application? On the other hand, no objection can be brought against the regulations issued on May 1st, 1886, nor those noted subsequently, intended to meet a special purpose. The regulation forbids the employment of any color prepared by chemical treatment of aniline or other coal-tar products. This enactment takes away the least doubt that the Government prohibits the use of all coal-tar colors for the purpose under consideration. The basis of the prohibition is entirely in accordance with the spirit of the law. It is the sense of the declaration that there are many coal-tar colors in commerce the action of which on the human organism is unknown and the adulteration to which they are liable suspicious. Such articles should not be employed in the preparation of food and drink.

Austrian regulations are the most radical in this field. It is to be assumed that the principle which has as yet found application only through executive action will take the form of enactment. Less severe than the Austrian law are those of France and Germany. The German law forbids the employment of certain enumerated colors and permits, therefore, the use of those not mentioned. In France the injurious and consequently forbidden colors are listed as well as those which are harmless and, therefore, permitted.* Without doubt, both these laws, which represent the results of toxicological and chemical research up to a certain time, have been of much service to public hygiene. As regards the effects of mineral colors on the human organism, we are sufficiently informed. The near future will not bring forth material changes in regard to these, but it is otherwise with the organic colors. Chemical technology moves by giant strides: new colors are brought into the market, and no inquiry is instituted as to the effect on the human body. If the new color is more beautiful than its predecessor, or cheaper, the tradesmen

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* The regulations by the magistrates of Milan, advance sheets of which were sent me by the courtesy of Dr. Carnelutti, permit the employment of certain definite—that is to say enumerated—coal-tar colors.

throw the older color to one side. This is not forbidden by law. The dealer is allowed the employment of any color not mentioned in the regulations, even though it may have been subsequently proved injurious. A characteristic illustration of this point may be found in the proclamation emanating from the Chamber of Commerce of Sonneberg. This body recommends for the preparation of children's toys, three colors, the poisonous character of which I can demonstrate. These are Martius' yellow, safranin, and Bismarck brown. Of course, the Chamber of Commerce could only abide by the law, and this did not allude to the above named materials. The law maker, however, is not to blame, for the facts to which I refer were not known at the time the law was prepared. Obviously, some amendment must be brought about. This can be done either by forbidding the use of all coal-tar colors in the preparation of food and drink, or by following the plan of the Italian law and providing for periodical investigations by a commission of chemists and physicians, to determine what are, and what are not, appropriate colors for such uses. Upon the reports of such commission, the legislature will regulate the use. Should the use of every one of the colors be forbidden, as has been done by the German government in the case of the coloring of wine, the problem is solved in the simplest manner. By this means we would bring about the same condition that prevails in Austria. Many serious difficulties beset the carrying out of the second plan. A commission can only act to advantage when it subjects colors to investigation before they come into commercial use.

Undoubtedly the whole matter must undergo a revision, probably in the shape of a general poison law affecting the entire Empire. I will return to a discussion of this topic in a later section of this treatise.

APPENDIX.

LEGAL ENACTMENTS CONCERNING THE USE OF COLORS IN THE PREPARATION OF FOOD.

GERMANY.

I. Laws concerning the use of unwholesome colors in the manufacture of food, drink, and other articles. July 5, 1887.

We, William, by the Grace of God, Emperor of Germany, King of Prussia, etc., order, in the name of the State, in accordance with the approval of the Federal Council and the Imperial Diet, as follows:—

1. Unwholesome colors are not permitted to be used in the preparation of articles of food and drink which are exposed for sale. Colors which contain antimony, arsenicum, barium, lead, cadmium, chromium, copper, mercury, uranium, zinc, tin, gamboge, corallin, picric acid, are unwholesome in the sense of this Act. The Chancellor of the Empire is empowered to set forth exact methods for determining the presence of arsenicum and tin.

2. Vessels, wrappers, or covers dyed with colors referred to in § 1 are not to be used for holding or protecting articles of food or drink. The present regulation does not apply to the use of the following: Barium sulphate (heavy spar, fixed white), barium colors free from barium carbonate, chrome green, copper, zinc, tin and their alloys when applied as metallic colors, cinnabar, tin oxide, tin sulphide in the form of mosaic gold, all vitrified colors in glass, glazes, or enamels, and colors on the outside of water-tight vessels.

3. In the preparation of cosmetics (materials intended for

the cleaning, care, or tinting of the skin, hair, or cavity of the mouth) put up for sale, the materials enumerated in § 1 must not be used. This rule does not apply to the use of barium sulphate (heavy spar, fixed white), cadmium sulphide, chromium oxide, cinnabar, zinc white, tin oxide, tin sulphide, nor to copper, tin, zinc, and their alloys in powdered form.

4. In the manufacture of toys (including picture-cards, picture-books, and water-colors, flower-pot covers, and artificial Christmas trees), the materials forbidden in § 1 are not to be used. This regulation does not apply to the articles excepted in § 2, nor to antimony sulphide and cadmium sulphide applied as color in gum; lead oxide, in varnish; white lead as a component of the so-called molded wax, if the same does not amount to more than one part in one hundred; lead chromate by itself or in association with lead sulphate, in oil or lacquer, covered by lacquer or varnish; zinc colors insoluble in water, in rubber toys, if used in the coloring of the rubber, or as lacquer or oil color, applied with lac or varnish, and all vitrified color applied with enamel. The provisions of §§ 7 and 8 are strictly applicable to the objects therein mentioned, when these enter into the composition of the toys.

5. In book printing and lithographing in connection with the manufactures enumerated in §§ 2, 3 and 4, only colors containing arsenicum are forbidden.

6. Water colors of all kinds are not to be sold nor offered for sale as non-poisonous unless they are in accordance with the requirements of § 4.

7. Arsenical colors shall not be employed in the manufacture of tapestries, upholstery, carpets, curtains, wearing apparel, masks, candles and artificial flowers and fruits. This regulation does not apply to the use of arsenical mordants for the dyeing and printing of textiles, but fabrics so prepared shall not be employed in the manufacture of the articles enumerated in the preceding paragraph, if the arsenical compound is soluble in water, or present in amount greater than 2 milligrams to 100 square cent. of the finished fabric. The Chancellor of the Empire is authorized

to formulate in detail the method for estimating the amount of arsenicum.

8. The provisions of § 7 apply to the manufacture of writing materials, lamp shades and lamp decorations.

The manufacture of sacred wafers is subject to the conditions specified in § 1, but as regards those not intended to be eaten, the use of barium sulphate (heavy spar, fixed white), chrome green and cinnabar is allowed.

9. Water colors, or gelatin colors containing arsenicum, are not to be used in the preparation of paints for floors, ceilings, walls, doors or windows of living or work-rooms, nor for shades, shutters, curtains, furniture, or other household articles.

10. The regulations given in § 1, do not apply to the ingredients there enumerated, if such are merely present as impurities unavoidable in the ordinary manufacture, and not essential constituents.

11. These regulations do not apply to the coloring of furs.

12. Whoever prepares, keeps or puts up food, drink or household articles in violation of the provisions of § 1 to 5, 7, 8, and 9, or sells or offers for sale articles prepared, kept or put up in violation of said provisions, or violates the requirements of § 6 or those of § 9, or sells or offers for sale articles made in violation of the provisions of § 9, may be punished by a fine not exceeding one hundred and fifty marks, or by imprisonment.

13. In addition to the penalties fixed by § 12, articles made, sold or exposed for sale in contravention of the provisions of this Act may be confiscated, whether the property of the accused person or not. If the prosecution or conviction of any particular person is impossible, the judgment may be limited to the confiscation.

14. The provisions of the law of May 14, 1879, relating to sale of food, drink, and household articles (Reichs-Gesetzbl., p. 146) remain undisturbed. The regulations given in § § 16 and 17 of that law, relating to violations of it, apply to the present enactment.

15. This law takes effect on May 1, 1888, at which date

the imperial decree relating to the employment of poisonous colors, dated May 1, 1882, (Reichs-Gesetzbl., p. 55), expires.

Given under our royal hand and imperial seal, Ems, July 5, 1887.
WILLIAM.
VON BOETTICHER.

II. The Sonneberg Chamber of Commerce and Trade announced in a bulletin of information, on December 4, 1887, an opinion as to the points in the law of July 5, 1887, touching the use of unwholesome colors in the manufacture of toys, and enumerated the following colors, which under that law may be employed unrestrictedly: All blue and violet aniline (that is, coal-tar) colors, all ponceaus, all orange colors, methyl green, brilliant green, malachite green, chrysoidin, naphthol yellow, Martius' yellow, eosin, phloxin, safranin, erythrosin, fuchsin, phenylene brown, and aniline black.*

III. Announcement concerning the examination of colors and fabrics for arsenic and tin. April 10, 1888.

By virtue of the provisions of § § 1 and 7, of the law relating to the use of injurious colors in the preparation of food, drink, or household articles, approved July 5, 1887 (Reichs-Gesetzbl., p. 277), I order that the following methods are to be pursued in the recognition of arsenicum and tin in the colors employed in food or drink and in the determination of the amount of arsenicum in fabrics containing arsenical mordants.

For the Chancellor of the Empire,
Berlin, April 10, 1888. VON BOETTICHER.

Appendix.

Directions for the examination of colors and fabrics for arsenicum and tin (§ § 1 and 7, of the law relating to the use of injurious colors in the manufacture of food, drink, and household articles, dated July 5, 1887.).

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* See publications of the Imper. Health Office, p. 132, No. 8.

A. Methods for detecting arsenicum and tin in artificially colored articles of food and drink.

I. Solids.—With solids which are colored through the entire mass, 20 grams are to be taken. If colored superficially, sufficient of the exterior is to be scraped off to be equivalent to 20 grams of the material. Smaller amounts of material are to be used only when the full quantity is not obtainable. The test-piece is to be reduced to powder in any suitable manner and placed in a Berlin porcelain dish with a convenient quantity of hydrochloric acid of sp. gr. 1.100 to 1.120 and a quantity of water equal to three times the quantity of acid added. In general, 25 c. c. of acid and 75 c. c. of water will be sufficient; 0.5 gram of potassium chlorate are then added, the dish heated on the water-bath, and, when the fluid reaches the temperature of the bath, small quantities of potassium chlorate are added from time to time until the liquid acquires a uniform light yellow tint and becomes clear. Two grams of potassium chlorate will usually suffice for the operation. Water lost by evaporation is to be replaced. When the proper condition has been reached, about 0.5 gram more of the chlorate are added and the dish taken from the bath, cooled, filtered into a 400 c. c. flask, and the filtrate heated on the water-bath until all odor of chlorine has disappeared. The filter, together with any precipitate, is washed with hot water, the washings evaporated to 50 c. c., and the liquid, with any precipitate that may be in it, added to the original filtrate. The total volume of the liquid at this point must be at least six times that of the hydrochloric acid taken. Thus, supposing that 25 c. c. of hydrochloric acid have been used, the volume must not be less than 150 c. c., preferably 200 to 250 c. c. The liquid is then maintained for three hours at from 60° to 80° C., while a slow current of pure well-washed hydrogen sulphide is passed through; the heat is then withdrawn, the gas being continued until the liquid is cold. It is transferred to a flask, the mouth of which is covered with a piece of filter paper, and allowed to stand for twelve hours in a moderately warm place. If a precipitate be formed, it is to be collected upon a filter, washed with hydrogen sulphide solution, and then, while still moist, treated with yellow ammonium sulphide which has been somewhat diluted with weak ammonium hydroxide. In general 4 c. c. of ammonium sulphide, 2 c. c. of ammonium hydroxide of sp. gr. 0.96, and 15 c. c. of water will be satisfactory. The residue on the filter, not dissolved by this mixture, is washed with water containing a little ammonium sulphide and the filtrate and washings evaporated to dryness at a gentle heat in a porcelain dish, not over six cm. in diameter. The residue treated with three c. c. of red fuming nitric acid, the dish being covered by a watch glass, and the acid evaporated at a gentle heat. If the residue is still dark, the treatment with nitric acid must be repeated until a mass appearing yellow when moist, is obtained. This is mixed, while still moist, with finely powdered sodium carbonate, until strongly alkaline, a mixture of one part of sodium nitrate and three parts of sodium carbonate added, and sufficient water to make a pasty mass, which is then thoroughly mixed. The mass is heated in a crucible to sintering or incipient melting; a high heat is to be avoided. A colorless or white residue should be obtained. If the mass is colored, it should be re-heated with a little sodium nitrate, until the colorless condition is reached.*

The melt is dissolved in warm water and filtered through a wet filter. If tin be present, it will be found on the filter, in the form of stannic oxide, while all the arsenicum will be in the filtrate in the form of sodium orthoarsenate. If there be a residue on the filter, it must be borne in mind that minute amounts of tin may pass into the filtrate. The residue is washed with cold water, then three times with a mixture of equal parts of alcohol and water, the washings evaporated so that the total volume including the filtrate does not exceed 10 c. c., and nitric acid added, drop by drop, until the liquid is acid. If a precipitate

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* If the melt persistently remains black it contains copper, owing to the slight solubility of copper sulphide in ammonium sulphide.

of stannic hydroxide appear it is filtered off and washed as described above. The further procedure for the detection of tin is given below.

For the recognition of the arsenicum, it is converted into ammonium arsenmolybdate. For this purpose, the liquid, rendered acid by nitric acid, as described above, is freed from carbonic and nitrous acids by warming, cooled, the clear (filtered, if necessary) solution, which should be about 15 c. c., mixed in a flask with about an equal volume of ammonium molybdate solution,* and allowed to stand without warming for three hours. If through incomplete washing of the hydrogen sulphide precipitate, any phosphate has been retained, a yellow precipitate of ammonium phosphomolybdate will separate; otherwise, the liquid will remain clear. The clear (if necessary, filtered) liquid is heated on the water bath for five minutes, at the boiling point.* If arsenicum be present, a yellow precipitate of ammonium arsenmolybdate, together with molybdic anhydride will separate.†

After standing for one hour, the liquid is decanted through a filter, the precipitate washed twice with a mixture of 100 parts of the molybdate solution, 20 parts nitric acid of sp. gr. 1.200 and 80 parts of water, and dissolved, by the aid of heat, in from two to four c. c. of ammonium hydroxide sp. gr. 0.96, four c. c. of water, filtered, if necessary, mixed with one-fourth its volume of alcohol, and then with two drops of the solution of ammonium chloride and magnesium chloride. The arsenicum separates on standing, as ammonium magnesium arsenate, more or less crystalline in form, which is to be collected on a filter and washed with as small as

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* Dissolve one part of molybdic anhydride in four parts of ammonium hydroxide (sp. gr. 0.96), and pour the solution into 15 parts of nitric acid (sp. gr. 1.200); allow the liquid to stand in a moderately warm place for several days and decant the clear portion for use.

† It is best to continue the heating until the molybdic anhydride begins to separate.

possible a quantity of a mixture of one part of ammonium hydroxide, two parts of water, and one part of alcohol. The precipitate is to be dissolved in the smallest possible quantity of dilute nitric acid, the solution evaporated to small bulk, one drop of it placed in a porcelain basin and another on a glass slide. To the first drop, a solution of silver nitrate is added, then a drop of ammonium hydroxide sp. gr. .096 is applied to the edge of the mixture. If arsenicum be present, a red-brown streak will appear. The drop on the object glass is made akaline with the smallest possible quantity of ammonium hydroxide, by which there appears very soon, if arsenicum be present, a crystalline precipitate of ammonium magnesium arsenate.

For the detection of tin, the filter or filters containing the stannic oxide are to be dried, burned in a porcelain crucible, and weighed.* Further examination for tin will be necessary only when the residue, after deducting the filter ash, weighs more than .002 gram. In this case, the residue is to be placed in a porcelain boat which is inserted in a tube of hard glass, one end of which has been drawn out to a fine jet. A stream of pure dry hydrogen is passed through the tube, the temperature being slowly raised and continued until no vapor of water escapes, that is, until all the oxide is reduced. The boat is allowed to cool in the stream of gas, removed, tilted slightly, a few drops of hydrochloric acid sp. gr. 1.10 to 1.12, placed in the lower end, again placed in the tube and subjected to a slow current of the hydrogen gas. The boat is inclined so that the hydrochloric acid comes in contact with the reduced tin, and is then slightly heated. The tin dissolves, forming stannous chloride, with liberation of hydrogen. The boat is allowed to cool in the current of gas, removed, if necessary, treated with a few drops of a mixture

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* If the residue is black, in consequence of the presence of copper oxide, it is to be warmed with nitric acid and evaporated in the water-bath to dryness, and a few drops of nitric acid with a little water added, the residue collected on a filter, washed, dried, ignited and weighed.

of three parts of water and one part of hydrochloric acid, and different drops of the solution tested for tin, by mercuric chloride, gold chloride and hydrogen sulphide, the latter test being tried both before and after the addition of bromine or chlorine water.

A black residue, insoluble in the acid, remaining after the treatment of the contents of the boat with hydrochloric acid, may be antimony.

II. Liquids, Fruit Jellies, and Similar Substances.—In such cases, a quantity of the material is to be weighed out that shall be equivalent to 20 grams of the dried substance. For raspberry syrup, 30 grams must be taken; for currant jelly 35 grams, and for red wine, vinegar and such fluids, from 800 to 1000 grams must be used. Smaller quantities may be used only when the full amount is not obtainable.

Fruit juices, jellies and such substances are treated exactly as directed above, with hydrochloric acid, potassium chlorate, etc.; dilute, non-acid liquids are concentrated by evaporation, to a small volume, and treated as before; acid liquids are distilled to a small volume, the distillate is mixed with hydrochloric acid and saturated with hydrogen sulphide, any precipitate so obtained being added to that obtained from the liquid in the retort similarly treated.

B. Procedure for the detection of arsenicum in yarn and fabrics (§ 7 of the law).*

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* It is allowable for the investigator to make a preliminary test by Marsh's method, using a sufficiently large quantity of the material, and thus determine the presence or absence of arsenicum. Should the result be negative further procedure is unnecessary. [In this and similar cases, Reinsch's test, which is much more convenient than Marsh's, will be found sufficient for preliminary examination. It is advisable to use a rather large amount of hydrochloric acid, otherwise arsenates may be overlooked. The processes given in the text for the destruction of the organic matter are now not much employed, since the methods involving the use of sulphuric acid with or without nitric, are more rapid and satisfactory. These methods will be found described in Fresenius' Quantitative Analysis and other works of similar scope. TRANSLATOR.]

Thirty grams of the material to be tested are cut fine and soaked in water at from 70 to 80° C. for from three to four hours. The liquid is filtered, any residue is washed, and the filtrate and washings are concentrated to about 25 c.c., cooled, mixed with 5 c.c. of pure sulphuric acid, and tested by Marsh's test, with due precautions. If an arsenical mirror is obtained it shows that arsenicum is present in the fabric, in a form soluble in water.

If the result by the above test is negative, a further quantity of 10 grams is taken and the superficial area determined. In the case of yarn the area is to be determined by comparison with a fabric woven from yarn of similar size. If the quantities necessary for the examinations are not to be obtained, smaller quantities may be used, and this part of the test may, in such case, be carried out upon a portion of that which has been treated with water and afterwards dried.

The yarn or fabric is to be cut fine, introduced into a hard glass retort of 400 c.c. capacity, and covered with 100 c.c. of hydrochloric acid sp. gr. 1.19. The neck of the retort is drawn out and bent at an obtuse angle, and the retort mounted so that the first portion of the neck points obliquely upward and the second portion sharply downward. The end of the neck is attached to a Liebig's condenser and the joint made tight with a caoutchouc tube. The condenser is attached by an air-tight joint to a receiver of 500 c.c. capacity, in which has been placed 200 c.c. of water, and which is immersed in a dish of cold water. The outlet tube of the receiver is connected in a suitable manner with a Péligot's tube.

About an hour after the addition of the hydrochloric acid, 5 c.c. of cold saturated solution of non-arsenical ferric chloride is introduced into the retort and heat applied. When the excess of hydrochloric acid has passed over the heat is raised until the liquid boils, and continued until the contents of the retort begin to foam. The liquid is allowed to cool, 50 c.c. of hydrochloric acid of sp. gr. 1.19 added, and the distillation resumed. The contents of the receiver, colored by organic matter, are mixed with the liquid that has collected in the Péligot tube, diluted with distilled water to about 600 c.c., and treated, first warm, and then in the cold, with pure washed hydrogen sulphide. At the end of twelve hours the brown precipitate, consisting in whole or in part of organic matter, is collected on an asbestos filter, which rests in a funnel provided with a stopcock, and washed briefly. The cock is closed and the mass treated with a few c.c. of a solution of bromine in hydrochloric acid of sp. gr. 1.19, a watch glass being placed over the top of the funnel to avoid loss. After action for half an hour the liquid is allowed to run from the funnel into the flask in which the precipitate was originally formed, on the sides of which some of the material remains. The residue on the filter is to be washed with hydrochloric acid of the usual strength. The filtrate and washings are to be mixed with excess of ferric chloride, the mixture introduced into a distillation apparatus of smaller size, but constructed as before detailed, the flask containing the solution being rinsed with hydrochloric acid of the usual strength, the rinsing being added to the contents of the retort. The distillation is conducted exactly as before described. The distillate is usually clear and colorless. It is diluted to about 700 c.c., precipitated with hydrogen sulphide, as before directed, and after twelve hours standing the precipitated arsenious sulphide is collected on a filter (which has been successively washed with dilute hydrochloric acid, water and alcohol, dried at 110° C., and weighed), washed with water, absolute alcohol, warm hydrogen sulphide solution, absolute alcohol again, dried at 110° C., and weighed. The quantity of arsenicum is calculated, and from the data obtained in the original measurement the proportion of arsenicum in 100 sq. cm. of material may be ascertained.

England.

In the Sale of Food and Drugs Act of 1875, paragraph 3, to which Mr. Otto Hehner, of London, has kindly referred me, is found to be to our purpose.

"3. No person shall mix, color, stain, or powder, or order or permit any other person to mix, color, stain, or powder, any article of food with any ingredient or material so as to render the article injurious to health, with intent that the same may be sold in that state, and no person shall sell any such article so mixed, colored, stained, or powdered, under a penalty in each case not exceeding fifty pounds for the first offence; every offence after a conviction for a first offence shall be a misdemeanor for which the person, on conviction, shall be imprisoned for a period not exceeding six months at hard labor."

FRANCE.

(This abstract is given by Dr. Weyl in the original French.)

LIST OF HARMFUL AND HARMLESS COLORS.

I. SUBSTANCES THAT MAY BE USED.

Mineral Colors.

White.—Chalk. Precipitated barium sulphate (to be used in small amount.)

Blue.—Prussian or Berlin blue, ultramarine.

Violet.—Violet ultramarine.

Brown.—Ochre, manganese brown.

Green.—Green ultramarine.

Yellow.—Yellow ochre.

Organic Colors.

White.—Farina flour, starch.

Red.—Cochineal carmine, carthamic acid (from saffron), redwood, artificial alizarin and purpurin, cherry and beet juices, lakes prepared with these substances.

Orange.—Annatto; mixtures of harmless red and yellow colors.

Yellow.—Saffron, safflower, turmeric, quercitron, extract of yellow wood, French berries; aluminous lakes prepared with these colors.

Green.—Spinach green, Chinese green; mixtures of harmless blue and yellow colors.

Violet.—Archil, India wood; mixtures of harmless blue and red colors.

Blue.—Indigo, litmus, Archil blue.

Brown.—Caramel, liquorice, extract of chestnut wood, extract of catechu.

II. SUBSTANCES NOT TO BE EMPLOYED.

Mineral Colors.

Containing Copper.—Mountain blue.

Containing Lead.—Massicot red lead, orange mineral, Paris yellow, Cassel's yellow, Turner's yellow, white lead, silver white, Naples yellow, chrome yellow, orange chrome.

Containing Barium.—Barium chromate, yellow ultramarine.

Containing Arsenicum.—Copper arsenite, Scheele's green, Schweinfurth green, mixed green, also mercuric sulphide (vermilion).

Organic Colors.

Gamboge, aconite, fuchsin, and derivatives, *e. g.*, Lyons blue, eosin. Colors containing nitro-groups, *e. g.*, naphthol yellow, Victoria yellow. Colors prepared from diazo-compounds, *e. g.*, tropæolins and xylidine red.

ITALY.

[An abstract of these regulations is given by Dr. Weyl in the original Italian. They provide that the sale, keeping for sale, or dealing in any article of food or drink which is known to be spoiled, diseased, adulterated, or otherwise injurious to health, and contrary to the regulations, may be punished by fine or imprisonment, maximum and minimum penalties and terms being enumerated.

The manufacture and sale of vessels, etc., intended to contain articles of food and drink, which vessels, etc., contain or are coated with any metal or varnish or other covering, which may be likely to make the food injurious, are forbidden.

The Superior Council of Health, with the approval of the Minister of the Interior, is authorized to issue a list of colors considered injurious, and which are not to be used in the preparation of food, drink, toys, household articles, etc. Heavy fines are imposed in case of the use of the substances so prohibited.]

Abstract from regulations of the administration of the municipality of Milan, (not yet proclaimed).

A. It is forbidden to add coloring matters of any kind to the naturally colored articles of food and drink, such as wine, wine-vinegar, fruit juices, preserved fruits, preserved vegetables, such as saffron, etc.

Paper, tissue, etc., used for wrapping articles of food, must not be colored with poisonous colors, and the colors denominated as poisonous in the law of the German Empire of July 5th, 1887, are hereby designated as poisonous.

For the coloring of articles of food and drink not naturally colored, and of which the practice of artificial coloring is well known, for instance, liquors and confections, the employment of the poisonous colors referred to above, as well as all coal-tar colors not cited below, is until further notice forbidden: certain azo-colors and purpurin are permitted. Inasmuch as several of the colors here designated occur in commerce under various names, any one who intends to employ such color will be obliged to ascertain whether it belongs to the permitted class.

AUSTRIO-HUNGARY.

In the official announcement of March 4, 1824, Z. 11379, the harmful colors which are not allowed to be used for painting toys, or for candies, and the harmless ones which are permitted for these purposes, are enumerated as follows:—

A. NOT ALLOWED FOR PAINTING TOYS.

White lead, zinc white.

Orpiment, king's yellow, Naples yellow, massicot, English yellow, mineral yellow, chrome yellow, and gamboge.

Verdigris, Braunschweig green, mountain green, Bremen green, Swedish or Scheele's green, mitis green, Vienna green, Schweinfurth green.

Mountain blue, mineral blue, smaltz, Berlin blue, when containing copper.

Vermilion, red lead.

HARMLESS AND THEREFORE PERMITTED.

Chalk, gypsum, white bone ash, ivory white, hartshorn ash.

Dutch pink, turmeric, yellow ochre, orlean (an infusion of yellow wood mixed with one-fourth of alum and gum.)

Sap green, all greens made from harmless yellow and blue colors, Veronese green.

Pure Berlin blue, new blue, indigo solution with starch, Saxon blue, solution of indigo in sulphuric acid, litmus, sap blue, and cornflower blue.

Carmine, lac, stick-seed, madder, and Florentine lac, Armenian bolus, pure ferric oxide, Pernambuco and Brazil wood infusion, mixed with alum and gum.

B. For candies the following colors are regarded as harmful: cinnabar and red lead, yellow, blue and green, colors above designated as harmful, with mixtures of such yellow and red colors and such red and blue colors, imitation gold and silver leaf. As harmless, the following: juice of red berries, kermes, bearberry, red-beet juice, onion peelings, infusions of cochineal with cream of tartar, of red poppies, of bluebottle (Centaurea cyanus, L.), saffron, safflower, turmeric, infusion of marigold flowers, expressed juice of blue flowers, such as bluebottles and violets, litmus, spinach juice, mixtures of harmless yellow and blue colors. Pomegranate yellow, decoction of oleander with sodium hydroxide, cochineal infusion with lime water, mixtures of harmless blue and red colors, genuine gold and silver leaf.

II. According to the ministerial announcement of September 19, 1848, Z. 3075, of a governmental order of October 5, 1848, Z. 53 169, only the following colors are to be used for painting edibles, confections, and tragacanth preparations, as well as all show pieces prepared by candy makers and not intended for consumption.

White.—Tragacanth.

Red.—Cochineal, carmine, kermes, infusion of red poppy.

Yellow.—Saffron, safflower, and turmeric.

Blue.—March violet, bluebottle, indigo, Prussian blue, ultramarine, sea blue (a form of artificial ultramarine).

Green.—Spinach juice, mixtures of permissible blue and yellow colors.

Violet.—Mixtures of harmless blue and red colors, cochineal infusion with lime water.

Gold Color.—Pure gold leaf.

Silver Color.—Pure silver leaf.

All other colors, no matter what name they may bear, are forbidden to the extent that even to keep them in stock in the business department or work rooms of any given establishment, will constitute an infringement of these regulations and bring about liability to the penalties provided.

III. In accordance with the orders of the government of lower Austria (January 23, 1859, Z. 55507), the provisions for the employment of Alpine red (murexide) as a color were designated as follows: "This color can only be made permanent by the employment of mercuric chloride. In its preparation the workmen come frequently and for considerable periods in contact with the mercuric chloride, and by neglect of the proper precautions, serious results must occur. To prevent, as far as possible, the injuries that must follow long contact with materials charged with this substance, it is necessary that the workmen engaged in using murexide avoid handling it with abraded hands; that they should not allow the mercuric chloride solution to remain in contact with the skin longer than is absolutely necessary, and as often as such contact occurs should rinse their hands with clean water, and take especial care to wash the hands prior to taking or preparing food. This information is given in order that those in charge of such establishments shall not neglect to give necessary instructions to workmen."

IV. Regulations promulgated, May 1, 1866, by the Imperial Secretary of State for Austria, relating to the employment of poisonous colors and unwholesome preparations in various articles of household use, and to the sale of the same. (R. G. Bl. Royal Austrian Empire, p. 137.) Quoted from publications of the Imperial Health Office, 1887, 351, No. 23. The employment of colors containing metals (except iron), gamboge, picric acid, or aniline, is forbidden for all articles of consumption, food or drink, including devices and figures made from starch and sugar. Preparations and colors containing arsenicum, antimony, lead, cadmium, copper, cobalt, nickel, mercury (with the exception of pure mercuric sulphide), zinc, or gamboge, are not to be employed for coloring or decorating children's toys. The materials, the employment of which is forbidden in the above paragraphs, or conditionally permitted, are not to be used on earthenware employed for holding food, except when the coloring material is burnt in. Artificial flowers colored with arsenicum compounds, or natural flowers of which any part may have been tinted by dipping in arsenical solution, are only allowed when the falling off of any of the material is completely prevented by varnish. Tapestry containing arsenical colors will only be allowed when the portions so colored are protected by a varnish coating. The employment of arsenical colors for the painting of walls of living rooms, or other places where persons collect, is forbidden. The employment of any substance which in any form or manner in which it is used endangers health, is forbidden in the preparation of articles of food, table and culinary ware, clothing, and all kinds of toilet articles. In addition to the manufacture of the articles which do not accord with the preceding conditions, trading, retailing, or other dealing in them is forbidden. Violations of these regulations which are not provided for by the general penal code are punishable by the provisions of the regular ministerial orders of September 30, 1881, R. G. P. L. 198. Signed, Count Belcredi, m. p.; Baron von Wüllerstorf, M. P.; Kt. von Komers, m. p.

V. In reply to a formal question as to what course is to be pursued when articles of food have been found to be colored with aniline red, free from arsenicum, and, therefore, not injurious to health, the Royal Imperial Secretary of the Interior, by a proclamation of November 21, 1881, Z. 16033 (State proclamation, December 19, 1881, Z. 75960) after consultation with the chief sanitary authority determined not to amend the regulations of May 1, 1866, since, although it is a fact that fuchsin free from arsenicum, is now in the market, no evidence is at hand that a preparation of poisonous quality is not in commerce under the same name. Further, the question as to the poisonous or non-poisonous character of the aniline colors free from metal is still in dispute, and observations are on record to the effect that the continued consumption of liquids colored by fuchsin free from arsenicum has resulted in material disturbances of health. The use of fuchsin as a coloring material in all kinds of food is all the less to be permitted since coloring matters are not wanting which suffice for the purpose and are unsuspicious from a sanitary point of view.

VI. Regulations of the Royal Imperial Austrian Secretary of the Interior concerning the employment of aniline or other coal-tar colors in the preparation of articles of food, dated March 1, 1886, R. G. P. L. (Reichsgesetzblatt für die im Reichrathe vertretenen Königreiche und Länder. Quoted from the publications of the Imperial Health Office, Germany, 1886, 348). The employment of colors produced by chemical treatment of the aniline or other coal-tar derivatives, including rosolic acid produced by various methods, in the preparation of all articles of food, is prohibited.

In accord with §§ 1 and 6 of regulations of May 1, 1866. Taaffe, m. p., Prezák, m. p., Pino, m. p.

VII. Supplement relating to the application of rosolic acid to the coloring of articles of food, added by the Royal Imperial Austrian Secretary of the Interior. (Quoted from the publications of the Imperial Health Office, 1887, 351, 23.) In answer to the formal question as to the permissibility of the use of rosolic acid for coloring articles of food, the following is issued with the consent of the chief sanitary authority: "In view of the more exact information acquired as to the composition of the compounds obtained from rosaniline by chemical action and applicable as coloring materials, the expression in § 1 of the regulations of May 1, 1866, 'the employment of colors which contain aniline,' etc., must not be taken in the sense that the said colors contain aniline, but rather the expression must be understood to mean colors produced by chemical action on aniline. In this sense, rosolic acid prepared from rosaniline must be regarded as a derivative of the latter, and hence, as an aniline color, is subject to the conditions of § 1 of the aforementioned regulations. As to the second variety of rosolic acid prepared by the action of oxalic acid upon carbolic acid, which differs as to composition and properties very slightly from the acid first named, § 1 of the aforementioned regulations does not apply, but § 6 of the same does apply all the more positively, since, apart from the absence of trustworthy knowledge of the action of pure rosolic acid upon the human organism, it comes into commerce contaminated by the injurious materials employed in its manufacture, and therefore, in the manner and form in which it is employed, it is actually liable to endanger health. The Secretary of the Interior takes this opportunity to advise that recently numerous organic substances, especially prepared from coal-tar and applicable as colors, have been prepared, which on the one hand, on account of their unknown action and unknown influence on the human organism, on the other hand from their contamination with substances of suspicious influence, must not be employed in the preparation of food and drink, and therefore, are to be dealt with in accordance with provision of § 6 of the regulations above quoted."

SCOPE OF THE INVESTIGATION.

The review of the existing literature shows that certainty as to the unwholesomeness or toxic nature of the coal-tar colors has not yet been attained, and cannot be attained because researches with definite purpose are almost entirely wanting. On the other hand, the majority of civilized nations have been constrained to forbid, by rules and regulations, the employment of certain colors in the preparation of food or household articles.

Since my labors in this field forced me to the conclusion that a rational legislative control of this question could only be based upon more comprehensive information than seemed to be attainable, I resolved to test the existing statements concerning certain coal-tar colors, and further, to carry out investigations on as many of these dyes as possible. Thus, following research was inaugurated, and as already stated was pursued in strictly practical relations. Frequently, to the regret of the experimenter, interesting lines of research must be passed by, which would lead to information concerning the ultimate products resulting from the ingested substances, the origin of the toxic symptoms, and the disturbances of metabolism under the influence of the foreign materials. The abundance of new observations offered added an additional reason for leaving these side-issues untouched, at least in the preliminary stage. No excuse should be needed for the frequent allusion to questions of theory, since the data herewith presented are not the result of mere chance, but have been developed under the guidance of those theoretical views concerning the constitution of the coal-tar colors which have been wrought out by modern chemistry.

METHODS.

Selection of Colors.—In consequence of the great number of these colors and the constant appearance of new ones in the market, it has been impossible to test all or even the greater portion. A selection must therefore be made, and it will be well to choose first those which are in some manner suspicious, from having caused poisoning in their intentional or unintentional use. Moreover, the colors most suitable for practical use must be taken into consideration. Even a tolerably complete list of such, however, is not easy to obtain, since the employment of a given color may be a matter of fashion, and the different makers have some interest in concealing from their competitors which colors they sell in largest amount, and, further, the consumer cannot always find out what colors are used to bring about a given tint. Perhaps it may become possible to pronounce upon the harmfulness of these colors by a sort of induction when tests have been made of many colors, including the most various groups, without subjecting every one to test. A connection between chemical composition and physiological action is certainly to be expected.

It remains to be considered whether the toxicological investigation should be limited to the color in a condition of absolute purity or only to the commercial form of it. Tests of the pure colors have preëminently theoretical significance, since the degree of toxic action and the relation between chemical constitution and physiological effect can be most clearly indicated. Tests of the commercial forms, however, have greater practical value, and only when a commercial article is found to be poisonous, will it be necessary to inquire further whether the poisonous action is an essential property of the color or arises from accidental admixture. This point will be made more clear by some examples. Fuchsin and its congeners, methyl violet and malachite green, are, as is now established, almost without poisonous action. Whoever would pronounce an arsenical aniline color poisonous without being aware of its arsenical contamination, would easily fall into the error of assuming that all colors analogous to fuchsin would be poisonous. The reverse is the case with the poisonous dinitrocresol (saffron-substitute). The commercial preparation contains usually about forty per cent. of ammonium chloride. This addition does not develop the poisonous action of the color, but, as is obvious, diminishes it materially. Therefore, according to the purpose of the investigation, whether it lean toward theoretical or practical information, the toxicological experiment must deal either with the pure product or the commercial form. Should the commercial article be found poisonous, a further inquiry will be needed to determine if it can be made harmless by the removal of any impurities.

Selection of the Animals for Experiment.—Only rarely will the toxicologist be able to make researches as to the effect on human beings. At the most, a case of poisoning which has come to chemical or legal notice will be investigated scientifically. Investigations, as far as they have practical value in relation to the human organism, must be carried out on animals which in their organization and chemical functions are as near as possible similar to human beings. Physiologists know, and it will not be necessary for me to stop to establish the fact, that these requirements are best fulfilled by the dog. The ape, by reason of costliness, scarcely comes into consideration. It is naturally of great scientific interest to examine the effect of any material upon as large as possible a number of animals of various types. Even the higher and lower plants may be taken into consideration in these experiments. It must also not pass unnoticed that occasionally conclusions may be drawn from experiments on other animals. For instance, for preliminary researches, frogs and rabbits have value for economical reasons. The conclusions derived from such experiments must be accepted with great deliberation, since it happens that rabbits will bear without injury doses which will seriously, nay, even fatally act upon the dog, as I have already shown to be the case with Martius' yellow. Fishes, for instance, are only affected after several hours by doses of curara to which frogs quickly succumb. Chickens bear more than ten times, Guinea pigs more than three times, the dose of strychnine that is fatal to rabbits. Human beings are more sensitive to morphine than are Guinea pigs. These and similar facts serve to make us cautious in interpreting results obtained in experiments on dogs. It is only because we have no other satisfactory method, that we use the dog as the animal for experiment and apply the results thus obtained to the human being.

Manner of Administration.—Of course, only exactly measured and weighed doses of the material of which the effect is to be studied, should be administered to the animal. This is necessary not only in order that the results obtained by one experimenter may be susceptible of confirmation by another, but more especially because most materials do not act the same in small as in large doses. Further, the material to be tested should, whenever possible, be administered in dissolved form. In case a suitable solvent is not available, the material should be given in fine powder, or suspended in water or other liquid. The selection of the solvent is consequently of importance. Such liquids only are applicable as are either without action when administered in moderate quantity, or at least of but feeble effect: water, very dilute acids, alkalies, or salt solution are suitable. Alcoholic, ethereal, and similar solutions have but a limited application and must not be employed unless absolutely necessary. In doubtful cases, control experiments are indispensable. Omitting special cases, a substance may be administered in four different ways: by the mouth, by direct injection into blood, by hypodermic, and by endermic application.

(1) *Administration by the Mouth.*—Administration by the mouth is to be preferred unless special reasons to the contrary exist. This is best accomplished by means of the food. Frequently, however, the animal refuses to eat food mixed with foreign matters. In such a case it can either be introduced by force, or the œsophageal tube can be used. The latter consists of an elastic rubber tube of a diameter corresponding to that of the gullet, the upper end terminating in a funnel. The introduction of the apparatus requires the aid of an assistant, but generally does not involve much difficulty. It is best that any solution introduced directly into the stomach by this apparatus, should be warmed to blood heat. The quantity of liquid introduced should not exceed thirty to fifty c.c. even with large dogs. Vomiting may easily be produced if larger quantities are introduced. In order to diminish the irritating action of the substances administered, a soothing menstruum such as milk or peptone solution should be employed. Vomiting takes place more quickly on an empty stomach than with one filled with food. The œsophageal sound can be employed with good results for pumping out the stomach. The action can be assisted by pressure over the region of the stomach and by suction.

(2) *Injection into the Blood—i. e.*, intravascular administration. Injection into the blood requires the exposure of a vein or an artery, an operation that should only be performed by a trained hand. Most substances produce their effect more quickly and more powerfully through the blood than through the stomach, and in such injections the solvent plays a most im-

portant part. Watery solutions, for instance, produce coagulation of the blood and destroy the experiment. The employment of a dilute solution—say about 0.75 per cent.—of sodium chloride is more satisfactory. The introduction of large volumes of water into the blood-vessels will produce spasm.

(3) *Hypodermic Administration, i. e.*, dissolved substances introduced beneath a fold of skin by means of a suitable syringe. The back is usually chosen, or some point on the surface of the body which cannot be reached by the tongue. The skin should be shaved at the point at which the injection is made, cleaned, and disinfected. The solution, the syringe, and the canula must be sterilized. The injection must not injure the deeper tissues such as fascia and muscles. Large volumes of solution must be avoided. Not more than 10 to 15 c.c. should be injected at one point even with large animals. The effect of the hypodermic method is generally as powerful as the direct injection into the blood-vessels, and may advantageously replace it.

(4) *Endermic Application.*—Administration of material by application to the surface of the skin, is but little employed in experiments on animals, since the absorptive quality of the unbroken skin is so slight that some investigators have denied it entirely. In every case the skin must be shaved and a point chosen which cannot be reached by the tongue. If, however, the upper layers of the skin are removed by blistering, or incisions, and wounds are made on the skin, substances applied at such points will be absorbed into the lymph or blood. We have in such a case conditions analogous to those under which a color or a mordant on a fabric in direct contact with the skin may produce poisoning. Many substances, for instance, quicksilver, may be forced through the unbroken skin by pressure.

Diagnosis of Poisoning.—Of the various symptoms which may be exhibited by the human organism under the influence of poisoning, the most important series is almost entirely lost in experiments on animals, namely, the subjective symptoms. In animals we cannot expect to appreciate the manifold disturbances of sensation and ideation, feelings of discomfort, slight disturbances of sight and hearing, which, among human beings, may alone constitute a clue to the poisoning. For instance, a particular form of local anæsthesia and amaurosis is typical of lead poisoning. Moreover, the recognition of the objective symptoms of poisoning, especially when they are not well developed, depends upon an exact knowledge of the special nature of the animal in a state of health. Pulse and respiration rate, normal temperature variations in different portions of the body, amount and number of the discharges, composition of the secretions and organs, all must be known to the one who would with certainty detect departures from the standard. Examination of the urine is of special diagnostic value. A dark, almost black, secretion is discharged in carbolic acid poisoning; an abundant but pale urine occurs in various disturbances of the circulation. A high specific gravity indicates increased tissue disturbances, such as occur in fever. An alteration of the chemical reaction occurs after the administration of the salts of the organic acids. These are converted into the alkaline carbonates and then excreted. This is the reason that the secretion in the case of vegetable feeders, in the food of which the salts of the organic acids are found, gives an alkaline reaction, while in meat-eating animals it generally exhibits an acid or neutral reaction. Moreover, changes in the blood, especially in the blood-coloring matter, may serve as a clue to the detection of poisoning, the method involving, as a rule, the employment of a spectroscope. Thus, in cases of poisoning by illuminating gas, the blood may contain in addition to normal hæmoglobin, the carboxyhæmoglobin; after large doses of potassium chlorate or potassium ferricyanide, methæmoglobin will be present. Inhalations of hydrogen sulphide produce a characteristic alteration of the blood-coloring matter. The appearance of abnormal ingredients in the urine will also frequently give most important information. Blood-coloring matters appear, for instance, in cases of poisoning by hydrogen arsenide; sugar is found in poisoning by carbon-monoxide and nitrobenzene; sulphates are wanting after toxic doses of carbolic acid, and the secretion is rich in phenol; albumin is frequently referable to an affection of the kidneys, as is noted in poisoning by cantharides and β-naphthol.

Bile acids and bile coloring matters are also observed in pathological urines. Scarcely less important than the observations on the living creatures is the anatomical investigation after death, especially with a view to determining the mode of action. Some poisons accumulate in the organism and may be detected after a long time. Lead, for instance, accumulates in the bones, kidneys, and liver; copper, principally in the muscles; arsenic in the intestines, kidneys, and liver. Many poisons, such as acids and alkalies, have a local corrosive action, other substances must enter the general circulation before they can produce pathological changes. To the latter class belongs phosphorus, which, on the one hand, modifies, in a most remarkable manner, the tissue metabolism; on the other hand, brings about an extensive fatty degeneration of liver, kidney, heart, and blood-vessels. There are also many poisons that produce death quickly without any pathological changes, that are up to the present time recognizable by us. These can be classified according to the points at which their effects are most distinctly manifested, into heart, nerve, and blood poisons. In the first class we place muscarine and several ptomaïnes closely related to it. Among the blood poisons we enumerate carbon monoxide, hydrogen sulphide, amyl nitrite. In the third class we find, pre-eminently, hydrogen cyanide; further, strychnine, nicotine, chloroform, curare, and probably most of the ptomaïnes. I may here point out a source of error which may be serious in observing cases of chronic poisoning in animals, that after a long time have perished or been killed after a prolonged delay. I refer to infection by reason of unclean instruments and unclean and insufficiently ventilated places of confinement. Only the greatest cleanliness and most exact anatomical investigation will avoid these sources of error. From this brief notice concerning the diagnosis of poisoning it will appear that the decision as to whether a substance is or is not poisonous can only be given by an expert.

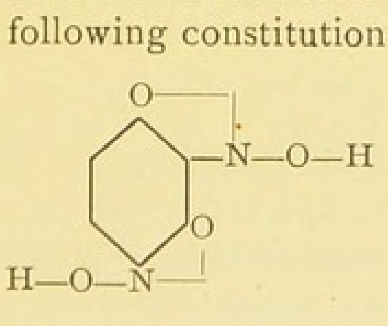
SPECIAL PART.

NITROSO-COLORS.

By the action of nitrous acid upon certain of the phenol derivatives and their sulphonic acids, bodies are produced which form salt-like combinations with iron, nickel, and cobalt. These have coloring qualities and are tolerably permanent. Iron, nickel, and cobalt can be detected only after ashing the material. These colors probably contain the dyad isonitroso-group NHO, and are, therefore, preferably called isonitroso-colors. The metals substitute the hydrogen atom of the isonitroso-group. These colors dye wool, silk, and cotton tolerably fast. They are either produced upon the fibre, as in the color known as solid green (see below), or the fibre is impregnated with a ready formed color, as is the case with naphthol green B. Investigations as to the effects of the nitroso-colors upon the animal organisms are apparently not yet on record.

Dinitrosoresorcinol.

This compound, preferably called diisonitrosoresorcinol, is produced by the action of sodium nitrite, at a low temperature, upon a solution of resorcinol in dilute acetic acid. According to Kostanecki it has the following constitution :—



It crystallizes from hot water, or hot dilute alcohol, in glistening, brownish-yellow plates containing two molecules of water of crystallization. It dissolves with difficulty in cold water, better in alcohol, more easily in hot water and hot alcohol. It is insoluble in benzene and ether. It explodes lightly at 115°. The alcoholic solution quickly becomes brown when exposed to the air.

Typical Reactions.—The green color which the ferrous salts produce with the aqueous solution is a test for this body. This green solution is bleached by reducing agents. The dye produces, on cotton, mordanted with iron salts, a dark green, which is fairly fast to soap and light. The color thus produced is known as resorcinol green, Alsace green, or solid green.

Exp. 1.—Dog weighing 11,550 grams. June 18th, two grams in a small amount of sodium hydroxide, administered by the œsophageal tube. June 19th, animal lively; urine scanty; neutral; dark brown; producing with ferrous salts a dark green color not destroyed by dilute acetic or muriatic acid. Two grams similarly administered. Urine 600 c.c.; dark brown, traces of albumin. Iron reaction very distinct, slightly alkaline, Fehling's solution not reduced. June 20th, two grams as usual; animal lively. June 21st, three grams; animal lively; no albumin. June 22d, condition same; weight, 11,140 grams; loss about 400 grams; experiment relinquished.

Exp. 2.—Dog weighing 5500 grams. July 13th, one gram by the tube. July 14th, very little eaten; urine dark brown, almost black. With ferrous sulphate produces green color and in time a green precipitate. July 15th, two grams by the tube. July 16th, urine colored green by ferrous oxide; no albumin; no reduction of alkaline solution. Acids produce a black flocculent precipitate. July 17th, animal lively; three grams administered; urine deep black in color. July 19th and 20th, animal lively; relinquished; urine contained some albumin and produced, with dilute sulphuric acid, a brown flocculent precipitate. This was collected on a filtrate and was found to be tolerably easily soluble in water, and again precipitated from the filtered solution by dilute sulphuric acid. This body was colored green by ferrous salts. The filtrate from the precipitation by acids did not produce, even after neutralization, any green color with ferrous salts.*

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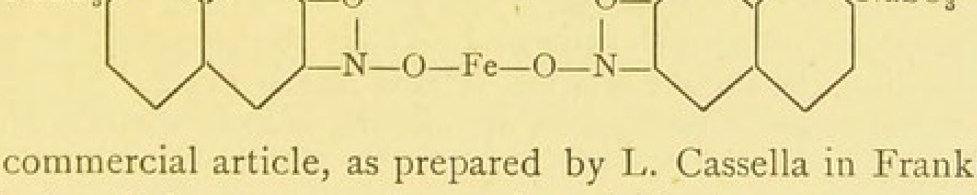
* I will refer elsewhere to this flocculent precipitate, as well as to another substance which is soluble in ether.

Exp. 3.—Dog weighing 5250 grams. July 4th, one o'clock in the afternoon, one gram dissolved in about ten c.c. of water, assisted by sodium hydroxide, introduced beneath skin of back. In the evening the animal was very weak. Urine 50 c.c.; almost black. No green color produced by ferrous salts. Sulphates present, also traces of albumin. On adding an acid, a brown flocculent precipitate appeared which was soluble in alkalies. On distilling in hydrochloric acid, no substance precipitable by bromine water passed into the distillate. July 5th, animal very dull, refused all food and died about two o'clock in the afternoon. Post mortem made on July 6th. Body rigid; all abdominal organs hyperæmic; lung hyperæmic; heart contained a good deal of non-coagulated blood. Vessels of the cerebral membrane strongly injected; brain substance œdematous. None of the organs tested exhibited the green color with ferrous salts.

According to the above experiments, diisonitrosoresorcinol is not dangerous to dogs when administered by the stomach even in large doses, while hypodermic administration proves fatal within twenty-four hours in the proportion of 0.19 grams per kilogram of the body-weight.

Naphthol Green B.

Naphthol green B, sodium ferrous nitrosonaphtholsulphonate, is produced from Schaeffer's acid (β-naphtholmonosulphonic acid) by the action of nitrous acid. According to G. Schultz, it has the following constitution:—



The commercial article, as prepared by L. Cassella in Frankfurt o. M., is a dark green powder, easily soluble to a green solution in water.

Typical Reactions.—Sulphuric acid added to the powder produces a yellow color, no precipitate appearing on diluting with water. Dilute acids do not alter the solution in water. Concentrated acids produce a yellow color. Alkalies restore the green color except when the acid has been acting for a considerable time. The green solution becomes yellow on being heated with sodium hydroxide. Ether shaken with alkaline solution does not take up the color. The green solution bleaches ultimately when heated with stannous chloride and hydrochloric acid. The powder heated on platinum foil leaves a residue containing ferrous sulphide.

I am indebted to Messrs. L. Cassella & Co. for the sample of naphthol green B with which the experiments given below were made, which show, so far as the administration by the stomach is concerned, the material to be harmless.

Exp. 1.—Dog weighing 5800 grams, the urine of which, on May 13th and 14th, contained traces of albumin. May 15th, one gram of naphthol green B, in small quantity of water administered by the tube. May 16th, animal quite lively; conjunctiva stained intensely green; urine greenish. One gram as usual. May 17th, one gram; urine green. May 18th, five grams by the tube; animal lively. May 19th, appetite undisturbed; animal lively; relinquished.

Exp. 2.—Dog weighing 4800 grams. May 12th to 14th, urine free from albumin. May 15th, naphthol green B, two grams by the tube; urine dirty yellowish green; no albumin; no iron by the usual reagents. After boiling for three-fourths of an hour with fuming nitric acid only traces of iron could be detected. May 16th, animal normal. May 17th, two grams by the tube; condition still unchanged; eats heartily; urine yellowish green; no sugar; no albumin. May 18th, animal quite lively; fæces normal, but colored green. The watery extract gives a green reaction with sodium or ammonium hydroxide, and red with acids. The yellowish green urine behaves in the same manner with acids and alkalies; no albumin; no sugar. On standing, the surface of urine became almost black. By mistake the animal received two grams of safranin, and the experiment was discontinued.

Exp. 3.—Dog weighing 5650 grams. May 20th to 23d, no albumin in urine. May 24th, two grams dissolved in twenty-five c.c., administered hypodermically; animal quite lively, taking food well. Conjunctiva, gums, and mucous membrane of the jaw colored green. May 25th, two grams in twenty-five c.c. hypodermically, animal lively. May 26th, 27th, and 28th, the same. May 29th, animal lively; no abscesses; relinquished.

Exp. 4.—Dog weighing 5015 grams. May 22d to 24th, doubtful traces of albumin. May 25th, two grams in twenty-five c.c., hypodermically; twenty minutes after the injection, conjunctiva, mucous membrane of the jaws and gums were colored green. Animal lively; urine scanty, intensely green in color. May 26th, two grams hypodermically; animal lively. May 27th and 28th, two grams, similarly; urine intensely red when acidified. May 29th, animal lost weight. No injection; wool is colored intensely dark green by the urine slightly acidulated with sulphuric acid. May 30th, animal weak and feverish; inner surface of the pinna green, as well as conjunctiva. June 1st, many abscesses on the back. June 2d, animal dead. Six pus sacs. Post-mortem presented same appearance as in following experiment.

Exp. 5.—Dog weighing 5600 grams. May 18th, hypodermic injection; in twenty minutes conjunctiva became intensely green. May 19th, similarly. Urine intensely green. May 20th and 21st, similarly, colors wool intensely green. May 22d, animal lively; no abscesses; weight 5450 grams, therefore about 150 grams lost. May 24th, several abscesses on the back. May 26th, animal very weak; killed. Post-mortem: Three large abscesses beneath skin on back, from which on pressure a greenish non-offensive pus escaped. Subcutaneous cellular tissue and the serous membranes, peritoneum, pericardium, endocardium, and pleura, colored deep green. Liver and spleen also colored green. In the kidneys, the glomeruli were not colored, but the uriniferous tubules were green.

Exps. 1 and 2, in which two to five grams per day of the color were introduced directly into the stomach, demonstrated its harmlessness in this method of administration. On the other hand, in the hypodermic administration, in two out of three cases, abscesses and septic fever were induced. Infection by means of the syringe is unlikely, since other animals for which the same instrument was employed, remained free from abscesses. The places of confinement also seemed free from suspicion. I must rather regard the color as poisonous when applied hypodermically, and assume that in the third experiment the animal, which seemed in good health when relinquished had not been kept sufficiently long under observation. The coloration of the conjunctiva and the inner surface of the pinna in about twenty minutes after the injection, is an interesting physiological phenomenon.

NITRO-COLORS.

Nitro-colors contain the monad nitro-group NO_2. They are produced by the action of nitric acid upon the benzene derivatives (nitration) and are, like most nitro-compounds, more or less explosive by heat or percussion. Reducing agents convert them, as a rule, into colorless amido-derivatives. Picric acid, for instance, a nitro-compound, produces by proper reduction triamidophenol, an amido-body.

The nitro-colors are mostly orange or yellow-colored salts of nitro-compounds. They dye wool and silk the corresponding color. They serve this purpose only in a restricted degree at the present time, since they have been replaced by faster colors. Picric acid is by far the most used of the nitro-colors and has long been known to be poisonous. With the exception of this, the use of which is now prohibited by Imperial enactment, these nitro-colors are now largely employed for coloring food. Most nitro-colors, that is the salts of the nitro-compounds, are not very freely soluble in water. *

The watery solution of these colors is mostly precipitated, even when largely diluted, by ammoniacal copper solution.† Warming with potassium cyanide generally produces the so-called iso-purpuric acid reaction. The copper salt of brilliant yellow (Schoellkopf) and dinitrocresol are very easily soluble, and are therefore precipitated only after long standing or not at all.

The following table will serve for the recognition of the more

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* Colors which contain a nitro-group are not necessarily nitro-colors. We include in the group rather those bodies the color of which depends upon the presence of the chromophorous nitro-group. The nitro-azo-colors, for instance, belong to the azo-group, since the azo-group, $-N=N-$, not the nitro-group, is the characteristic structure.

† The behavior of the following colors with ammoniacal copper solution was tested by the author: picric acid, dinitrocresol, Martius' yellow, naphthol yellow S, brilliant yellow, aurantia.

important nitro-colors. The solution to be tested must contain at least 1 per cent. of a salt of the color.

The watery solution of the color is treated with sodium hydroxide.

(A) A precipitate appears either promptly or after standing.

(1) The original solution produces with hydrochloric acid a precipitate soluble in ether to a pale yellow color. With ferric chloride a flocculent yellowish-white precipitate is produced. The substance is free from sulphur: *Martius' yellow.*

(2) The original color remains clear upon addition of hydrochloric acid and becomes a bright green. The original solution is momentarily colored red-brown by ferric chloride, then permanently dark green. The body contains sulphur:

Brilliant yellow (Schoellkopf).

(B) The solution treated with sodium hydroxide remains clear.

(1) Ammoniacal copper solution produces no precipitate, or only after long standing.

Hydrochloric acid bleaches the original solution. Ferric chloride produces a flocculent precipitate easily soluble in water. On boiling with ferric chloride, the solution becomes red; on cooling a flocculent precipitate is separated:

Dinitrocresol (*saffron-substitute*).

(2) With ammoniacal copper solution a precipitate, mostly crystalline, is formed.

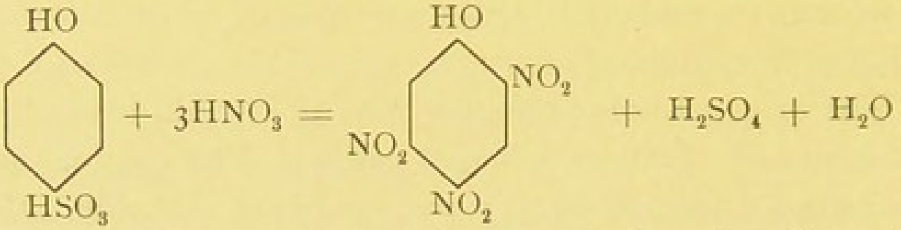
Hydrochloric acid produces a precipitate in the original solution, which is soluble in ether to a yellow color: *Aurantia.*

Hydrochloric acid produces no precipitate in the original solution. By reduction with stannous chloride and hydrochloric acid, and subsequent addition of ferrous chloride, a golden yellow solution is produced: *Naphthol yellow S.*

By reduction with hydrochloric acid and stannous chloride, and subsequent addition of ferrous chloride, a blue solution is produced: *Picric acid.*

Picric Acid.

This is produced by the action of nitric acid upon phenolsulphonic acids, ortho- or paranitrophenol, α- or β-dinitrophenol and certain resins. The action of nitric acid upon silk, wool, leather, and similar substances also gives rise to picric acid. The commercial article is almost entirely prepared by the action of nitric acid upon phenolsulphonic acid :—



Pure picric acid crystallizes from water in pale yellow shining plates, from ether, in rhombic prisms. By cautious heating it sublimes unchanged, but strongly heated, it explodes. It melts at 122.5. It is difficultly soluble in cold water ; easily soluble in hot ; also in alcohol, ether, and benzene. These solutions are yellow and intensely bitter. Picrates explode by percussion and on heating. Sodium picrate is much more soluble than the potassium salt.

Typical Reactions.—In concentrated sulphuric acid the powder dissolves without color, and the watery solution is not changed by a few drops of dilute hydrochloric acid. (Distinction from brilliant yellow, Martius' yellow, aurantia, and dinitrocresol.) Ether shaken with the acid solution extracts the picric acid and becomes yellow in color ; potassium cyanide added to this solution produces a red-brown color. The test with potassium cyanide is due to formation of isopurpuric acid ; it can also be applied to watery solution of the color. This isopurpuric reaction is shown by all the nitro-colors tested. Picric acid, when treated with ammoniacal copper sulphate, consisting of equal volumes of copper sulphate solution (1 : 12) and ammonium hydroxide, produces, even in dilute solutions, a yellow crystalline precipitate, which dissolves in hydrochloric acid to a clear liquid (distinction between Martius' yellow and aurantia). The solution in hot water is colored dark brown-red by boiling with potassium cyanide. Copper picrate is insoluble in alcohol. Ammonium picrate produces with sodium hydroxide no precipitate (distinction from brilliant yellow). Picric acid, by reduction with alcoholic solution of ammonium sulphide, forms a red solution of picramic acid (dinitroamidophenol). Hydrochloric acid solution of stannous chloride produces triamidophenol, which, by addition of small amount of ferric chloride, becomes diimidoamidophenol (distinction from all remaining nitro-colors). Ferric chloride produces with picric acid a reddish yellow precipitate, rather easily soluble in water. To detect the acid in textiles and foods, it must be extracted. This is best accomplished by producing an ethereal solution and shaking it with a little alkali. The alkaline picrate can then be tested for by reactions numbers two, four, and seven just mentioned.

Applications.—Picric acid was formerly largely used, either alone or in association with other colors, for dyeing silk, wool and artificial flowers, yellow. It has also been employed in foods, and has had some applications in medicine. In Germany its employment for coloring food is forbidden by the Imperial enactment of 1888, on account of its poisonous character. The poisonous qualities of picric acid have been much exaggerated. Erb gave a rabbit weighing 1700 grams, .06 gram of potassium picrate daily for ninety days. Slight loss of weight and, occasional diarrhœa were noted, but nothing more serious. A rabbit weighing 2065 grams died at the end of nineteen days, after having taken 2.52 grams of the substance.

A very young dog received daily, from April 21st to 26th, .24 gram of sodium picrate. From April 28th to May 9th, .36 gram daily of the same, and, therefore, received in the course of about two weeks 5.76 grams of sodium picrate without the appearance of any serious phenomena. May 13th, the same animal received in one dose 1.2 grams of sodium picrate. On the following day it was quite weak, marked diarrhœa and dyspnœa appearing. May 14th, .6 gram were administered, which caused vomiting. About evening .36 gram were administered. May 15th, animal lively; .24 gram was again given, and in the evening of the same day, .72 gram. May 16th, marked weakness was manifested, and .16 gram of the salt was administered. Marked vomiting ensued. On May 17th, .72 gram was given. May 18th and 19th, animal had distinctly recovered, and, with the exception of a strong yellow tinge of the conjunctiva and skin, no abnormal conditions were manifest. Not until May 20th did the animal finally succumb, after the administration of 1.32 gram of potassium picrate. This dog had taken the enormous dose of 10.5 grams in the course of four weeks, of which .9 gram of sodium and potassum picrate, respectively, had been administered hypodermically. Even after the administration of 8.5 grams the dog was tolerably well. Dogs are, therefore, resisting to this substance, notwithstanding the prostration and the blood disorganization. (Note.—.6 gram administered May 14th was not taken into consideration in the experiment, being mostly expelled by vomiting.

We are also tolerably familiar with the action of picric acid and picrates upon human beings by reason of the therapeutic applications and also from some cases of poisoning. Daily doses from .54 to .90 gram of potassium picrate are easily borne by healthy adults for a considerable time. Generally after twenty-four hours a distinct yellow tint of the skin and conjunctiva ensues. The urine is dark-colored and contains, among other substances, small amounts of the acid. Children and weak adults bear picric acid badly. Picric acid was formerly employed in place of quinine in cases of intermittent fever. Doses of from 0.3 to 0.9 gram were administered three times per day, apparently without results. It has also been employed as an anthelmintic. It is valueless for the removal of trichinæ and cysticerci, but has been commended in the treatment of some other intestinal parasites. It has also been employed in the treatment of coughs, dyspepsia, chlorosis, etc. Few cases of picric acid poisoning are recorded, and none of them were fatal.* In a case reported by Adler, a school-girl, aged sixteen, took from three to five grams of the acid. Vomiting and diarrhœa occurred promptly. She became chlorotic and the skin of the whole body

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* L. Lewin ("Lehrb. f. Toxicol.," 1885, p. 229) found record of only three cases of poisoning by picric acid. Since then the case quoted above, reported by Adler, has occurred.

became intensely dark yellow, almost brown, so that the patient appeared to be jaundiced. The visible mucous membrane was pale. The fingers of both hands were flexed at the metacarpo-phalangeal articulations, but the fingers themselves remained straight and rigid and could not be actively moved by the patient. The blood contained many white and few red corpuscles. Ludwig found picric acid in the urine. The girl recovered in about a week.

The foregoing statements show that while the acid must be considered poisonous, its injurious character is far less than has generally been assumed. Nevertheless, the legal prohibition of its use as a coloring matter for food or drink is just.

Dinitrocresol. Saffron-substitute.

The color variously known as saffron-substitute, golden yellow, Victoria yellow, Victoria orange, and aniline orange, consists of the potassium or ammonium salt of dinitrocresol. It is obtained by the nitration of cresolsulphonic acid:—

$$C_6H_3(CH_3)(HO)(HSO_3) + 2HNO_3 =$$
$$C_6H_2(CH_3)(HO)(NO_2)_2 + H_2SO_4 + H_2O,$$

and corresponds to the formula:—

$$C_6H_2(CH_3)(KO)(NO_2)_2 \text{ or } C_6H_2(CH_3)(NH_4O)(NO_2)_2.$$

The Victoria yellow, produced by the nitration of orthocresol, is distinguished by its yellow color from the redder saffron-substitute produced from paracresol. The potassium and ammonium salts dissolve in alcohol and water rather easily. The concentrated solutions are orange; by dilution they become yellow. The dry color explodes on heating. The commercial article is mixed with about forty per cent. of ammonium chloride to prevent explosion and make the materials transportable.

Typical Reactions.—The powder dissolves in concentrated sulphuric acid without color. The addition of water produces no precipitate (distinction from Martius' yellow). The watery solution of the potassium or ammonium salt becomes colorless or weak yellow by addition of hydrochloric or sulphuric acid, and the free dinitrocresol separates in pale yellow needles (distinction from picric acid). The precipitate is soluble in alcohol. Ether extracts the color acid from the acidified solution and becomes pale yellow (distinction from picric acid). Alkali added to the ethereal solution produces a yellowish brown color. The aqueous or alcoholic solution of the color produces a dark brown on heating with potassium cyanide. The aqueous solution of the commercial saffron-substitute is not precipitated even after prolonged standing by the above mentioned ammoniacal copper solution (distinction from Martius' yellow, naphthol yellow S, aurantia, and picric acid). Occasionally, after twenty-four hours, a small amount of flocculent precipitate separates. (Weyl.) (See brilliant yellow.) The dry salts of dinitrocresol explode when heated. Ferric chloride produces, in the aqueous solution, a pale yellow precipitate easily soluble in water. Heated with ferric chloride, the solution becomes red; on cooling a flocculent precipitate separates. Sodium hydroxide produces no precipitate (distinction from brilliant yellow). Hydrochloric acid solution of stannous chloride produces, in the presence of ammonium hydroxide, a red color; in the presence of ferric chloride, an orange yellow solution (compare picric acid).

The uses of these colors are almost entirely limited to the coloring of food and drink, such as noodles, cakes, and liquors. The orange color produced by dinitrocresol on silk and wool rubs off easily, and it is, therefore, not in favor. Saffron-substitute is, as the following experiments show, a powerful poison. My investigations were conducted with six samples, the sources of which were as follows:—

(*a*) From the collection in the laboratory of organic chemistry at the Berlin Polytechnic, kindly placed at my disposal by Professor Liebermann. This sample consisted almost entirely of potassium dinitrocresol.

(*b*) A sample kindly furnished by Dr. Martius, of Berlin.

(*c*) The commercial article from Schuster & Co., of Eutrisch, near Leipzig.

(*d*) The commercial article from Ed. Sauppe, in Doebeln.

(*e*) The commercial article from M. Mittenzwey, in Poelbitz.

(*f*) A sample from the case of poisoning in Bremerhaven.

c, *d*, and *e* each contain about forty per cent. of ammonium chloride.

The various preparations were very similar. They were yellowish-red micro-crystalline powders. The sample from the collection of the Berlin laboratory consisted of distinct crystals which had a silver lustre in reflected light.

Experiments on Rabbits.—Animals to which .25 gram of dinitrocresol salt, dissolved in a small quantity of water, were administered by the œsophageal tube exhibited the following symptoms: For a short time after the administration they were not visibly depressed. They hopped about the room and showed no abnormal condition. The respirations, however, soon became more rapid. The animals became quiet, and occasionally fell to one side. In forward movements, the hind limbs dragged. The muzzle touched the ground, but could again be raised, and the animal was still able to move forward. The pupils were generally dilated, in some cases contracted just before death. The breathing gradually became more rapid, and occasionally ceased for a time, the animal at this time lying on one side, the head touching the ground. The eyes, the bulbs of the conjunctiva, were insensitive, and the pupils strongly dilated. The extremities exhibited twitchings. Finally, spasms supervened. As a general rule, Cheyne-Stokes respiration occurred. The intervals between the respirations increased slowly until they reached from ten to fifteen seconds, at which time death ensued from asphyxia. Usually, the head was drawn backward and there was general but brief spasm of the extensors. In two cases, Exps. 1 and 3, as the annexed table shows, these symptoms ran their courses in from twenty to thirty minutes, and in these cases the preparation used was, as stated above, a nearly pure potassium dinitrocresol. In the ninth experiment death occurred after two hours. The following notes on experiments will give more precise information :—

EXPERIMENTS ON RABBITS—ADMINISTRATION BY STOMACH.

No.	Weight of Animal.	Amount of Dose Actually Administered.	Proportion of Dose per Kilometre.	Duration of Case.	Sample Used.
1	890	0.24	0.27	10 minutes.	a
2	670	0.08	0.12	not fatal.	a
3	640	0.16	0.25	15 minutes.	a
4	670	0.17	0.25	21 "	b
5	1360	0.34	0.25	30 "	b
6	1880	0.47	0.25	46 "	c
7	750	0.187	0.25	25 "	c
8	680	0.17*	0.25	143 "	d
9	1797	0.45	0.25	20 "	d
10	1610	0.40	0.24	120 "	f
11	1970	0.50	0.25	165 "	f
12	1870	0.45	0.24	135 "	f
13	1750	0.42	0.24	140 "	e
14	1690	0.42	0.25	150 "	e

* Some of the material was lost in the administration.

Exp. 4.—Rabbit weighing 680 grams received .17 gram of the preparation from Ed. Sauppe, the administration taking place at 12.22 P. M. At 12.30 the animal was not yet affected. At 12.54 it had become still. At 1.16 was breathing with dilated nostrils. 1.52, head dropped to the ground. 2.00, long respiratory pauses. 2.10, Cheyne-Stokes respirations, pauses of from ten to twelve seconds. 2.45, death.

Exp. 9. Animal weighing 1797 grams received .45 gram of the same preparation at 12.00 o'clock. At 12.03, marked dyspnœa. 12.10, lateral decubitus. 12.12, chronic spasm. 12.20, head bent strongly backward. 12.25, death.

I tested the hypodermic action of the preparation from Bremerhaven only. The symptoms were as given above, with the exception that death occurred more quickly.

Exp. 15.—A rabbit weighing 1825 grams received hypodermically .2 gram of the Bremerhaven preparation, dissolved in lukewarm water, the proportion being .11 gram per kilogram of the body weight. The injection was made at 2.04. At 2.10 there was marked dyspnœa and convulsive movements; strong expiratory efforts; marked weakness; the extremities constantly moved to and fro beneath the body of the animal. 2.40, the head falls to the side; eyes remaining widely open. 3 o'clock, animal lies quietly on the side; deep breathing with long pauses; almost typical Cheyne-Stokes respiration; pupil reflexes wanting. 3.15, death. A second animal, to which only .06 gram per kilo of body weight had been administered subcutaneously, exhibited marked dyspnœa and escaped fatal poisoning.

An autopsy of the animal killed by administration by stomach exhibited marked yellow staining in that organ. Its contents were acidified with hydrochloric acid and extracted with ether. The ether extract was colored green by the presence of chlorophyll, as was shown by the spectroscope, and, on shaking the liquid with sodium hydroxide, the latter took up a body which was soluble in alcohol to a yellowish-red color. The green ethereal solution showed a red fluorescence. The alkaline solution, being freed from ether by warming and acidulated with hydrochloric acid, deposited a crystalline precipitate having the properties of dinitrocresol. Most of the viscera, especially the liver and lungs, were highly congested.

Experiments on Dogs.—*Administration by Stomach.*—Animals to which the saffron-substitute has been administered by means of the œsophageal tube exhibit characteristic symptoms. At first, in all cases, more or less vomiting occurs, and diarrhœa is frequently induced. If by these actions the greater part of the poison is expelled from the animal, it begins in from about ten to fifteen minutes to resume the normal condition. It runs about, responds to calls, and takes food readily. Generally, however, sufficient of the dinitrocresol remains in the system to develop the remaining symptoms of poisoning. In such cases the vomiting is followed in about ten to twenty minutes by a peculiar trembling of the entire frame. Spasmodic, and frequently ineffectual, attempts at vomiting occur, with the discharge of a tough, somewhat yellow-colored mucus. The breathing is labored, with forced expirations. The animal is unable to stand upright, and excessive salivation appears. The animal then falls upon its side, and clonic spasms of the extremities occur, during which the animal paws the air. Death ensues usually in the third and fourth attacks. The following are details from some experiments :—

Exp. 1.—Dog weighing 6230 grams received at 12.20 P.M., January 8th, 1888, by means of the œsophageal tube, about 1.5 gram of dinitrocresol from the Polytechnic laboratory, the material being dissolved in from fifty to sixty c.c. of lukewarm water. 12.30, frequent vomiting. 12.40, marked muscular tremors. The animal stood upright with difficulty and continued to vomit. 12.45, after rapid spasmodic efforts at vomiting the animal lay down. 12.49, clonic spasms while lying on the side. 12.52, salivation, diarrhœa. 1 o'clock, the animal was sleeping. 2 o'clock, completely recovered.

Exp. 3.—Dog weighing 5500 grams received January 21st, 1888, at 12.10 P.M., 30 grams of dinitrocresol, same sample as above, administered by the œsophageal tube. 12.15, vomiting. 12.20, diarrhœa. 12.25, animal fell upon its side and pawed the air; renewed vomiting, by which a rather tough white mucus was discharged. 12.27, strong tonic spasm; the animal lay on the side, the mouth opened by tetanic spasm. 12.35, third spasmodic seizure. 12.45, fourth spasmodic seizure. 12.50, death; muscles stiff. Post-mortem showed very little material in the stomach except a few crystals of dinitrocresol. Liver, intestines, and lungs hyperæmic. No methæmoglobin detected in the blood.

Exp. 5.—A Newfoundland dog weighing 14500 grams received at 1.55 P.M., January 22d, .7 gram of dinitrocresol, same sample as above, administered in milk by means of the œsophageal tube. 2.20, animal was quiet. 2.35, dyspnœa, loud complaining. 2.40, salivation. 2.45, urine passed containing dinitrocresol salt. 2.46, vomited. 2.50, very restless. 3, tonic spasms of the extremities, loud cries. 3.03, vomiting. 3.15, marked dypsnœa, animal lying upon its side; strong, spasmodic seizure; animal does not react to strong irritation. 2.35, animal lively. 2.31, very little dyspnœa. 4, completely restored (see further experiment, No. 7).

A summary of all the experiments is given in the table below. I hoped by means of the hypodermic injection to avoid the vomiting brought about by the administration by the stomach. The experiments showed, however, that this expectation could not be realized.

Exp. 6.—Dog weighing 6230 grams received subcutaneously January 24th, 1888, 1.21 P. M., 0.1 gram of dinitrocresol, same sample as above, dissolved in about ten c.c. of water. This animal had previously received .3 gram by the œsophageal tube, but, in spite of well-developed symptoms of poisoning, had recovered. 1.30, marked dyspnœa with vomiting. 1.40, tremors and slight spasm. 1.57, salivation and slight spasm. 2 o'clock, clonic spasms of the extremities, tetanic spasm of the masseters, thick mucus expelled from the mouth. 2.05, marked dyspnœa, animal lying upon its side. 2.10, recurring clonic spasm; animal does not respond to calls or to strong irritation. 2.15, death, muscles stiff. Post-mortem as above. No methæmoglobin in blood.

Exp. 7.—To the animal that had been employed in experiment No. 5 the following doses of dinitrocresol (same sample as above) were administered subcutaneously. At 10.40 A. M., 0.1 gram. At 12.15, animal was somewhat weak, then improved. 12.20, 0.1 gram administered; animal became weak. At 2 o'clock, .2 gram. At 2.30, active expiration, abdominal breathing. At 2.45, dyspnœa, responds to call by wagging tail; slight cramps, and subsequent complete recovery.

Exp. 8.—Dog weighing 3420 grams, received, subcutaneously, at 10.30, on January 27, 1888, 0.1 gram of the Bremerhaven sample dissolved in ten c.c. of water. 11.06, vomiting. 11.27, renewed vomiting. 12 o'clock, vomiting. 12.50, 0.2 gram subcutaneously. 12.55, vomiting of yellow masses. 1.10, spasmodic retching, yellow masses expelled. 1.11, weak clonic seizure. 1.16, animal lay upon its side; strong clonic seizure; tetanus of the masseter muscles, mouth wide open. 1.18, very marked dyspnœa, continuous spasm. 1.20, death, muscles stiff. Post-mortem showed the usual appearances.

Exp. 9.—Dog weighing 5690 grams received, subcutaneously, at 10.40 A. M., 0.1 gram of saffron-substitute, made by Mittenzwey, dissolved in twenty-five c.c. of lukewarm water, the proportion being 0.17 gram per kilo of body weight. At 10.51, breathing very rapid. 11.35, animal was sitting quietly. 11.50, apparently normal.

12.15, 0.2 gram subcutaneously. 12.25, respirations accelerated. 12.26 to 12.30, vomiting followed by tremors. 12.31, vomiting of a tough yellow mucus. 12.32, weak clonic seizure. 12.35, strong clonic seizure, spasm of the masseters, white foam issuing from the mouth. 12.36, strong clonic spasm ; pupils sensitive. 12.40, the seizures are not relieved by irritation of sensitive surfaces. Very rapid breathing ; animal lay upon its side. Successive clonic seizures occurred at the following periods : 12.05, 12.49, 12.52, 12.55, 1, 1.02, 1.05, 1.08, 1.15, 1.26, respirations 108 ; 1.22, respirations 120 ; 1.38, respirations 148 ; 1.39, respirations 180 ; 1.45, respirations 120 ; 1.50, breathing slower, animal lay upon its side with eyes open. 1.52, spontaneous movements. 2, breathing much quicker; 2.10, respirations 90. 2.25, spontaneous movements of head. 2.30, wags its tail somewhat. 2.45, animal recovered, but still lay on its side. Following day alive and apparently well.

EXPERIMENTS ON DOGS.

No.	Weight of Animal.	Dose.	Proportion to Kilogram.	Sample.	Duration of Case.	Remarks.	Method of Administration.
1	6,230	1.5	0.2	a	. . . .	Recovery.	By stomach.
2	5,500	0.3	0.055	a	. . . .	"	"
3	5,500	0.3	0.055	a	40 minutes.	. . .	"
4	6,230	0.3	0.048	a	. . . .	Recovery.	"
5	14,500	0.7	0.05	a	. . . .	"	"
6	6,230	0.1	0.016	a	75 minutes.	. . .	Hypodermically.
7a	14,500	0.1	0.007	a	. . . .	Recovery.	"
7b	"	0.1	0.007	a	. . . .	"	"
7c	. . .	0.2	0.014	a	. . . .	"	"
8	3,420	0.1	0.029	f	170 minutes.	. . .	"
9a	5,690	0.1	0.017	e	. . . .	Recovery.	"
9b	. . .	0.2	0.035	e	. . . .	"	"

The preceding table needs but little explanation. It is clearly apparent that the animals which received .05 gram of dinitrocresol salt by the stomach, in Experiments 2 to 5, did not die in all cases. These phenomena will, however, be easily understood when we recollect that the dosage of such a substance is deceptive in view of the frequent vomitings which it produces. It depends upon accident, not entirely under the control of the experimenter, whether much or little, or even none, of the material administered reaches the system proper. This is especially true of Exp. 1. With the subcutaneous administration the conditions were as follows:—Exps. 6 and 7 were comparable, since the same preparation was employed. The animal lived that received seven milligrams per kilogram of body weight (Exps. 7 a and 7 b.). Sixteen milligrams per kilogram killed in Exp. 6. Fourteen milligrams per kilogram was not fatal in the case of the very large dog in Exp. 7 c. In Exp. 8 twenty-nine milligrams were required for a fatal effect, therefore it took almost double the dose that was sufficient in Exp. 6. The Bremerhaven preparation employed in Exp. 6 contained, as was ascertained, about thirty-three per cent. of ammonium chloride while the material used in the other experiments, obtained from the Polytechnic College laboratory, was nearly pure potassium dinitrocresol. The animal used in Exp. 9, to which the Mittenzwey preparation was given, was also dangerously affected, as is shown in the notes of this experiment. Dogs upon which the experiments were made exhibited the following characteristic toxic symptoms. Whether the color was introduced directly into the stomach or beneath the skin, nausea and vomiting invariably ushered in the poisoning. Active inspiratory movements; and dyspnœa succeeded these, then followed excessive salivation and characteristic trembling of the entire frame. At this period the animal generally lay helpless on one side. The first convulsive seizure then showed itself and was especially exhibited by pawing the air. A second and even a third convulsive seizure followed, and in the latter the animal generally succumbed. The muscles became rigid a few moments after death. In some cases the animal recovered after one or two hours' suffering.

The toxic dose for dogs is from seven to ten milligrams per kilogram of body weight in hypodermic administration. The fatal dose is sixteen milligrams with a perfectly pure potassium dinitrocresol: twenty-nine milligrams per kilo of body weight of the commercial preparation, which contains about thirty per cent of ammonium chloride. The following formulæ show that the saffron-substitute is related to phenol and picric acid :—

C_6H_5HO Phenol. $C_6H_4CH_3HO$ Cresol.
$C_6H_5HO(NO_2)_3$ picric acid. $C_6H_2HOCH_3(NO_2)_2$ dinitrocresol.

The symptoms of poisoning by dinitrocresol agree in several material points with those of phenol, as E. Salkowsky has shown in the case of rabbits and J. Munk in the case of dogs. Indeed, poisoning by saffron-substitute could almost be designated as phenol poisoning, except that the dinitrocresol is the more poisonous, as the following comparison indicates :—

Material.	Method of Administration.	Lethal Dose per Kilogram.	
		Rabbit.	Dog.
Phenol, ...	Stomach.	0.45	0.5
Dinitrocresol, commercial, .	Subcutaneously.	0.25	0.029
" pure, ...	"	0.25	0.016

In this table doses administered by the mouth are compared with those administered subcutaneously. This has been done because saffron-substitute administered by the mouth causes vomiting, and the doses cannot be accurately estimated. Moreover, the lethal dose of phenol administered subcutaneously to dogs seems not to have been determined. If we assume that phenol has fifty per cent. more activity when acting through the subcutaneous cellular tissue, which is certainly more than the necessary allowance, dinitrocresol will still be materially more active. A characteristic difference between dinitrocresol and phenol poisoning is the vomiting which the former substance develops.*

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* Picric acid also produces vomiting.

The experiments given indicate the poisonous nature of dinitrocresol. They justify the hope that the State may restrict the sale of so dangerous a material and prohibit its employment for the coloring of food and drink. This opinion will be still more strengthened by the notes of a case of fatal poisoning by saffron-substitute, for information of which I am indebted to the kindness of Dr. With, Police Surgeon of Bremerhaven.

On August 9, 1887, Mrs. J., a married woman of Bremerhaven, obtained fifteen pfennings' worth of "safran" with the intention of employing it as an abortifacient. She took the red powder at eight o'clock in the morning, was seized with vomiting, and died at one o'clock of the same day. A post-mortem examination was made on the next day and exhibited the following appearances: The abdomen, conjunctiva, and mucous membrane of the mouth were pale yellow; no corrosion was observed in the mouth. The heart contained a dark yellow serum. There was no liquid in the pleural cavity. The bronchi and lungs contained a yellowish-green liquid. Nothing abnormal was observed in the intestines. The mucous membrane of the stomach was covered with a brownish-yellow material, and the contents of the stomach on being diluted with water exhibited, in thin layers, an intensely yellow color; in thick layers, a brown-yellowish red. The contents of the bladder had the same peculiar yellow color as the skin. No bile colors were found in the urine. I have no information in regard to the condition of the uterus. The authorities at Bremerhaven sent me about ten grams of the powder remaining from that which the woman had taken, which I subjected to a toxicological and chemical investigation.* I have already given a report of the former (see p. 78). In order to present a synopsis of the actions of these substances, I place here in tabular form the result of the investigations of the Bremerhaven preparation, together with those of the commercial article from Mittenzwey, because,

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*I am also under obligations to Professor Otto, of Brunswick, and Mr. Techner, an apothecary in Bremerhaven, for furnishing me small specimens of the same powder.

as will appear later, the two preparations were found to be identical.

COMPARISON BETWEEN EFFECTS OF SAMPLES "E" AND "F."

No.	Sample.	Animal.	Method of Administration.	Weight of Animal.	Dose.		Remarks.
					Actual.	Per Kilo.	
1	f	Rabbit.	Stomach.	1610	0.4	0.24	Died in 2 days.
2	f	"	"	1970	0.5	0.25	" " 165 mins.
3	f	"	"	1870	0.45	0.24	" " 135 "
4	f	"	Subcutan.	1825	0.2	0.109	" " 71 "
5	e	"	Stomach.	1750	0 42	0.24	" " 140 "
6	e	"	"	1690	0.42	0.25	" " 150 "
7	f	Dog.	Subcutan.	3420	0.10	0.029	" " 150 "
8a	e	"	"	5690	0.10	0.017	Recovery.
8b	e	"	"	"	0.20	0.035	"

These experiments show that the Bremerhaven preparation is capable of killing rabbits and dogs in small doses whether administered by the stomach or subcutaneously. The characteristic symptoms to which the animals succumb are exhibited above.

Chemical Investigation.—The Bremerhaven preparation was a loose, orange-red, distinctly crystalline powder. Heated in a test tube, it was decomposed with evolution of nitrous vapors. Heated on platinum foil, it decomposed with a hissing noise. On treating it with water at ordinary temperature, a portion of the powder dissolved to an orange solution, another portion remaining undissolved as a brownish-black, tar-like mass. The latter, by warming, was nearly all dissolved. The watery solution dyed silk and wool orange, but the color could be almost entirely withdrawn by washing with hot water. The aqueous solution was not precipitated by ammonium hydroxide. The ammoniacal copper solution produced, after twenty-four hours' standing, a minute flocculent precipitate. Addition of dilute sulphuric or hydrochloric acid to the watery solution produced a crystalline precipitate. This was recrystallized several times from hot water, and yellow needles were obtained having a melting point of 79–80°. Pure dinitrocresol salts melt at 84°; orthodinitrocresol, at 86°. The crystals contained nitrogen, exploded lightly by quick heating, and dissolved in alcohol and alkalies to an orange color. It was clear that I had here a mixture of para- and ortho-dinitrocresol. A more complete separation and ultimate analysis was not possible by reason of the scantiness of the sample. The quantitative analysis of the materials present in the Bremerhaven preparation was carried out by the following methods:—

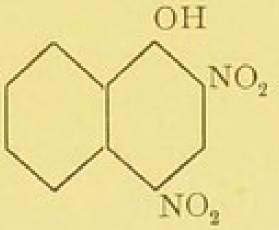
(*a*) Two grams of the powder were dissolved in 300 c.c. of hot water mixed, while yet warm, with dilute sulphuric acid and allowed to stand for twenty-four hours. The precipitate was then collected on a tared filter, washed with some water, dried in vacuo, and weighed. The yellow filtrate was then shaken with ether until decolorized and the ether evaporated in a weighed dish. The residue was treated in vacuo with sulphuric acid, weighed, and the weight calculated with that upon the filter as dinitrocresol. The watery filtrate, now practically colorless, was freed from ether, made up to one-half of a litre. The solution contained potassium, ammonium, and chlorine. The chlorine was determined by titration with silver nitrate and calculated to ammonium chloride, while the potassium was calculated to potassium dinitrocresol from the weight of the dinitrocresol obtained as above. I obtained from two grams of dinitrocresol by precipitation, 0.7065, from the ether extract, 0.33; total, 1.0365; hence, 51.8 per cent. of dinitrocresol. Chlorine by titration, .4524, equivalent to .67 of ammonium chloride, hence 33.5 per cent.

(*b*) In the second analysis, two grams of the powder were dissolved in 300 c.c. of water and excess of dilute sulphuric acid, and the liquid rapidly extracted with ether until colorless. The residue from the ethereal extract was dried in vacuo from sulphuric acid and weighed. There was obtained dinitrocresol, .984 gram, 49.2 per cent. The mean of the two experiments would, therefore, give 50.5 per cent. of dinitrocresol, which corresponds to 60 per cent. of potassium dinitrocresol. Adding to this 33.5 per cent. of ammonium chloride, the difference between this amount and 100 (6.5 per cent.) may be reckoned as moisture and loss. By comparing the Bremerhaven powder with the commercial saffron-substitute in my collection, it was shown that the preparation from Mittenzwey agreed completely in its color as well as its chemical properties with the specimen from the Bremerhaven case. This chemical identity was completely confirmed by the similarity of the toxicological action of the two preparations. This point is fully presented above. Furthermore, a judicial inquiry disclosed the fact that the Bremerhaven preparation had been obtained from Mittenzwey. The toxicological and chemical investigations which I have stated demonstrate with certainty that the Bremerhaven woman died of poisoning by saffron-substitute. With the intention of bringing about an abortion by using saffron, she had taken, in the place of the well-known drug (*Crocus sativus*), the artificial color, saffron-substitute. The material had cost 15 pfennings. Since the dye-stuff is sold by the manufacturer for 23 marks per kilo, and the retailer will expect in such small sales at least 50 per cent. profit, the woman obtained about 4.5 grams for 15 pfennings. Assuming that she weighed 75 kilo, the fatal dose of the Mittenzwey preparation may be reckoned at .06 gram per kilo of body-weight. It must here be noted that the Bremerhaven preparation could not have contained appreciable amounts of other nitro-compounds, especially picric acid.

I have satisfied myself that the ordinary and commercial samples of nitro-colors, with the exception mentioned, yield, even when largely diluted, a precipitate with ammoniacal copper sulphate. Even brilliant yellow, which forms a relatively easily soluble copper compound, could not have been present, since it is precipitated by sodium hydroxide and would have given a characteristic reaction with ferric chloride. For human beings, therefore, as the Bremerhaven affair shows, dinitrocresol is highly poisonous even in small amounts, and the sale of such a substance should be restricted by legal provision.

Martius' Yellow.

This color is named after its discoverer, Dr. C. A. Martius, of Berlin. It is also known as naphthol yellow, naphthalene yellow, Manchester yellow, saffron yellow, and golden yellow. It is dinitro-α-naphthol. The structural formula is as follows:—



Several methods are available for its preparation.

1. α-amidonaphthalene is treated with hydrochloric acid and sodium nitrite (diazotized), and the resulting diazonaphthalene chloride is boiled with nitric acid, when the color separates in fine yellow crystals. The reactions are as follows:—

$$C_{10}H_7NH_2 + 2HCl + NaNO_2 = C_{10}H_7N{=}N{-}Cl + NaCl + 2H_2O$$
$$C_{10}H_7{-}N{=}N{-}Cl + 2HNO_3 = C_{10}H_7HO(NO_2)_2 + N_2 + HCl + 2H_2O.$$

2. α-naphthol is treated with sulphuric acid, by which α-naphtholsulphonic acid is produced, and this, on being heated with dilute nitric acid, yields the color.

$$C_{10}H_7HO + H_2SO_4 = C_{10}H_6HOHSO_3 + H_2O$$
$$C_{10}H_7HOHSO_3 + 2HNO_3 = C_{10}H_5HO(NO_2)_2 + H_2SO_4 + H_2O.$$

In commerce, calcium, sodium, and, more rarely, ammonium salts of the preparation are seen. The first mentioned is a yellowish orange powder difficultly soluble in water. The sodium salt forms reddish crystals, tolerably soluble. These substances are usually reduced by admixture with dextrine.

Typical Reactions.—The powder dissolves in sulphuric acid to a reddish-yellow color. The solution becomes turbid on dilution. Ether added to this liquid becomes only very slightly tinged with yellow. If the ether be removed carefully and treated with sodium hydroxide or sodium carbonate, it becomes decidedly yellow. The solution in water, rendered alkaline, becomes brown-yellow. After long boiling with potassium cyanide, the aqueous solution of the dye takes on a brown color and then becomes intensely dark brown (naphthylpurpuric acid). This reaction with potassium cyanide takes place, as it appears, with all nitro-colors. Heat causes it to explode slightly. The watery solution becomes turbid by the addition of a small amount of acid (distinction from naphthol yellow S, picric acid, and aurantia, (see also brilliant yellow). The watery solution gives with sodium hydroxide after some delay a flocculent red precipitate. (Compare brilliant yellow.) (Picric acid, dinitrocresol, naphthol yellow S, and aurantia are not precipitated by sodium hydroxide.) With ammoniacal copper solution a crystalline precipitate occurs, even when very much diluted. The copper compound is soluble in hot water, and with strong hydrochloric acid gives a precipitate of free dinitronaphthol which may be tested with the procedure with ether given above.

Reduction by means of hydrochloric acid solution of stannous chloride produces, in the presence of ammonium hydroxide, an orange-red liquid ; in presence of ferric chloride, a fuchsin-red solution. Ferric chloride produces a yellowish precipitate which, together with the liquid, turns red on boiling.

Since Martius' yellow rubs off easily and is also very volatile on heating, it is now but little employed for dyeing wool or silk. According to G. Schultz, it is employed in printing on textiles. It is used for the coloring of food (maccaroni) in France and Italy.* Concerning the action of Martius' yellow upon the animal organism, reliable investigations were made by Cazeneuve and Lépine. These observers employed the sodium salt.

A dog weighing 7 kilos received daily .05 gram (probably per kilo) of the powder introduced into the throat. On the second day oc-

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* According to a report made by Dr. Erhardt, Sanitary Officer, to Count Solms, German Minister to Italy, and kindly placed at my disposal.

curred diarrhœa and vomiting of yellow masses. The animal refused nourishment, except milk. On the fourth day dyspnœa and a temperature of 41° was noted. The symptoms continued to increase in intensity and the respirations became croupy. Temperature 42°, appetite gone. Urine contained the color and was albuminous. Animal died on this day. Post-mortem showed the intestines colored yellow. In a second experiment a dog weighing 22 kilos received .4 gram (probably per kilo) suspended in syrup. On the following day .5 gram was administered. The symptoms were as in the first case. The animal was killed. Post-mortem showed no discoloration of the intestines, but an extensive congestion of the same.

Further investigations were carried out upon dogs weighing from 10 to 25 kilos, to which proportions of the color varying from .3 to .6 per kilo of the body weight dissolved in .7 per cent. solution of sodium chloride were injected into the femoral vein. The temperature rose to 44°. Marked dyspnœa was developed. Death resulted in 45 to minutes to 1½ hours. Doses of .1 gram per kilo injected into the blood were followed by the same symptoms, but the animal recovered. I gave to two rabbits, weighing 1797 and 2100 grams respectively, .55 gram of the ammonium salt and 1 gram of the potassium salt respectively. No symptoms of poisoning appeared in these cases. The following investigations were undertaken with dogs. The easily soluble sodium salt was fed to the animal. The material was in yellowish-red needle-shaped crystals, and was manufactured from the calcium compound obtained from Kuhnheim & Co., in Berlin.

Exp. 1.—Dog weighing 6850 grams received by the œsophageal tube on March 10, 1888, one o'clock, .5 gram Martius' yellow sodium salt suspended in about 25 c.c. of water. 1.10, strong efforts at vomiting. At 6 o'clock vomiting occurred. March 11th, 10 o'clock A. M., animal very weak, rectal temperature 40.8°, vomiting and diarrhœa, urine rather darker than the salt administered and containing traces of albumin. Strongly acidulated with sulphuric acid, it yielded a weak, yellow-colored extract ether. Sodium hydroxide solution added to the ether colors it a pure yellow and becomes itself colored. Addition of hydrochloric or sulphuric acid renders the urine turbid by separation of free dinitronaphthol. No injection was made at this date. March 12th, one o'clock, .5 gram was given by the œsophageal tube. 1.10, vomiting; animal was then lively with normal breathing. March 13th, diarrhœa, but lively and ate at midday; albumin in urine. March 14th, 11 o'clock, 1 gram by the œsophageal tube. Efforts at vomiting, but up to three o'clock in the afternoon no actual vomiting occurred. March 15th, animal was found dead in its cage. Post-mortem was accidentally omitted.

Exp. 2.—Dog weighing 5700 grams received, March 22d, 0.1 gram by the œsophageal tube. March 28th, five living pups were born. March 24th to 29th, animal and progeny remained in good health.

Experiment No. 1 indicates the poisonous quality of Martius' yellow when administered by the stomach, since any other cause of death seems to be excluded. The following experiments, in which the color was administered subcutaneously, are more positive in their indications.

Exp. 3.—Dog weighing 5800 grams received, April 30th, 10 A. M., .1 gram dissolved in about 25 c.c. of water injected subcutaneously at various points on the back. The animal remained lively, but in the afternoon had diarrhœa. On May 1st and 2d .1 gram was administered in the same manner. Diarrhœa continued, urine contained much albumin; addition of acid caused a precipitate of dinitronaphthol. Ether shaken with the liquid became feebly yellow. Addition of alkali to the ether extract caused it and the alkaline solution to become deep yellow. The feebly acidified urine dyed wool a yellowish brown. May 3d, .1 gram subcutaneously. May 4th, .15 gram subcutaneously. Urine contained albumin. Dyeing of wool took place very satisfactorily. This experiment shows that small doses of Martius' yellow administered subcutaneously produced albuminuria.

Exp. 4.—Dog weighing 8800 grams received, April 30th, .1 gram subcutaneously. May 1st and 2d, the same. Great thirst was exhibited. May 3d, same dose administered. Thirst and poor appetite. May 4th, 10 A. M., 0.2 gram subcutaneously. Urine was dark brown, contained albumin, and died wool yellow. At four o'clock, six hours after the injection, strong dyspnœa and great thirst. At seven o'clock the animal was quite apathetic, with marked dyspnœa. Died during the night. Post-mortem showed venous congestion of the liver, spleen, kidneys, and lungs, incipient pneumonia, intestines and skin not tinged.

This experiment demonstrates beyond cavil that the poisoning was the sole cause of death, since the operation of subcutaneous administration cannot be reckoned as contributing to the results. The animal took in the course of five days nearly .6 gram of the sodium salt of Martius' yellow; therefore, nearly .07 gram per kilo of the body weight.

Poisoning by this color presents the following symptoms: Administered by the stomach it causes vomiting; animals suffer from intense thirst, high fever, with marked dyspnœa. After the first dose, albuminuria appears. Generally, the animal succumbs, and, as it seems, by asphyxia. If the substance be introduced directly into the blood (Cazaneuve and Lépine) or injected subcutaneously, similar symptoms, with the exception of vomiting, are noted.

Martius' yellow, therefore, belongs to the injurious colors. As a coloring matter for food and drink its use should be wholly prohibited. For dyeing materials that may come in contact with the skin, its use is also inadvisable, since an abrasion of the skin, even if superficial, may permit an injurious action of the poison. The experiments in which the animals either sickened or died by introduction of the Martius' yellow into the blood or skin demonstrates this point. The color introduced with the food is, in part, at least, excreted in the urine unchanged. The wool dyed by the urine showed a somewhat darker tint than that obtained from the pure color, doubtless due to the action of coloring matters proper of the urine.

Naphthol Yellow S.

This color, known also as acid yellow S, fast yellow, aniline yellow, succinine, saffron yellow, citronine, new yellow, and solid yellow, is calcium, sodium, or ammonium dinitro-α-naphthol-sulphonate. $C_{10}H_4HO(NO_2)_2NaSO_3$. It may, therefore, be regarded as a sulphonated Martius' yellow. The production of naphthol yellow S is as follows: The action of fuming sulphuric acid upon α-amidonaphthalene produces α-amidonaphthalenetrisulphonic acid. $NH_2C_{10}H_4(HSO_3)_3$. By boiling this with nitrous acid (diazotizing) α-naphtholtrisulphonic acid, $C_{10}H_4HO(HSO_3)_3$, is produced, and, by heating this with nitric acid, dinitro-α-naphtholsulphonic acid, $C_{10}H_4HO(NO_2)_2HSO_3$, is formed. α-naphthol can also be converted directly into the trisulphonic acid by the action of fuming sulphuric acid and by suitable treatment of this with nitric acid.

The commercial form, which is usually the sodium salt, is an orange yellow powder easily soluble in water. It is commonly sold mixed with dextrin or some similar diluting agent.

Typical Reactions.—The powder dissolves in concentrated sulphuric acid with greenish-yellow color, and the solution, on dilution with water, remains clear. (Distinction from Martius' yellow and aurantia.) Ether shaken with this solution remains colorless, even when an alkali is added (compare Martius' yellow), because the color acid is insoluble in ether. By this means, an admixture of Martius' yellow, which, by reason of its lower cost, is occasionally substituted for naphthol yellow S, may be detected. The aqueous solution is not precipitated by hydrochloric acid (distinction from dinitrocresol, Martius' yellow, brilliant yellow, and aurantia), and gives no precipitate with sodium hydroxide (distinction from Martius' yellow and brilliant yellow). Potassium cyanide produces, as with all other nitro-colors, the iso-purpuric acid color. The aqueous solution is precipitated, even when very highly diluted, by ammoniacal copper solution. The solution of the crystalline precipitate in hot water remains clear upon addition of strong hydrochloric acid, and yields nothing to ether. Hydrochloric acid solution of stannous chloride produces, on addition of ammonium hydroxide, an orange color; on addition of ferric chloride, a red color. Ferric chloride produces a Burgundy red precipitate, which, in part, dissolves on heating and reappears on cooling.

The color is used as a substitute for picric acid in the dyeing and printing of wool and silk, and also for the coloring of articles of food.

Cazeneuve and Lépine gave a dog, weighing 15,000 grams, .5 gram of naphthol yellow S, daily for fourteen days; then, for ten successive days, 2 grams daily, and 4 grams daily for ten more days. The animal gave birth to nine pups, of which eight lived. No disturbance was noticed in the animal and the urine was free from albumin. Occasionally the coloring matter was directly injected into the blood. Symptoms of poisoning were not manifested. With human beings, 2–4 grams of the color per day produced colic and diarrhœa.

The above-mentioned authors regard the color as non-poisonous and slightly purgative. It is to be noticed, however, that Cazeneuve and Lépine state that the naphthol yellow used (Jaune NS.) was difficultly soluble, so that they, probably, experimented with another substance. My own investigations were made on dogs, with a preparation for which I am indebted to the kindness of Dr. G. Schultz, of the Aniline Manufacturing Co., of Berlin. It was purified by precipitation and recrystallization.

Exp. 1.—Dog weighing 4800 grams received, May 7th, by the œsophageal tube, 2 grams dissolved in water. May 8th, appetite good, quiet breathing, fæces normal, urine neutral and free from albumin; wool could be easily colored by the urine. 5.75 grams were administered on this date in the same manner. May 9th and 10th, no albumin in the urine; no injection made. May 11th, 2 grams injected, animal normal, doubtful traces of albumin in the urine. May 12th, 2 grams injected, animal normal; traces of albumin in the urine; fæces normal.

In spite of the undoubtedly large dosage of 7.75 grams in six days, 1.6 grams per kilo of the body weight, the animal exhibited no symptoms of poisoning and only extremely limited albuminuria, which perhaps existed prior to the experiment. The following experiment, which was carried out with a dog and its 3½ weeks' old pup, shows that even by the subcutaneous injection of the naphthol yellow S, no symptoms of poisoning are produced.

Exp. 2.—Animal weighing 5800 grams received, May 11th, subcutaneously, .2 gram in about 32 c.c. of water. Animal remained in good spirits and had good appetite. May 12th, .2 gram subcutaneously. May 13th to 16th, animal continued lively; appetite not diminished; nursed its young.

Exp. 3.—Dog 3½ weeks old, weighing 1040 grams, received, May 11th, .1 gram in about 15 c.c. of water, subcutaneously. May 13th, .1 gram in same manner. Animal was lively, and continued so on the following day.

This experiment shows that even repeated doses of .1 gram per kilo. of body weight in a young animal, even when injected subcutaneously, does not produce any perceptible disturbances.

The harmlessness of naphthol yellow S is all the more interesting in view of the fact that it differs from the markedly poisonous Martius' yellow, merely by one sulphonic group (HSO_3), the introduction of which into a color renders it soluble.

Naturally, one would suppose that a soluble color would prove more poisonous than the insoluble color from which it was produced. Clearly, therefore, we are not in a position to decide as to the poisonous or non-poisonous qualities of any body except from actual research, even when we correctly know the constitutional formula. That poisonous bodies are rendered non-poisonous by the introduction of a sulphonic group, which attaches itself to the carbon atom, has been established by a series of investigations (compare, for instance, E. Salkowsky's observations on phenol-sulphonic acid, Pfluger's Archiv, 4, 92, 1871). Further, Cazeneuve and Lépine found that colors containing the sulphonic group are non-poisonous. From information kindly communicated to me verbally by E. Salkowsky, I learn that *p*-amidobenzenesulphonic acid is not poisonous. The investigations of Stolnikow refer to the influences of the sulphonic group attached to the oxygen.

Brilliant Yellow (Schoellkopf).

I am indebted to the kindness of G. Schultz, of Berlin, for a sample of this beautiful color. Brilliant yellow is, apparently, a dinitro-α-naphthol sulphonic acid, isomeric with naphthol yellow

S. The commercial form is a sodium salt, which is a yellow powder rather easily soluble in water. It is obtained by the treatment of naphtholdisulphonic acid with nitric acid, according to the following reaction:—

$$C_{10}H_5HO(HSO_3)_2 + 2HNO_3 = C_{10}H_4HOHSO_3(NO_2)_2 + H_2SO_4 + H_2O.$$

Typical Reactions.—The yellow-brown solution in water is rendered a paler yellow by hydrochloric acid, but not precipitated. Ether, shaken with this solution, becomes pale yellow. Sodium hydroxide produces an orange red crystalline precipitate. Ferric chloride produces a dirty greenish-yellow color, which, by reflected light, is opaque, almost black. Before the appearance of the dark color the solution appears, for a brief period, red-brown. (Distinction from picric acid, naphthol yellow S, Martius' yellow, and aurantia.) Ammoniacal copper solution produces, after similar treatment, a crystalline precipitate. With stannous chloride and subsequent addition of ammonium hydroxide, or ferric chloride, and with potassium cyanide, brilliant yellow behaves like Martius' yellow.

Exp. 1.—July 26th, a dog weighing 5650 grams, the urine of which contained a trace of albumin, received by means of the œsophageal tube 3 grams of the color suspended in water. July 27th, the animal was in good spirits and ate freely. The urine was colored intensely orange-yellow. The urine, slightly acidulated with sulphuric acid, dyed wool easily. It contained brilliant yellow and doubtful traces of albumin. Treated with hydrochloric acid, it yielded to ether a pale yellow color. Sodium hydroxide solution decolorized the ether almost entirely and was itself colored yellow. On July 28th the animal was in good spirits and appetite. Urine contained a small amount of the color. Three grams were administered by the œsophageal tube, dissolved in a little peptone to avoid corrosion of the mucous membrane of the stomach. July 29th, animal quite lively; urine almost free from albumin, but containing much coloring matter; dyeing of wool was easily done. July 30th, 2½ grams administered in the same manner, in peptone. The urine was alkaline, almost free from albumin; animal in good spirits and appetite good; wool easily dyed by the urine acidulated with sulphuric acid. July 31st, 3 grams administered as above. August 5th, animal quite normal and had again during the course of the experiment 180 grams. The brilliant yellow in the urine was detected, in addition to the dyeing of the wool in the acidulated liquor, by the following method. The liquid was rendered strongly acid with hydrochloric acid and shaken with ether. The ether extract yielded the color to sodium hydroxide solution and in the latter it was detected by the reactions given above.

Exp. 2.—A dog weighing 11600 grams was selected on July 27th, and the urine determined to be free from albumin and sugar. July 28th, 0.2 gram of brilliant yellow suspended in ten c.c. of water were injected. July 29th, urine intensely orange yellow in thin layers, in thick layers orange red, but free from blood and albumin; the animal was lively and had good appetite. July 30th, 0.3 gram were injected subcutaneously. Animal's condition the same, but urine contained a little albumin. July 31st, animal in good spirits and appetite. August 5th, animal lively, urine contained very little albumin. The dog had gained about 300 grams in body weight since the beginning of the experiment. Further investigations were omitted for want of material.

Brilliant yellow is not poisonous, even in large doses, when administered by the stomach. The dog which had received comparatively large doses subcutaneously was, at the end of the eighth day after the last injection, in quite good spirits and appetite. The albuminuria was very slight. In this color, as in naphthol yellow S, we observe the influence of the sulphonic group in diminishing the poisonous action.

Aurantia.

Aurantia, or imperial yellow, is the ammonium or sodium salt of hexanitrodiphenylamine:—

$$NH_4N[C_6H_2(NO_2)_3]_2.$$

It is produced by the action of nitric acid upon diphenylamine or methylphenylamine, according to the following reaction:—

$$(C_6H_5)_2HN + 6HNO_3 = HN[C_6H_2(NO_2)_3]_2 + 6H_2O.$$

The commercial article, usually the ammonium compound, reduced by admixture with dextrin, appears in brownish-red needles.

Typical Reactions.—The powder dissolves in concentrated sulphuric acid to a weak yellowish color. Addition of water produces a flocculent precipitate. Solution of aurantia produces with strong hydrochloric acid, a precipitate of the free color acid. Ether dissolves the precipitate and acquires a yellow color. Sodium hydroxide solution decolorizes the ether and becomes itself yellowish brown, almost red. Sodium hydroxide produces no precipitate. (Distinction from Martius' yellow and brilliant yellow.) Ammoniacal copper solution produces a cinnabar red precipitate. This gives, with fuming hydrochloric acid, a precipitate which behaves toward ether as described above. With potassium cyanide, and with hydrochloric acid solution of stannous chloride, with the subsequent addition of either ammonium hydroxide or ferric chloride, aurantia behaves like other nitro-colors. (Compare, however, picric acid.) Ferric chloride produces a fawn-colored precipitate.

Aurantia is used for the orange-dyeing of wool, silk, and leather. Its poisonousness has been often asserted and often denied. According to Gnehm, the preparation made by Binschedler and Busch is poisonous, since those engaged in the manufacture of the color, and the dyers who employ it, suffer from vesicular eruptions and marked swelling of the hands and arms. On the other hand, according to Martius, the preparation of the Aniline Manufacturing Company of Berlin is non-poisonous. E. Salkowsky and Ziurek, in a formal opinion based upon experiments made on rabbits, with a very much reduced preparation, agree with this latter view. To the same effect, is the opinion expressed by the Royal Medical Convocation of the Rhine Provinces, April 18, 1880, as I infer from a decree of the said Convocation, dated April 18, 1880. It appears from this communication that the opinion refers to a preparation furnished under the name of aurantia, or imperial yellow, by the Aniline Manufacturing Company of Berlin. The text of this opinion is, unfortunately, not accessible to me. It is to be found among the Acts of the Prussian Educational Bureau. Perhaps the two preparations mentioned above, the Berlin and Basle, are different, or the color acts differently on different individuals. Unfortunately, for want of material, I could not conduct the investigations on this point.

Other Nitro-Colors.

The remaining nitro-colors, mentioned by G. Schultz (Chemistry of Coal-tar, second edition, 4to, p. 48, et seq.), flavaurin, phenyl brown, garnet brown, salicyl yellow, salicyl orange, palatin orange, and heliocrysin, are no longer produced on a commercial scale and are not important.

Conclusions.—The researches which are on record concerning the action of the nitro-colors upon the animal organism point to the following conclusions. Only the sulphonated colors, naphthol yellow and brilliant yellow, are harmless and applicable to the coloring of food and drink. Picric acid, dinitrocresol (saffron-substitute), and Martius' yellow are poisonous ; aurantia, suspicious.

AZO-COLORS.*

Chemical Considerations.

Historical.—Peter Griess must be regarded as the discoverer of the azo-colors by reason of his thorough investigations of the diazo-compounds, which are the sources of the azo-bodies. In 1859 he prepared the first azo-color, aniline yellow (amidoazobenzene). On March 12, 1878, he took out the first German patent (No. 3224, class 22) on the "preparations of colors through conjugate combinations of diazophenols with phenols." Shortly after Griess' discovery, Mène (1861) and Simpson, Maule, and Nicholson (1863) obtained aniline yellow by the action of nitrous acid on aniline. They introduced the color into the market without indicating its constitution. Griess and Martius made this known in 1866.

The second azo-color produced artificially and introduced into use was Bismarck brown, also known as phenylene brown and vesu-

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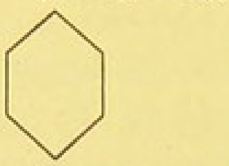
* The investigations described herewith were carried out in the Hygienic Institute in Berlin. I desire to express my sincere thanks to Professor Robert Koch for his kind interest in my work.

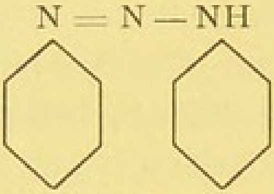
vin, discovered by C. A. Martius in 1865. In 1877 Caro and Griess determined this to be triamidoazobenzene. Ten years elapsed after the discovery of Bismarck brown, when another azo-color (chrysoidin) was prepared. This was discovered in 1875 by H. Caro, and in the early part of 1876 by N. O. Witt, being obtained by the action of diazobenzene chloride on metadiamidobenzene. Discoveries began to follow in quick succession. Roussin prepared orange I and II, in 1876 and 1877, in Poirrier's establishment. Then Griess and Witt prepared tropæolin, and since 1878 a large series of azo-colors has appeared, principally prepared in German factories, and especially in that of Meister, Lucius & Brüning, at Hoechst o. M., in the Baden Aniline and Soda Manufactory, and by the Aniline Manufacturing Company of Berlin. A new phase in the production began in 1884, when Paul Böttiger took out a patent (No. 28,753, Class 22) for the "preparation of azo-colors by the combination of tetrazodiphenyl salts with α- and β-amidonaphthalene, or their mono- and disulphonic acids. Up to that time the known azo-colors dyed wool alone in acid solution, and could be fixed on cotton only when it was previously mordanted. The azo-colors prepared from tetrazodiphenyl and its homologues will dye cotton without a mordant. The first of these series of colors was brought into the market in 1884 by the Aniline Manufacturing Company of Berlin under the name of "Congo." Since that time the number of Congo colors has increased rapidly. According to Friedlander, sixty per cent. of the patents for color preparations taken out in the last two years—from 1886 to 1888—relate to the preparations of these colors. The manufacturing of azo-colors has slowly reached an almost incredible extent. The well-known table of G. Schultz and P. Julius shows that there are 120 different azo-colors in the market, and the known colors amount to ten times that number.

Chemical Constitution.—The azo-group (—N = N—) is found in two classes of organic bodies—the azo-compounds and the diazo-compounds. In the first, it is joined on either side by a benzene residue which satisfies the valency. In the second series, but one benzene residue is present, while the other valency is satisfied by a radicle of another type—hydroxyl, amidogen, etc.

Diazo compounds.

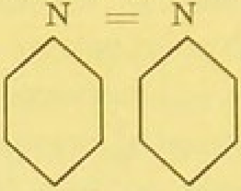


diazobenzene chloride

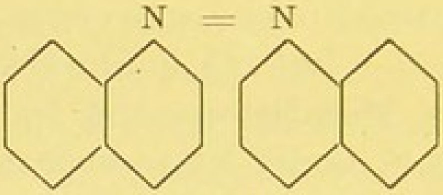


diazoamidobenzene

Azo compounds.



azobenzene



a-azonaphthalene

The diazo-bodies possess no coloring power, but as sources of the azo-colors they are of the utmost importance. For the most important points concerning their preparations and properties, see below. The azo-bodies, on the other hand, are coloring substances, but not dyes.* Their functions as dye-stuffs are developed only by the introduction of an acid or basic group into them. Azobenzene, for instance, is a yellow body that has no affinity for fibres. The azobenzenemonosulphonic and disulphonic acids, produced by the introduction of the sulphonic group into the azobenzene, are bodies of, at least, weak dyeing power. More powerful influences in determining the coloring value of the azo-bodies belong to hydroxyl or amidogen. Amidoazobenzenedisulphonic acid, which arises from the simultaneous introduction of amidogen and two sulphonic groups into azobenzene, is a useful yellow dye. Its sodium salt is sold under the name of acid yellow, or fast yellow. Hydroxyazobenzenesulphonic acid, produced by the simultaneous introduction of

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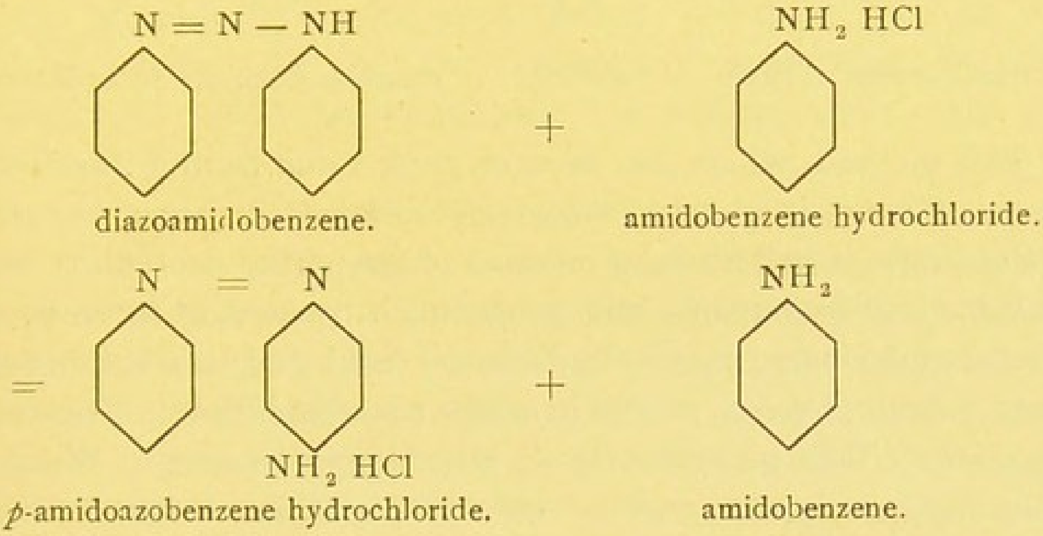
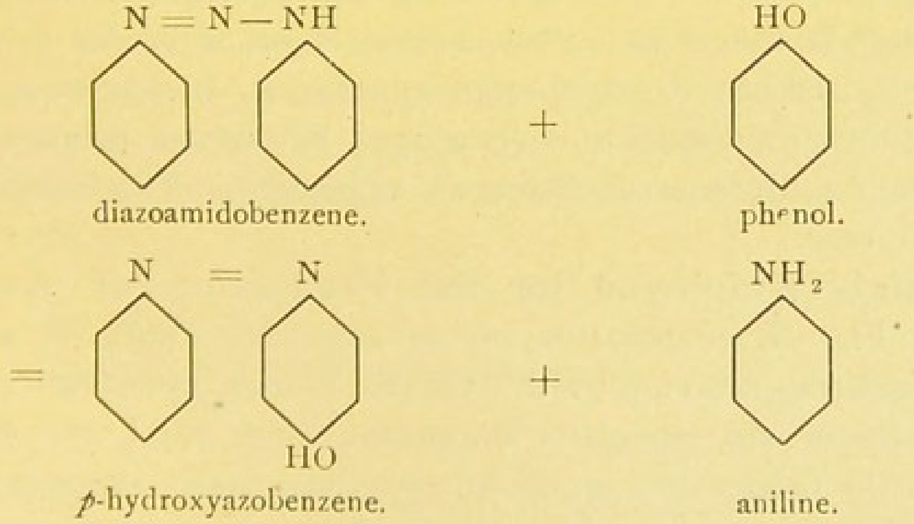
* For an account of some of the structural conditions on which the formation of dye-stuffs depends, see Appendix.

hydroxyl and a sulphonic group, occurs in the form of a sodium salt under the name of tropæolin Y.*

Production of the Azo-colors.—Two methods only need receive notice. First, transformation to diazoamido-compounds, by the action of amines on amidoazo-compounds, and by phenols to hydroxyazo-bodies. For instance, diazoamidobenzene, by prolonged heating with aniline hydrochloride at 30 to 40° becomes amidoazobenzene hydrochloride. (Kukelé.)



In the same manner the action of diazoamidophenol produces parahydroxyazobenzene together with aniline. (K. Heuman and Oeconomeides.)



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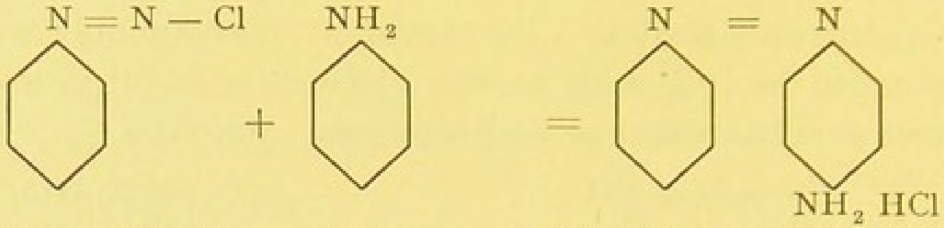
* The azarines are included in the azo colors, although they more probably contain the group —NH — N = rather than the typical azo-group — N = N—.

The second method of producing azo colors is by the action of the salts of the diazo-compounds upon primary, secondary, and tertiary amines. These produce amidoazo-compounds. (See Appendix.)



diazobenzene chloride. aniline. *p*-amidoazobenzene hydrochloride.

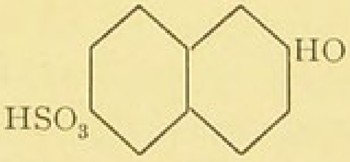
This method, which has been of great value from a theoretical point of view, is almost exclusively followed in manufacturing operations. Concerning a method of preparing azo-colors from quinone and hydrazines, which has much theoretical interest, see a subsequent paragraph. Phenols are employed in alkaline solution. Amines react in the neutral or acid solution. The color separates either immediately or after long standing. When it does not precipitate, sodium chloride, sodium acetate, and occasionally acetic acid, or hydrochloric acid are added. The color is purified by re-solution, or by re-precipitation. The commercial azo-colors are almost chemically pure. As appears from the method of preparation, they cannot contain injurious substances. Should they be found to act injuriously, it would be due to the color itself, and not to any foreign substance. In additions by way of dilution or reduction (coupage) it must, of course, be understood no injurious substances are to be used. This is almost always the case.

Materials Employed for the Production of Azo-colors.—For the preparation of the azo-colors, inorganic and organic materials are employed. Of the former, potassium and sodium nitrites are especially important, since these are employed in the production of the intermediate diazo-compounds. Sodium chloride, sodium hydroxide, and sodium acetate are also employed for purposes of precipitation and for formation of sodium salts. Sulphuric acid is employed for sulphonation. A few other bodies of little importance are also used. Of the organic bodies two classes are used: First, the substances that are to be diazotized; secondly, substances which are to be united with azotized materials. To the first group belong amines and their sulphonic acids. To the second group, primary, secondary, and tertiary amines, phenols, hydroxy-acids, and the sulphonic acids derived from these. It is not my purpose to enumerate more minutely the substances employed in the manufacture of these bodies, especially as in view of the constantly increasing list the enumeration would be incomplete. I will mention only the following:—

Group I. Aniline, toluidine, xylidine, cumidine, meta- and paranitraniline, and meta- and paramidobenzenesulphonic acids, α- and β-amidonaphthalene and their sulphonic acids, metadiamidobenzene and benzidine, tolidene, dianisidene, and diamidostilbenedisulphonic acid. Of the second class I may mention resorcinol, salicylic acid, α- and β naphthol, and their sulphonic acids, and diphenylamine. It will be necessary to discuss briefly the important naphtholsulphonic acids, and amidonaphthalenesulphonic acids, since a knowledge of these is very important in comprehending the azo-colors.

α- and β-naphtholsulphonic Acids.—By the action of concentrated sulphuric acid on β-naphthol there are formed several isomeric mono- and disulphonic acids, the relative proportion depending upon the temperature and the duration of the process.* Four isomeric β-naphtholmonosulphonic acids are known:—

I. Shaeffer's acid.
β-naphthol-β-monosulphonic acid.



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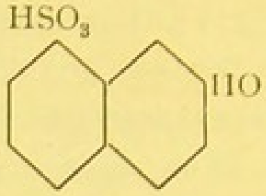
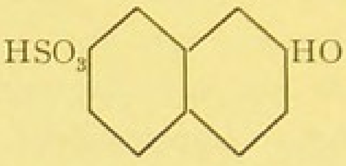
* According to Armstrong, with β-naphthol and sulphuric acid, the ether, β-naphthyl acid sulphate is first formed and then decomposed into the two isomeric acids.

II. Bayer's acid.
β-naphthol-α-monosulphonic acid.

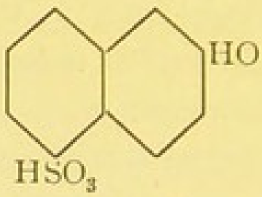


These are much used in manufacturing operations.

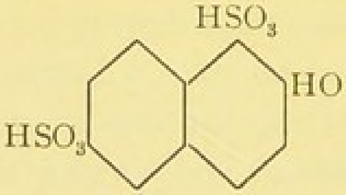
III. F-acid (L. Cassella & Co.).
β-naphthol-δ-monosulphonic acid.



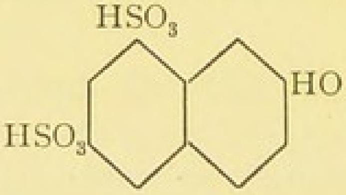
IV. Dahl's acid.
β-naphthol-γ-monosulphonic acid.



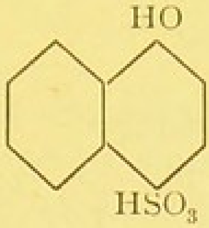
By further treatment of these monosulphonic acids with concentrated sulphuric acid, naphtholdisulphonic acids are obtained, of the β-forms of which three isomers are known. The exact constitutional formulæ are not perfectly clear. The so-called G- acid of Meister, Lucius & Brüning is probably—



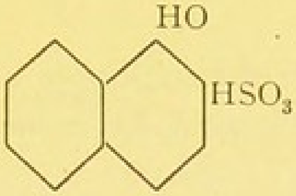
It forms a sodium salt soluble in alcohol (G-salt). The R-acid of Meister, Lucius & Brüning, the sodium salt of which (R-salt) is insoluble in alcohol, is probably—



It furnishes specially useful azo-colors. A third disulphonic acid (F-acid) has not yet been closely investigated. The three known isomeric α-naphtholmonosulphonic acids are of much less importance in the color-making industry than the corresponding β-derivatives. α-naphtholmonosulphonic acid, NW. (Neville & Winther) is prepared from α-amidonaphthalenesulphonic acid by diazotizing and subsequently decomposing by boiling. It has the composition :—

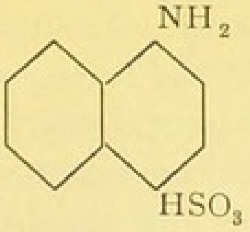


The second, α-naphtholmonosulphonic acid C., discovered by Cleve, has probably the constitution :—

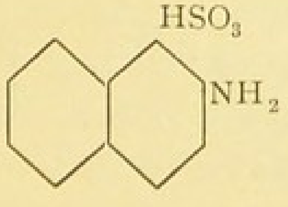


Two α-naphtholdisulphonic acids are also known, one prepared by Leo Vignon, known as LV., and another by Schöllkopf & Co., known as Sch.

Of the α-amidonaphthalenesulphonic acids, practically only one is used in manufacturing operations. This is Piria's, commonly known as naphthionic acid. Its constitution is probably

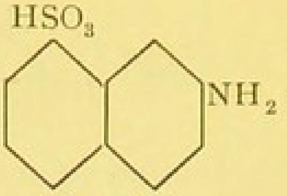


β-amidonaphthalenesulphonic acids are largely employed in the preparation of the Congo group. Three isomeric acids of this constitution are better known. First, the α-acid corresponds to the Bayer's acid :—



The β-acid corresponds to Schaeffer's acid.

The γ-acid is probably



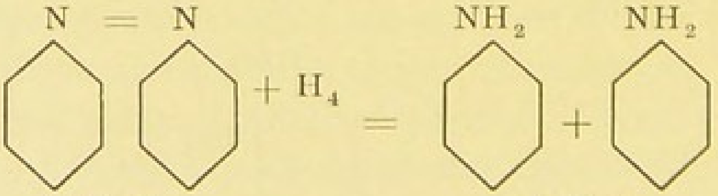
The δ-acid is doubtless a mixture of the β-acid with a new (F-)acid.

A β-amidonaphthalenedisulphonic acid prepared from β-nitronaphthalenedisulphonic acid by reduction has been used in the arts.

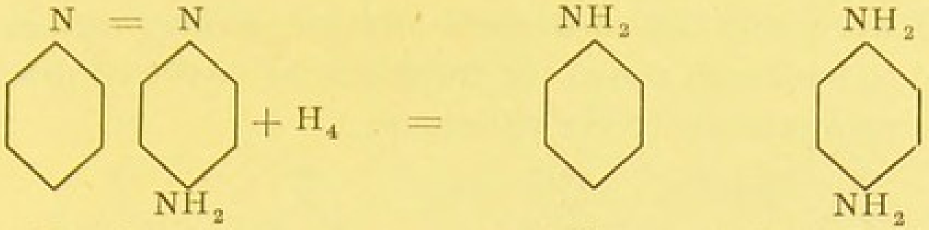
It is established that many of the materials enumerated above as employed in the manufacture of azo colors are poisonous, or at least, injurious. It would be unsafe, however, to infer *a priori* from the poisonous nature of the materials employed, a poisonous character in the colors, since any excess of these bodies is entirely removed during the process of manufacturing and purification, as has been noted above.

Decompositions and Transformations. — Reducing agents, for instance, zinc dust mixed with water, ammonium hydroxide, sodium hydroxide or dilute acids; stannous chloride or ammonium sulphide, decompose the azo-colors by separating the two nitrogen atoms in the azo-group and forming two amidogen groups.

$$R - N = N - R' + H_4 = R - NH_2 + R'NH_2.$$

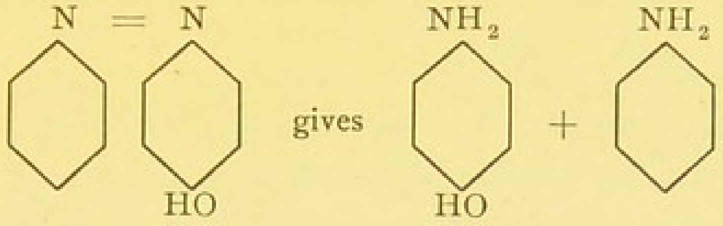


Azobenzene. Aniline.

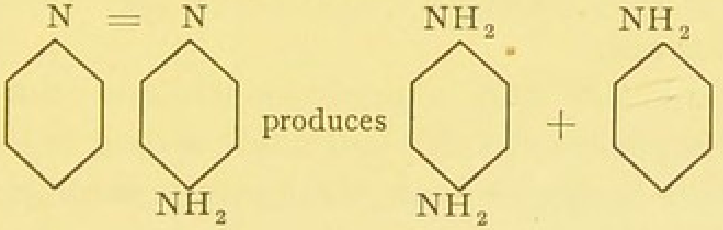


p-amidoazobenzene. Aniline. p-diamidobenzene.

This reaction is especially important, because it has in many cases enabled us to determine the constitution of the azo-colors. When, for instance, hydroxyazobenzene is converted by reduction into paramidohydroxybenzene and aniline, the nitrogen and hydroxyl groups will assume the para-position.

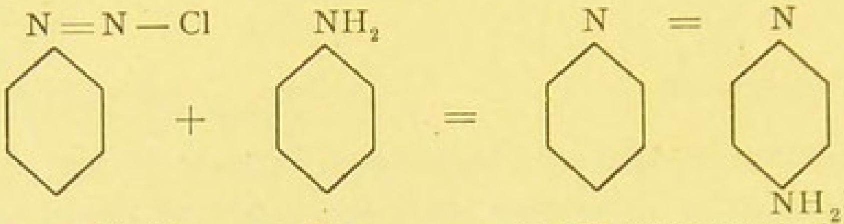


Amidoazobenzene gives by reduction paradiamidobenzene; therefore, the nitrogen and amidogen groups must have occupied in this color the para-position, thus:—



Azo-colors with free hydroxyl groups dissolve generally in sodium hydroxide, and give characteristic reactions. (For exceptions see below.) Concentrated sulphuric acid gives with most azo-colors very distinct color reactions, which are advantageously used for distinguishing various dyes. Spectroscopic examinations of these solutions may be employed in the practical recognition of these substances.

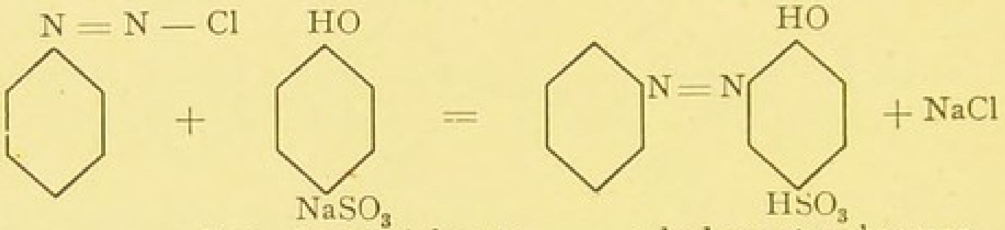
Constitution.—In the junction of a diazo-compound with a phenol or amine the position of the azo-group ($-N=N-$) in reference to the hydroxyl or amine is dependent upon the following conditions: When the carbon atom which is joined to the azo-group has, in the para-position, another carbon atom joined to hydrogen alone, the amidogen or hydroxyl group will take a para-position to the azo-group.



diazobenzene chloride. aniline. *p*-amidazobenzene hydrochloride.

This is the most frequent and most important class.

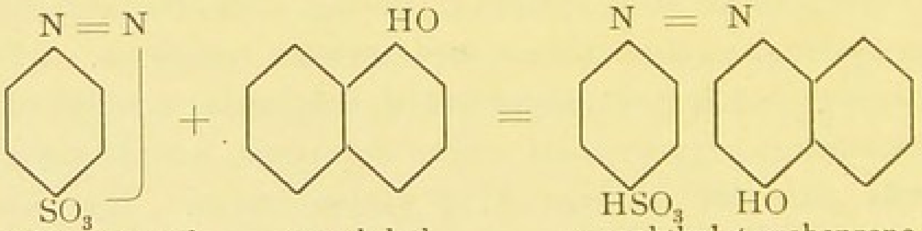
If the para-position, *i.e.*, the hydrogen at that point, is replaced by a radicle, the azo-group takes the ortho-position.



sodium phenolsulphonate. *o*-hydroxy-*p*-azobenzene sulphonic acid.

The attaching of the azo-group to the meta-position when other radicles are present in the ortho- or para-position has not yet been observed.

With *α*-naphthol and *α*-amidonaphthalene the azo-group takes the para-position to the hydroxyl as long as this is unsubstituted. If the hydrogen atom of the para-position is substituted, the azo-group takes the ortho-position.*



p-diazobenzene sulphonic anhydride. *α*-naphthol. *α*-naphthol-*p*-azobenzene sulphonic acid.

β-naphthol and *β*-amidonaphthalene have no hydrogen atom standing in the para-position to the hydroxyl group. When

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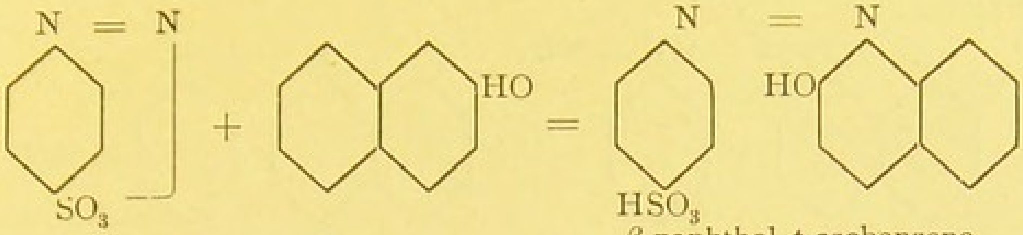
* According to Friedländer, ortho- as well as para-compounds are formed when the para-position is unsubstituted.

β-naphthol is joined, the azo-group takes the adjoining β-position (ortho-position) to the hydroxyl.



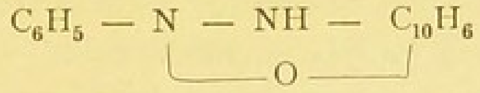
β-naphthol-*p*-azobenzene-sulphonic acid.

The correctness of the constitutional formulæ assumed in the above reactions is inferred from the reduction products of the resulting azo-colors, instances of which have already been presented. However, the close study of these reduction products, as far as the more complex forms are concerned, has just begun.

Those azo-bodies which result from a conjugation of diazo-salts with β-naphthol and β-amidonaphthalene must have a different constitution from the colors heretofore indicated. If the azo-colors prepared from β-naphthol were true hydroxyazo-compounds they should be by reason of the free hydroxyl group soluble in alkali, as are the derivatives of β-naphthol, but they are insoluble. For this reason C. Liebermann has formulated anilineazo-β-naphthol, not—

$$C_6H_5 - N = N - C_{10}H_6\ HO\ (\beta)$$

but as

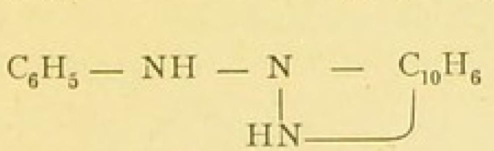


$$C_6H_5 - \underbrace{N - NH - C_{10}H_6}_{O}$$

Zincke formulated the corresponding product from diazobenzene chloride and β-amidonaphthalene, not

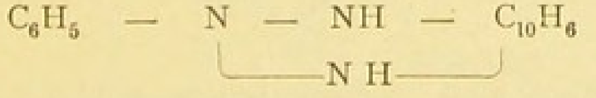
$$C_6H_5 - N = N - C_{10}H_6\ NH_2\ (\beta)$$

but



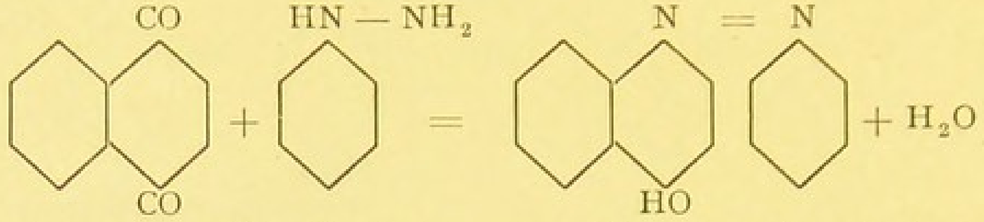
$$C_6H_5 - NH - \underbrace{N - C_{10}H_6}_{HN}$$

or as



$$C_6H_5 - \underbrace{N - NH - C_{10}H_6}_{NH}$$

A different formula is also supposable for the α-naphthol azo-colors, when we consider their origin from quinone and phenyl hydrazine:—



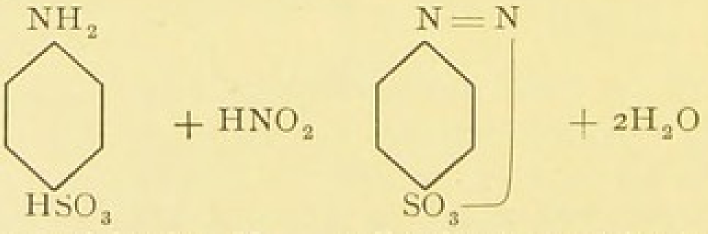
α-naphthoquinone. Phenylhydrazine. α-naphthoquinonephenylhydrazine = benzene-*p*-azo-α-naphthol.

The α-naphthoquinonephenylhydrazine obtained in this reaction is wholly identical with the benzeneazo-α-naphthol obtained from diazobenzene chloride and α-naphthol, while the products of the action of diazobenzene chloride and β-naphthol, and phenylhydrazine and β-naphthoquinone, although isomeric are different in properties.

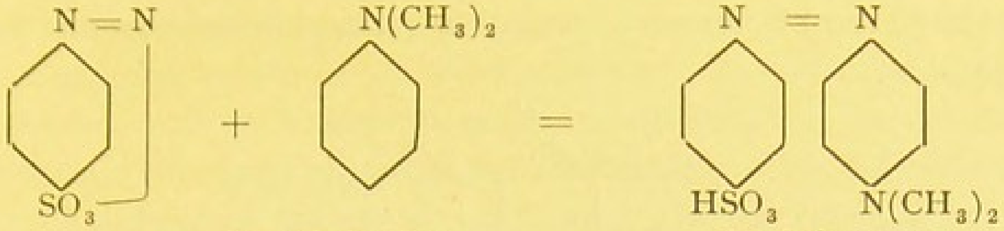
Solubility, Color, Deportment with Fibres.—The azo-colors employed in the industries are mostly soluble in water. They owe this solubility to the presence of one or more sulphonic groups. For instance, dimethylazobenzene (butter-yellow) is soluble only in alcohol, "spirit soluble," while the sulphonic acid derived from it (helianthin, methyl orange) is easily soluble in water. To introduce sulphonic groups into azo-colors, three methods are available:—

(*a*) The prepared but insoluble color is treated directly with strong sulphuric acid (sulphonation).

(*b*) The sulphonic group is first introduced into the diazotized body, or into the phenol or amine which is to unite with the diazo-salt. Thus, by diazotizing pure amidobenzene-sulphonic acid, and joining it with dimethyl aniline, we obtain a soluble methyl orange.



p-amidobenzene sulphonic acid. *p*-diazobenzene sulphonic anhydride.



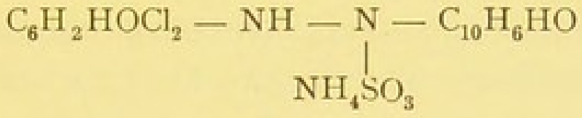
Dimethylaniline.

Methyl orange.
Helianthin.

Recently a third method was discovered for producing soluble azo-colors. E. Spiegel showed that insoluble azo-colors could be converted into soluble forms by the addition of ammonium acid sulphite, or sodium acid sulphite, which combinations are called azarines.

$$C_6H_2HOCl_2 - N = N - C_{10}H_6HO \quad + \quad NH_4HSO_3 =$$

Dichlorphenol-azo-β-naphthol. Acid ammonium sulphite.

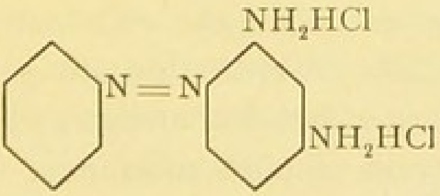


$$\underset{\displaystyle NH_4SO_3}{C_6H_2HOCl_2 - NH - \overset{}{N} - C_{10}H_6HO}$$

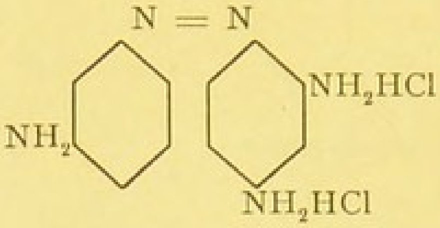
Azarine S.

The azarines decompose by the influence of heat or alkali readily into the original color and neutral sulphite. This property is utilized in dyeing and printing. The azarine is dyed or printed on the fibre and the compound is then split by heat or an alkaline bath. The color is fixed in the insoluble form and the soluble sulphite is washed out.

Yellow, red, brown, blue, violet, indeed, almost black, azo-colors have been obtained, but the production of a green azo-color seems to be as yet unaccomplished. Most of the azo-colors are acid, the basic members being quite limited in number. Among these latter are included chrysoidin, metadiamidoazobenzene hydrochloride,



and Bismarck brown, probably triamidoazobenzene hydrochloride,



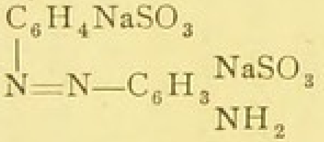
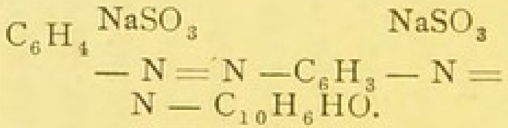
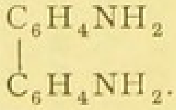
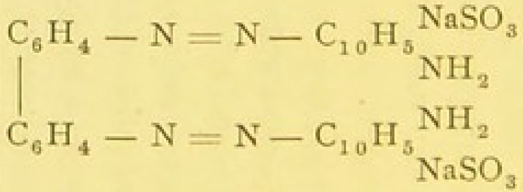
The soluble azo-colors which contain sulphonic groups find widest application in wool dyeing. The color vat is charged with sulphuric acid and sodium sulphate, practically sodium acid sulphate, technically known as cream of tartar preparation. By this, the color becomes less soluble and deposits more slowly upon the fibre. Silk is but rarely dyed with azo-colors. Up to a recent period, cotton could not be dyed with them except with the employment of a mordant, but lately a class of azo-colors known as Congo dyes have been obtained, which dye cotton in the ordinary soap bath. Metallic compounds of the azo-colors (lakes) serve for the coloring of paper. The colors insoluble in water but soluble in alcohol are used for the painting of wood, leather, and metals, being dissolved in lacquer or varnish. Azo-colors, both water and spirit soluble, are used in considerable amount for the coloring of food and drink. The spirit soluble are used, for instance, for the coloring of alcoholic beverages and liqueurs. Of the water soluble forms, aniline yellow (spirit yellow) is employed for coloring noodles.

Cazeneuve indicates the following colors as being used for the coloring of wines: Bismarck brown (phenylene brown), chrysoidin, aniline yellow, acid yellow, (solid yellow), various ponceaux, fast red, (roccellin), rouge purple, tropæolin, metanil yellow, azoflavin.

Typical Reactions of the Group—A characteristic reaction common to all azo-colors and easily performed is as yet unknown. By reducing, they are, as is the case with many other colors, decolorized. The products of reduction are generally only to be recognized by an intricate chemical analysis and with the employment of, at least, a gram of pure substance. In most cases the reduction products do not yield by oxidation the original material but indigo and azines (*e. g.*, safranine) yield by reduction colorless bodies, and by oxidation, even when standing in contact with the air, the original color is reproduced. The colorless reduction products of the rosolic acid series are not reconverted to rosolic acid, etc., by oxidation, but these bodies are free from nitrogen, and, therefore, easily distinguished from the azo-colors. The alkalies change the tint of azo-colors in a variety of ways, but decoloration never takes place, as in the case of fuchsin.

From these considerations it will appear that the recognition of any body as an azo-color is, even for the expert, no easy task, especially when little material is at hand, or when the determination is to be made upon the fibre. The artificial coloring of food can be detected, therefore, only under specially favorable conditions. The first practicable method for determining these colors was that given by Witt. Weingartner, Lepetit, and Martinon worked in the same direction. Further assistance in these, to say the least, not very satisfactory investigations, has been furnished by Kertész, G. Schultz, and P. Julius. When we are examining the secretions and excretions of animals for a color that has been exhibited with the food, a task with which the author of this book has been much concerned, the practical methods, outside of chemical and spectroscopical tests are the dyeing of wool, silk, or cotton by the color. Of course, for such a test the liquid examined, generally urine, must be prepared in the same manner as the dyer prepares the bath. Occasionally, mordanting the fibre will be advisable. I need not recall the fact that this method has been used by other investigators for the detection of small quantities of colors, being often used for the detection of fuchsin in wine, or of picric acid in beer. The color precipitated upon the fabric may then be recognized and identified by chemical reaction. On the detection of azo-colors in wine, we have a considerable number of investigations mostly of French origin. Caution against too great confidence in the spectroscope for these observations must be expressed, for it is known that constant

CONSTITUTION AND NOMENCLATURE OF AZO-COLORS.

COMMERCIAL NAME AND EMPIRICAL FORMULA.	MODE OF FORMATION.		STRUCTURAL FORMULA.	SYSTEMATIC NAME.
	Diazotized Body.	Conjugated Body.		
Chrysoidin. $C_{12}H_{13}N_4Cl.$	Aniline. $C_6H_5NH_2.$	*m*-diamidobenzene. $C_6H_4(NH_2)_2.$	$C_6H_5-N=$ $N-C_6H_3(NH_2)_2HCl.$	Aniline-azo-*m*-diamido benzene hydrochloride.
Archil-substitute. $NaC_{16}H_{11}N_4O_5S.$	*p*-nitraniline. $C_6H_4NH_2NO_2.$	Naphthionic acid. $C_{10}H_6NH_2HSO_3.$	$C_6H_4NO_2-N=$ $N-C_{10}H_3NII_2NaSO_3.$	Sodium *p*-nitraniline azo-*a*-amidonaphthalene sulphonate.
Biebrich scarlet. $NaC_{22}H_{14}N_4O_7S_2.$	Sodium amidoazo-benzene disulphonate.  $C_6H_4NaSO_3$ $\vert$ $N=N-C_6H_3\begin{matrix}NaSO_3\\NH_2\end{matrix}$	*β*-naphthol. $C_{10}H_7HO.$	 $C_6H_4^{NaSO_3}$ $-N=N-C_6H_3^{NaSO_3}-N=$ $N-C_{10}H_6HO.$	Sodium azo-*β*-naphthol amido-azo-benzene disulphonate.
Congo red. $NaC_{32}H_{22}N_6O_6S_2.$	Benzidine.  $C_6H_4NH_2$ $\vert$ $C_6H_4NH_2.$	2 molecules of naphthionic acid. 2 $(C_{10}H_6NH_2HSO_3).$	 $C_6H_4-N=N-C_{10}H_5\begin{matrix}NaSO_3\\NH_2\end{matrix}$ $\vert$ $C_6H_4-N=N-C_{10}H_5\begin{matrix}NH_2\\NaSO_3\end{matrix}$	Sodium benzidine disazo naphthionate naphthionate.

conditions of solvent, concentration and illumination must be observed. I wholly agree with Cazeneuve's statement: "We may observe, that although the spectra of the azo-colors differ but little among themselves, they are distinguished sharply from those of fuchsin, cochineal, and archil."

Commercial and Scientific Designations.—As set forth above, the artificial colors bear in commerce mostly arbitrary names, and justly, for scientific names, while they express the molecular structure, are so long, intricate and unpleasant that their use is prevented. Examples are given above. Proposals for simplying the nomenclature have not been lacking, and none of these accomplish the purpose better than the one proposed by G. Schultz.

As has been set forth, each azo-color consists of two parts, a diazotized base and a phenol or amine, which is joined to it. In Schultz's method for naming the azo-colors the body from which the diazo-compound has been prepared is first named, then follow the syllable "azo," then the name of the phenol or amine to which the diazo-compound is joined. In the diazo-colors containing the azo-group (— N = N —) twice, the diazotized base is separated from both the components by the word disazo. I have adopted this proposal since it has shown itself to be practical. A few samples are given in the annexed table. From the instances there given it will appear that even so complicated a compound as Congo-red receives a name relatively simple and intelligible to the chemist.

Classification of the Azo-colors.*—As a basis for classifying the azo-colors we can take the number of the azo-groups contained in a molecule, distinguishing two classes, *monazo-* and *disazo-*, accordingly as they contain one or two such groups. The former class can be subdivided into *hydroxazo-compounds* and *amidoazo-compounds*, according to whether they arise from the junction of a diazo-salt with a hydroxy- or an amido-com-

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* For illustrative formulæ and reactions of the main groups of azo-colors, see Appendix.

pound. Both these classes of bodies may be either sulphonated or not. This group includes a large number of azo-colors, and, in fact, those first discovered. It includes the azarins, which were sufficiently described previously.

In agreement with Schultz, we may divide the disazo-colors into three groups:—

(*a*) *Primary Disazo-colors.*—These originate from the action of two similar or dissimilar diazo-salts upon a single amine or phenol. Fast brown belongs here. It is produced by the action of two molecules of diazonaphthalenesulphonic acid upon one molecule of resorcinol.

(*b*) *Secondary Disazo-colors.*—These arise by the diazotizing of a diazo-compound containing a free amidogen group, and a junction of the compound so obtained with amines or phenols. Some very valuble dyes are included in this group. Biebrich scarlet, for instance, is produced by the diazotizing of amidoazobenzenesulphonic acid, and the junction of the diazo-compound so obtained with β-naphthol.

(*c*) *Azo-colors of the Congo Group.*—These are so called from the principal member of the group, Congo red. They are derived from benzidine, and its homologues by diazotizing and joining to similar and dissimilar molecules of a phenol or amine. By diazotizing benzidine, the so-called *tetrazo-compounds* arise, which name is derived from the four nitrogen atoms the molecule contains. Bodies of the Congo group are, therefore, also called tetrazo-dyes. They dye cotton fast to washing, without a mordant, which property distinguishes them from all other known azo-colors.

OBSERVATIONS ON ANIMALS.

Records from Other Experimenters.—We are indebted to Cazeneuve and Lépine for able researches as to the effect of azo-colors upon human beings and the lower animals, the results of which are exhibited in the following list[*]:—

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[*] The name in quotation marks is the title given in the original French work. The titles in parentheses are the synonyms.

"Rouge soluble" (azorubin S, fast red C, carmoisin) is not poisonous to human beings.

"Rouge poupre" (new coccin, brilliant ponceau, cochineal red, or fast red D, Bordeaux S, amaranth, acid azorubin 2B), not poisonous to human beings.

"Bordeaux B" (fast red B), not poisonous to human beings.

"Ponceau R" (ponceau 2R, xylidin red, xylidin ponceau), not poisonous to dogs, either by administration by stomach nor injection into blood.

"Orange I" (*α*-naphthol orange, tropæolin OOO), same as ponceau R.

"Solid yellow" (fast yellow R, acid yellow R, yellow W), not poisonous to dogs, either when administered by the stomach or injected into blood. Poisonous to human beings (?).

The azo-colors included in the above investigations belong to the monazo-group and are all harmless.

Weyl's Researches.—My own investigations on monazo-colors are set forth in the following list:—

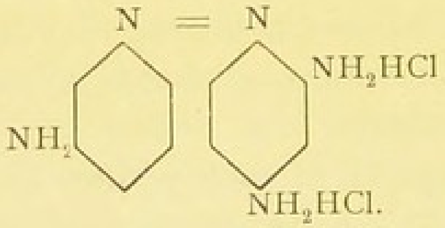
Non-poisonous: Bismarck brown, Soudan I, ponceau 4GB, archil-substitute, chrysoidin, diphenylamine orange, azarin S, *m*-nitrazotin, *p*-nitrazotin.

Poisonous: Orange II, metanil yellow.

To this I make the following comment concerning the selections of the colors. R — N = N — R — Gr. denotes an azo-color. R stands for C_6H_5, R′ for $C_{10}H_6$, Gr. for a salt-forming group. I desired to learn if the entrance of certain groups (Gr.) into the azo-color exercise an influence upon its toxic action. To this end, I started with the color which had been produced by the combination of diazobenzene chloride with *β*-naphthol (Soudan I). I introduced into this color, a nitro-group which stood in the benzene nucleus in the meta-position to the azo-group. The azo-color (*m*-nitrazotin) was thus produced. The influence of the sulphonic group could be thus indicated. This may be attached either to the benzene or to the naphthalene nucleus. *p*-nitrazotin contains at the same time a nitro- and a sulphonic group, while archil-substitute, which is derived from the *α*-amidonaphthalene, also contains nitro- and sulphonic groups. Unfortunately, further investigations directed to the introducing of other groups into the color molecule, in order to obtain information as to their influence upon the toxic action of the body so produced, were frustrated, because other intermediate products were not obtainable by me. Bismarck brown and chrysoidin are much used. Azarin S has not been examined. Diphenylamine orange and metanil yellow are isomeric.

Bismarck Brown.

This color, also known as Manchester brown, phenylene brown, Vesuvin, aniline brown, leather brown, cinnamon brown, canelle, English brown, and golden brown, is produced by the action of two molecules of sodium nitrite on three molecules of *m*-diamidobenzene hydrochloride in watery solution. It is not positively established whether it is triamidoazobenzene hydrochloride, as usually assumed,



or, more probably, a compound of *m*-diamidobenzenedisazo-*m*-diamidobenzene. The latter form is the more probable from the mode of formation, and in this case Bismarck brown would belong to the disazo-colors.

Typical Reactions.—Dark-brown powder, producing a brown solution in water, which gives with hydrochloric acid a brown precipitate easily soluble, and with acetic acid a brown solution, but no precipitate; with sodium hydroxide, a brown precipitate difficultly soluble; with ammonium hydroxide, a brown precipitate soluble in excess, and with ammoniacal copper solution, a brown precipitate difficultly soluble in hot water, reappearing on cooling. The powder dissolves in concentrated sulphuric acid to a brown solution which becomes reddish on dilution. Bismarck brown is one of the earliest-discovered azo-colors, but is still used to a large extent for the coloring of wool, leather, and jute. Cotton is dyed only after previous mordanting with tannin and tartar emetic. The specimens used in the experiment were from the Aniline Manufacturing Company of Berlin.*

Exp. 1.—Dog weighing 5690 grams, selected June 11th, and on that and the following day showing no albumin in the urine. On June 13th, at 10.30 A. M., 2 grams were administered by the œsophageal tube. At 12 vomiting occurred. June 14th, 10 o'clock, 2 grams: vomiting at 12, no food taken. June 15th, no food taken, animal moved about a little. June 16th, 2 grams, two hours after which marked vomiting occurred. June 17th to 20th, no nourishment taken except water. June 21st, food taken, animal more lively, albumin in urine. June 22d, 5 grams, animal vomiting for one-half hour after administration. June 23d to 27th, almost no food taken, albumin in urine. June 28th, improving. June 30th, food taken, albumin in urine. Animal was under observation until July 15th. Finally only slight traces of albumin were detected in the urine and the appetite was restored.

Exp. 2.—Dog weighing 29500 grams, selected April 29th, was found to have no albuminuria. On April 30th, received 5 grams by the œsophageal tube. May 1st, urine brown, animal lively, appetite normal. May 2d, 5 grams by the tube. Bismarck brown was recognized in the urine by dyeing wool and chemical tests. May 4th, 5 grams administered. Urine brownish, no albumin. May 5th, urine normal, no color, no albumin. May 8th, 15 grams administered. Animal vomited once after the administration. May 12th, ate little, seemed sick. May 14th, seemed lively. May 15th, 15 grams given; vomited after the administration. May 16th, no food taken, no albuminuria. May 18th, animal normal. May 22d, normal. Weight 28900 grams.

Exp. 3.—Dog weighing 5500 grams, received during an entire month, daily, .25 gram of Bismarck brown with its food. The animal continued in good health during the entire time, did not vomit and ate as usual. It gained during the experiment about 350 grams.

Exp. 4.—Dog weighing 6300 grams, received in the course of 20

[* I have found traces of copper in all the commercial samples of Bismarck brown I have tested.—TRANS.]

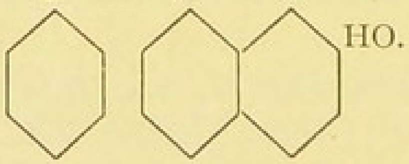
days, 9 injections, each .1 gram, of Bismarck brown in 8-10 c. c. of sterilized water inserted below the skin of the back. The animal remained entirely normal. Urine was normal color and contained no albumin.

Exp. 5.—Same animal received three injections of .1 gram each of Bismarck brown in 8-10 c. c. of sterilized water introduced into the abdominal cavity. Animal showed slight elevation of temperature and refused food. Urine remained uncolored, and in a week the animal had completely recovered.

Bismarck brown produces, when administered to dogs by the stomach, even in doses of .35 gram per kilo of body-weight, vomiting and albuminuria. Further disturbance is not noted, even with large doses. Small doses, .045 gram per kilo of body-weight, even when frequently administered, seem to be entirely harmless. Doses of .016 gram are harmless, even when introduced into the subcutaneous cellular tissue. The same dose introduced into the abdominal cavity induces slight disturbances. With small doses the urine remains uncolored. Only when considerable quantities are administered does the unaltered color appear in the urine.

Soudan I.

This was first prepared by C. Liebermann from diazobenzene chloride and β-naphthol. The material used in my investigations was prepared by myself in this manner. I obtained the color by recrystallization from 90 per cent. alcohol in beautiful red crystals. It is employed in coloring lacquers, oils, and liqueurs. It is aniline-azo-β-naphthol :—



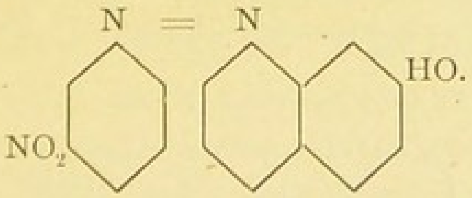
Typical Reactions.—In the pure form it is in red crystals, insoluble in water, soluble in alcohol, to an orange-red solution. The alcoholic solution produces, with aqueous sodium hydroxide or ammonium hydroxide, a red-brown solution. With ammoniacal copper solution, a brown precipitate. The powder dissolves in concentrated sulphuric acid to a fuchsin-red liquid, which on dilution with water yields an orange-yellow precipitate.

Exp. 1.—Dog weighing 11900 grams, selected June 7th, 1888. Urine alkaline, no albumin. June 8th, 2 grams administered by the tube. June 9th, no administration. Urine normal color, alkaline, no albumin, sulphates abundant. The distillate obtained from the urine, strongly acidulated with hydrochloric acid, gave a distinct precipitate with bromine water. June 10th, no administration. June 11th, 2 grams by the tube. Animal lively, normal fæces. June 12th, vomiting, but otherwise lively. Urine almost free from phenol. Two grams by the tube same date. June 13th, 2 grams administered. Urine now dark brown, alkaline, albumin distinctly present, also sulphates. June 15th, 2 grams. June 16th, animal lively, took food. Weight 11550 grams, therefore lost 350 grams in ten days. June 22d, animal lively. Urine normal in color, no albumin. June 23d, 5 grams administered. Urine rather darker than normal. June 24th, took little food. June 25th, 5 grams administered, but little food taken, June 26th, fæces yield to hot alcohol much of the unchanged dye stuff, which by cooling with the solvent is deposited in red crystals and gives the above reaction. Very little albumin in the urine. June 27th, animal lively, but little appetite. June 29th, food taken, urine uncolored. June 30th, animal lively, very little albumin in the urine.

The color, in the doses administered, is not entirely harmless, since a limited albuminuria seems to be brought about. From want of a suitable solvent, subcutaneous injections could not be made.

Metanitrazotin.

This an azo-color, which seems not to have been described. I obtained it by the conjugation of diazotized *m*-nitraniline with *β*-naphthol. Its mode of formation suggests the following formula :—



It may be called *m*-nitranilineazo-*β*-naphthol.

It is scarcely soluble in 90 per cent. alcohol, difficultly soluble in benzene and glacial acetic acid. It is dissolved in warm alcoholic solution of sodium hydroxide, filtered, and precipitated with hydrochloric acid. The precipitate is freed from the adhering liquid by the aspirator and washed with hot water. It presents the form of a red powder. The alcoholic solution produces, with sodium hydroxide and ammonium hydroxide, a Burgundy-red solution which is changed to yellow by acids. The powder dissolves in concentrated sulphuric acid to a fuchsin-red liquid which changes to orange-yellow by dilution with water, and gives a greenish-yellow fluorescence, possibly by reason of a very finely divided precipitate.

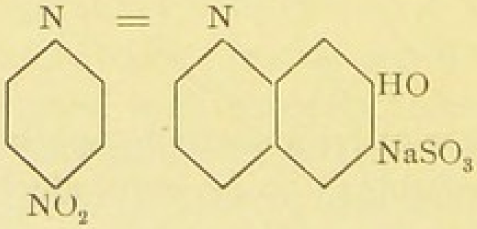
Exp. 1.—Dog weighing 12600 grams, selected July 11th, showed traces of albumin in the urine. July 12th, same condition. One gram by the œsophageal tube. Urine pale, alkaline, traces of albumin, but phenol hardly recognizable. July 13th, 2 grams administered. Urine abundant, pale yellow, turbid, strongly alkaline; addition of acid causes strong effervescence; no sugar, traces of albumin, no phenol. July 14th, 2 grams by the tube. Urine strongly alkaline. July 15th, 2 grams by the tube. Urine abundant. July 16th, animal lively; weight, 12,450 grams, consequently a loss of 150 grams in five days.

A second dog, weighing 5600 grams, received ten doses of 1 gram each during twenty days. Animal remained lively, urine free from albumin and not abnormally colored. It was under observation for five weeks.

I supposed, in view of the observations made on nitro-colors, that metanitrazotin would be poisonous, but, in spite of the nitro-group that is present, it is shown to be harmless.

Paranitrazotin.

I prepared this color from diazotized *p*-nitraniline and from β-naphtholmonosulphonic acid S. The color is sodium *p*-nitranilineazo-β-naphtholmonosulphonate. Its constitution is probably:—

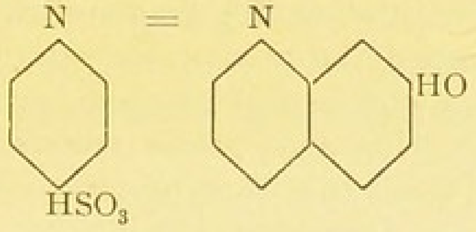


Typical Reactions.—It is a red-brown powder, producing with water an orange-brown solution. This solution gives with sodium hydroxide and ammonium hydroxide a fuchsin-red color; with copper sulphate, no change; with ammoniacal copper solution, a red-violet precipitate soluble to the same color in ammonium hydroxide. The powder dissolves in concentrated sulphuric acid to a bright red liquid which changes to orange-yellow by dilution with water. The mode of formation suggests the name, paranitrazotin.

A rabbit weighing 1500 grams received two doses of 2½ grams each by the œsophageal tube in the course of three days. It remained lively. Further investigations were prevented by a want of material.

Orange II.

This color is also known as orange 2, *β*-naphthol orange, tropæolin OOO 2, mandarin, mandarin G extra, chrysaurin, and golden orange. I obtained this color myself from *p*-diazobenzensulphonic acid and *β*-naphthol. It crystallizes from water in orange-yellow plates. It is azo-*β*-naphthol-*p*-azobenzenesulphonic acid.



Wool and silk are colored orange in an acid bath; cotton only after previous mordanting.

Typical Reactions.—Orange-red crystals easily soluble in water to an orange-red solution. The watery solution gives with hydrochloric acid a brownish precipitate, dissolving in alcohol to an orange-red liquid. Sodium hydroxide and ammonium hydroxide give red-brown solutions. Ammoniacal copper solution produces a gelatinous red-brown precipitate. The powder dissolves in concentrated sulphuric acid to a fuchsin-red liquid, which, on dilution with water, gives a brownish-red precipitate.

Exp. 1.—Dog weighing 10500 grams received, July 4th, 5 grams by the tube. Urine red, diarrhœa, (?) vomiting. (?) The red urine was decolorized by warming with stannous chloride and hydrochloric acid. July 5th, no administration. Urine colored by the dye stuff, vomiting (?). July 6th, urine red. July 7th, urine weak red with much sediment. July 8th, urine scanty, much sediment. July 9th to 12th, urine alkaline, turbid, contains albumin. July 13th, 7 grams by the tube. July 14th, urine orange-red, no food taken, diarrhœa. July 15th, animal ate little, urine weak reddish. July 17th, 2 grams administered. No food taken; diarrhœa; urine neutral, weak red, very turbid, doubtful traces of albumin. July 18th, animal very miserable, eyelids adherent. July 19th, no administration, animal in bad condition. July 20th, much albumin in the orange-colored urine; animal very miserable; 40° rectal temperature. July 27th, animal very weak; urine orange-red, colored dark red by sodium hydroxide; acid turns it yellow. Cotton easily dyed. July 23d, animal found dead in its cage. July 24th, post-mortem showed much fatty tissue of normal color, muscles normal in color, stomach and intestines pale; in the stomach and upper section of the intestines numerous abscesses, recent and just cicatrizing; liver somewhat fatty degenerated; kidneys pale; epithelium fatty; lungs normal; heart pale, containing much white coagula; brain not tinged.

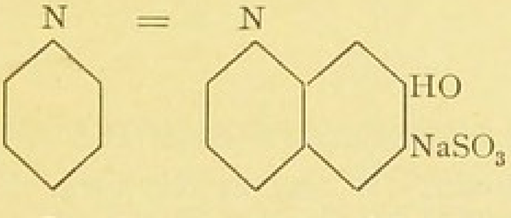
Exp. 2.—A white rabbit, weighing 2250 grams, died within twelve hours after the administration of 3 grams of the color. Four hours after the administration the animal was running about the room, lively. Post-mortem was, through accident, omitted.

Exp. 3,—Dog weighing 4300 grams received, December 12th, .5 gram dissolved in about 10 c. c. of lukewarm water, injected under the skin of the back. December 12th to 14th, urine alkaline, some albumin, no sugar; color weak orange. December 15th, no abscess at the point of injection, animal lively and took food. December 16th, .25 gram subcutaneously on the opposite side of the back. Urine orange red, acid, traces of albumin. Wool easily dyed in the liquid acidulated with sulphuric acid. Dec. 17th, .5 gram subcutaneously. No abscesses, some diarrhœa. Dec. 18th, rectal temperature 39.5°; right eye closed and inflamed; traces of albumin; urine strongly orange; dyes wool easily. Dec. 19th, coryza better, but cataract appearing. .5 gram administered subcutaneously. Urine red orange; animal lively. Dec. 20th, no injection; little albumin; animal trembled. Dec. 21st, but little albumin. .75 gram given in two places on the back. Dec. 22d, animal very miserable; trembled and snarled; but little albumin. Dec. 23d, continued the same. Dec. 25th, abscesses developed at the point of injection of Dec. 21st. Dec. 26th, animal livelier. Dec. 27th, abscesses opened spontaneously; animal weighed 3840 grams, having lost, therefore, 460 grams in fifteen days. Jan. 2d, abscesses nearly healed; animal lively; took food. Jan. 3d, animal began to lose hair. Jan. 14th. almost without hair. Weight, 3890 grams; lively; ate well. Jan, 17th, slept well, ate heartily. Jan. 26th, animal had completely recovered; weight 5120 grams.

β-naphthol orange is, therefore, according to experiment 1, poisonous in small doses when administered by the stomach, and suffices to kill a moderately strong dog. The rabbit, experiment 2, serves as a control. In contrast to β-naphthol orange, Cazeneuve and Lépine found the corresponding α-naphthol orange, distinguished from β-naphthol orange only by the position of the hydroxyl group, non-poisonous. The β-color seems almost to show its poisonous action when administered subcutaneously, but the animal did not succumb to the experiment.

Ponceau 4 GB.

This color is also known as croceïn and brilliant orange. I prepared this color myself from diazobenzene chloride and sodium β-naphtholsulphonate S. (Schæffer's salt.) It has probably the constitution:—



Typical Reactions.—In the pure condition a red crystalline powder that dissolves not very easily in water to a red solution which produces, with hydrochloric acid, a yellowish-brown precipitate, easily soluble to yellowish-red color in alcohol. With sodium hydroxide and ammonium hydroxide, a yellow solution. With ammoniacal copper solution, a dirty, yellowish-brown precipitate. Concentrated sulphuric acid dissolves the powder to an orange-yellow liquid, which deposits a yellowish-brown precipitate when diluted with water. In acid solution, wool is colored orange yellow.

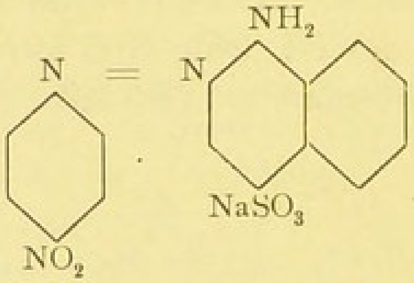
Exp. 1.—Dog weighing 12400 grams; received, June 19th, 2 grams dissolved in water by the tube. Urine rose-colored. June 20th, 2 grams administered. Urine reddish. June 21st, 2 grams in water. Animal lively; urine reddish, no blood, no albumin. June 22d, 2 grams. Animal lively; urine alkaline, no albumin, no phenol. June 23d, 4 grams. Urine normal color, alkaline, turbid, no albumin. June 24th, animal lively, took food. June 27th, 4 grams. June 28th, urine normal color, free from albumin.

In a second investigation a dog weighing 8500 grams received for an entire month 1 gram daily by the œsophageal tube. Urine remained uncolored, animal lively, with undisturbed appetite. The loss of weight, 200 grams in thirty days, need not be considered.

This color can be regarded as non-poisonous.

Archil-substitute. Naphthion red (now obsolete).

This color is prepared from diazotized *p*-nitraniline and naphthionic acid and has, therefore, the constitution :—



My preparation was obtained from the Aniline Manufacturing Company of Berlin. It was in the form of a red liquid which contained 8.2 per cent. of the color.

Typical Reactions.—The color has the form of a brown paste soluble in water to a red-brown color, which solution gives with hydrochloric acid a bluish-red precipitate which is soluble in water and in 96 per cent. alcohol to a red brown. Acetic acid produces a reddish-brown solution. Sodium hydroxide produces a bluish-red precipitate difficultly soluble in water but easily soluble in alcohol to a brownish-red liquid. Ammonium hydroxide produces a brownish-red solution. Ammoniacal copper solution produces a dirty red precipitate which is soluble in hot water. The paste dissolves in concentrated sulphuric acid to a fuchsin-red solution, which, on dilution with water, gives a red-brown precipitate. It colors wool, in acid solution, archil red.

Exp. 1.—December 24th and 26th, dog weighing 3810 grams, urine weakly alkaline, some albumin, no mucin. Dec. 27th, 20 c.c. of the solution equals 1.64 grams of the color administered with peptone. Tendency to vomit, but no actual vomiting. Urine normal, nearly colorless, slightly alkaline, traces of albumin. No characteristic changes with acids or alkalies, or concentrated sulphuric acid. Dec. 28th, 20 c.c. of the solution with peptone. Urine as above, animal lively. Dec. 30th, 40 c.c. of the solution equals 3.28 grams of the color. Dec. 31st, animal lively, took food; urine as above; weight 3980 grams, consequently a gain of 170 grams in seven days. Jan. 1st, 1889, urine uncolored, some albumin, much sulphates. Jan. 2d, 50 c.c. of the solution equals 4.1 grams of the color. Urine alkaline, otherwise, as above, no color. Jan. 3d, urine gives a rose color to filter paper; alkaline, with very little albumin, dyes wool when acidified; animal lively; experiment relinquished.

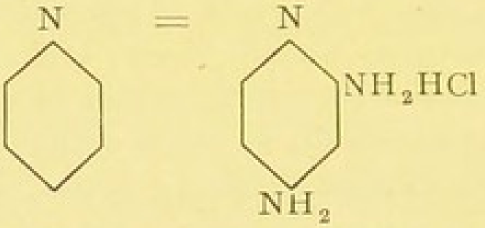
In a second investigation, a dog weighing 4500 grams received daily for one month 10 c.c. of the color solution, which equals .82 gram of the color,—therefore, altogether, 24 grams, which showed the same results as experiment No. 1, except that the urine remained uncolored.

Exp. 2.—Dog weighing 4980 grams, on Jan. 2d showed urine of normal color, very little albumin, and received 10 c.c. of the color subcutaneously, which equals .82 gram. of the color. Jan. 3d, urine reddish, no injection. Jan. 4th, urine reddish, traces of albumin. 10 c.c. of the solution administered on left side of the back. Jan. 5th, urine reddish, hardly any albumin, much sulphates; animal lively, no abscesses. Jan. 6th to 7th, no abscesses, animal lively; little albumin. Jan. 8th, animal normal; urine uncolored; little albumin. Jan. 9th, food taken; no abscesses; 20 c.c. (equals 1.64 grams) injected in two places on the back. Jan. 10th, no food taken; conjunctiva not colored; urine reddish; no albumin. Jan. 11th, no abscesses; urine uncolored, little albumin. Jan. 12th, urine colorless, little albumin. Jan. 14th, weight 4950 grams, therefore, no reduction in weight in twelve days; animal lively, no abscesses. Jan 17th, animal lively; very little albumin.

This color, in the doses indicated, must be regarded as not poisonous when administered by the stomach or subcutaneously, in spite of the fact that it contains a nitro-group. Probably, as is the case with naphthol yellow, the action of the nitro-group is ameliorated by the simultaneous presence of a sulphonic group.

Chrysoidin.

This color is prepared from diazobenzene chloride and *m*-diamidobenzene, and has, therefore, probably, the constitution:



It colors wool and silk without a mordant, and cotton after mordanting, orange. My specimen was obtained from the Aniline Manufacturing Company of Berlin, and was in the form of a reddish-brown crystalline powder easily soluble in water to a brownish-red liquid.

Typical Reactions.—The watery solution produces with hydrochloric acid a brown gelatinous precipitate easily soluble in water to an orange-yellow liquid. Acetic acid produced no change. Sodium hydroxide and ammonium hydroxide produced orange-brown precipitates difficultly soluble in water, easily in alcohol, to orange-yellow liquids. Ammoniacal copper solution produced a brownish-red precipitate soluble in hot water and insoluble in alcohol. The powder dissolved in concentrated sulphuric acid to a yellowish-brown liquid which by dilution with water became ponceaux.

Exp. 1.—March 24th and 25th, dog weighing 26600 grams. Urine uncolored, containing albumin. March 25th to 26th, 3 grams by the tube. March 26th to 27th, urine colored strongly orange-brown; albumin distinctly present. March 29th to 30th, urine slightly colored, animal lively. April 1st, 10 grams by the tube. April 2d to 5th, urine colored very strong brown; little albumin. April 6th to 7th, 10 grams administered. Animal took food, did not vomit. April 8th to 10th, urine dark brown, albumin distinct.

In a second investigation, a dog weighing 9500 grams took daily, for one month, 1 grain of chrysoidin. Animal remained lively; urine uncolored and free from albumin. It lost during this time about 1200 grams, therefore about one-eighth of its body weight.

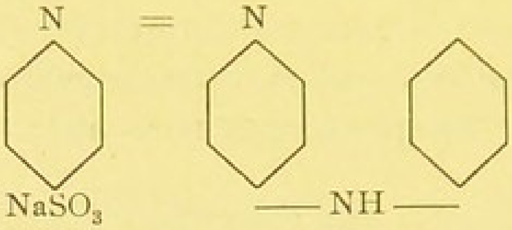
Exp. 3.—April 12th, dog weighing 58500 grams; urine uncolored, and traces of albumin present. April 13th to 14th, .1 gram subcutaneously in 10 c.c. of sterilized water. April 15th to 27th, urine uncolored, little albumin; animal lively; appetite as usual. April 29th to 30th, .1 gram subcutaneously. May 2d to 3d, animal lively; urine uncolored. May 5th, urine uncolored; very little albumin. May 8th, .1 gram subcutaneously. May 10th, urine normal; no abscesses; appetite good; weight 4620 grams; therefore, lost about 1230 grams, or one-fifth its body weight. May 5th, animal normal; ate well; urine nearly free from albumin.

Injection into the abdominal cavity.—Dog weighing 4500 grams received, three times in the course of 10 days, .1 gram of chrysoidin in sterilized water injected into the abdominal cavity with a sterilized syringe. The urine remained uncolored, but contained some albumin. The animal, three weeks after termination of the experiment, was entirely well and had good appetite.

Chrysoidin produces, according to my investigations, a slight albuminuria and notable reduction of the body-weight, but further disturbance has not been noted. With large doses introduced into the stomach, a portion of the color appears in the urine. In contrast to the experiment with dogs, Blaschko describes a frequently occurring eczema among workmen engaged in the manufacture of the color. To determine if this skin affection is caused by the color itself, or rather by the materials required for its manufacture (especially the *m*-diamidobenzene might be suspected) requires, I think, further investigation.

Diphenylamine Orange.

This color, known also as acid yellow D, diphenyl orange, orange IV, tropæolin OO, orange B, aniline yellow, orange G S., new yellow, helioxanthin (?), is produced from diazotized *p*-amidobenzenesulphonic acid and diphenylamine. The commercial article has probably the following constitution :—



It is sodium azodiphenylamine-*p*-azobenzenesulphonate. The specimen I used was obtained from the Aniline Manufacturing Company of Berlin, and was an orange-yellow powder dissolving in cold water, but not very easily, to an orange-red liquid.

Typical Reactions.—The watery solution produced with hydrochloric acid a reddish-violet precipitate which was difficultly soluble in water, but easily soluble in 96 per cent. alcohol and produced an orange-red liquid. Sodium hydroxide produced a yolk-of-egg color and dissolved with difficulty in water to the same color; in 96 per cent. alcohol, to an orange-yellow color. Ammonium produced an orange precipitate tolerably easily soluble in excess of the precipitants. Ammoniacal copper solution produced a yellow precipitate which dissolved in hot water to a brown liquid and reprecipitated on cooling. The powder dissolves in concentrated sulphuric acid to a bluish-violet solution which on dilution with water gives a violet precipitate that is soluble in excess of water to a reddish-violet liquid. In acid solution wool is colored orange-yellow. The color serves as an indicator in titration, since in the presence of small amounts of free acid, except carbonic, it is changed to red.

Exp. 1.—January 16th–18th, dog weighing 27350 grams; little albumin in urine. January 19th, 5 grams in peptone by the tube. Urine on standing became dark colored from the surface downward; albumin present, sulphates abundant, reaction alkaline; animal was lively and took food. January 20th, urine almost black, otherwise as the day before. January 21st, 5 grams administered. Urine alkaline, almost black. When treated with strong hydrochloric acid and distilled, it gives only traces of phenol. The original urine gives with ferric chloride no characteristic reaction. Addition of hydrochloric acid produces a flocculent precipitate insoluble in water, but soluble in hot alcohol. The filtrate from the acidulated urine gives a distinct albumin reaction. January 23d, the substance precipitable by the addition of acid was no longer present; albumin abundant, 3 grams administered. January 24th, precipitable substance still missing; urine almost colorless; albumin scanty. January 25th, urine very dark, gives precipitate with hydrochloric acid; albumin scanty. January 26th, urine uncolored, albumin scanty. January 27th, same. January 28th, 10 grams administered; urine abundant, strongly black, contains albumin and sulphates, alkaline. January 29th and 30th, urine dark colored, albumin abundant; very little food taken. January 31st, much albumin; weight, 2635 grams; therefore, 1000 grams lost,—that is to say, 1-27 of the body weight in fourteen days. February 2d, fifteen grams administered; urine deep color; albumin abundant; animal lively. February 3d, urine dark brown; albumin distinct; appetite good. February 7th, urine almost normal in color; animal lively.

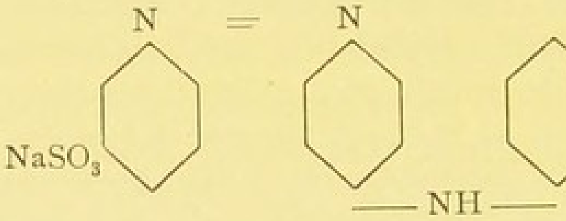
Exp. 2.—January 15th to 18th, dog weighing 9730 grams, showing but little albumin in the urine. January 19th, 3 grams in peptone. January 21st, 3 grams. January 22d, no administration; animal lively. January 23d, 2 grams; food taken. January 27th, animal lively, took food; 3 grams of the color administered. January 28th to 30th, 3 grams each day; animal lively. January 31st, 3 grams, animal took food and was lively; weight, 9820 grams. Animal received, from February 2d to 15th, daily, 3 grams; urine contained unchanged color and albumin; animal remained lively.

Exp. 3.—March 20th, dog weighing 5450 grams; albumin distinctly present. March 21st to 22d, urine colorless, contained distinct amount of albumin; .1 gram administered subcutaneously. March 22d to 23d, no abscesses; urine uncolored; animal lively. March 24th, .1 gram subcutaneously; urine uncolored, little albumin. March 25th, urine uncolored, contained but little albumin; exhibited no change on addition of hydrochloric acid or sodium hydroxide. March 26th, no abscess; animal took food. March 29th to 30th, no abscesses, urine uncolored. March 31st to April 4th, .1 gram subcutaneously; took food. April 4th, animal lively; weight, 5220 grams; therefore, lost 230 grams in fourteen days, or 1-24 of the body weight. April 12th, no abscesses; animal lively.

According to the above investigations, diphenylamine orange causes albuminuria, but further disturbances did not appear during the several weeks' observations on the animals used.

Metanil Yellow.

This color, also known as orange MN, is produced by diazotizing *m*-amidobenzenesulphonic acid and the conjugation of the resulting compound with diphenylamine. It has, therefore, probably, the constitution:—



The commercial form is the sodium azodiphenylamine-*m*-azobenzenesulphonate. My specimen was obtained from the Aniline Manufacturing Company, of Berlin, and exhibited the form of a yellowish-brown powder, smelling strongly of diphenylamine.

Typical Reactions.—It dissolves in water to a yellowish solution. Hydrochloric acid produced a violet precipitate, which slowly dissolved to a fuchsin-red liquid in an excess of hydrochloric acid or water. Sodium hydroxide does not immediately affect the watery solution. In time a yellow crystalline precipitate separates, which is soluble in warm water to an orange-red liquid. The dried color dissolves in concentrated sulphuric acid to a violet solution, which is changed to a fuchsin red by dilution with water. Ammoniacal copper solution produces, in watery solution, a heavy, flocculent, pale-yellow precipitate difficultly soluble in water.

For purification the color was dissolved in water, filtered, and separated by the addition of sodium acetate. The yellow mass was freed from the adherent liquid by the filter pump and dissolved in hot alcohol, in which it is difficultly soluble, and obtained from this in the form of yellow crystals. The material used for the experiments was almost pure, as the following analytical statement shows: 0.4895 gram of the color dried in 105° gave 0.084 sodium sulphate. Sodium, required, 6.1; found, 5.6. Like diphenylamine orange, this color, in acidified solution, dyes wool orange-yellow.

Exp. 1.—Dog weighing 11600 grams. April 2d, urine almost free from albumin. April 4th, 10 grams by the tube; animal vomited and did not take food. April 5th, 10 grams; animal vomited and did not take food. April 7th, animal very miserable and did not take food; labored respirations. April 8th, died during the night of the 7th day. Post-mortem:—Body stiff, skin not colored, mucous membrane yellowish, intestines pale, not stained; kidneys pale, not stained; liver red, contained much unchanged color since it becomes red with concentrated sulphuric acid; much unchanged color in the stomach; lungs contained a circumscribed focus in which tubercle bacilli were recognizable, but were otherwise normal. The deposit was on the anterior surface of the lower lobe of the right lung. The animal took, in the course of four days, 20 grams of the color, therefore, 1.7 grams per kilo of the body weight, and was killed by this dose.

Exp. 2.—March 19th, dog weighing 11250 grams. Albumin distinctly present. March 21st, 1 gram. Urine colorless, albumin distinct. March 22d, urine colorless, developed dark color from the surface; albumin distinct. March 25th, urine in thin layers, orange-yellow, became bluish-violet with hydrochloric acid, and orange-red with sodium hydroxide. Animal lively; conjunctiva not tinged. March 26th, 10 grams. About one hour after the administration strong vomiting occurred. March 27th, very little food taken; urine dirty greenish yellow. March 28th to 29th, urine normal in color, albumin distinct. April 1st, 5 grams administered. Animal took little food and died on the night of April 1st. Weight 8750 grams. Post-mortem; skin and subcutaneous cellular tissue, serous membranes and intestines, and contents of intestines yellow. Intestinal contents became colored ruby-red with concentrated sulphuric acid, and therefore, contained the unchanged color. The liver was hyperæmic, dark red, and gave the reaction with concentrated sulphuric acid.

Kidneys were deep yellow; conjunctiva yellow. Contents of the bladder were orange-yellow and were turned red by concentrated sulphuric acid, and contained, therefore, the unchanged color.

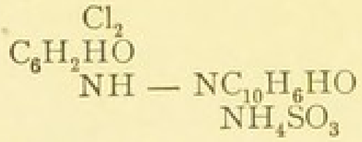
This animal received in the course of twelve days twenty-one grams of the color, or 0.53 gram per kilo of the body weight. This dose is fatal.

Exp. 3.—Dog weighing 5220 grams, on April 3d, had traces of albumin in the urine. April 6th, .1 gram in 10 c.c. of sterilized water administered subcutaneously. Animal trembled a great deal. April 9th, .15 gram subcutaneously at two points. Animal trembled, but ate freely. April 11th, .15 gram. No abscesses, animal livelier, trembling no longer observed: urine contained traces of albumin. April 14th, weighed 4790 grams, was lively and took food.

Metanil yellow must be considered poisonous when administered by the stomach, from the indication of Experiments 1 and 2. The lethal dose, which is determined by Experiment 2, is 0.53 gram per kilo of the body-weight. The isomeric diphenylamine orange is, on the other hand, non-poisonous.

Azarin S.

Azarin S is obtained by the diazotizing of amidodichlorphenol, joining the compound with β-naphthol, and treating the resulting color with ammonium acid sulphite. The operation, therefore, takes place in two steps: one, the production of the azo-color; secondly, addition of the ammonium acid sulphite. For the product of this reaction, the following formula is generally assumed.*



$$\begin{array}{l} \quad Cl_2 \\ C_6H_2HO \\ \quad NH - NC_{10}H_6HO \\ \qquad\qquad NH_4SO_3 \end{array}$$

The color itself is insoluble, but becomes soluble through the addition of the acid sulphite. If the azarin S so prepared is printed together with aluminum acetate on cotton goods, and

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* [The formula for azarin is given differently by different authorities.—Trans.]

the fabric treated with warm water in the presence of an alkali or an acid, the material is split up into a soluble sulphite, or free sulphurous acid, and an insoluble dichloramidophenolazo-β-naphthol. The latter is fixed upon the fibre as a color. My preparation, for which I am indebted to the kindness of Mr. v. Gerichten, was manufactured by Meister, Lucius & Brüning. It was a thin, yellowish-orange, strongly acid paste, smelling of sulphurous acid. It was not entirely soluble in water.

Typical Reactions.—The watery solution produced with hydrochloric acid a yellow precipitate which dissolved in alcohol with a yellow color. Ammonium hydroxide produced a brown-red solution: sodium hydroxide, a bluish-violet solution, which by warming became reddish-violet and retained this color on cooling. Concentrated sulphuric acid produced a dark-red solution, sulphurous acid escaping. On diluting the solution with water a brown solution appeared which was easily soluble in alcohol to a brown color. Ammoniacal copper solution produced a violet precipitate appearing in thin layers as reddish.

Exp. 1.—A large dog weighing 25600 grams received, in the course of twenty-five days, a total of thirty-five grams of the color suspended in water administered by the tube. The urine was colored a weak yellow and contained a distinct amount of albumin. Sulphurous acid was produced on adding hydrochloric acid to the urine. The appetite of the animal was not diminished. In a second experiment, a dog weighing 10,300 received, in the course of twenty days, twenty grams of the color administered in the same manner. Results the same as in experiment 1.

Exp. 3.—A dog weighing 4700 grams received, in the course of eight days, three injections of 1 gram each of the azarin paste suspended in 10 c. c. of water inserted under the skin of the back. During the period of observation (three weeks) no abscess appeared at the point of injection, nor was there albumin or abnormal coloring matter found in the urine. The appetite was unimpaired.

Another dog received, on May 15th, 5 c.c. of the paste in 5 c.c. of sterilized water, therefore altogether 10 c.c. of liquid, which was injected by means of the Koch syringe into the abdominal cavity. On the following day the animal had no appetite, but the urine remained uncolored. On the third day the animal seemed very miserable and took no food. There was a little albumin in the urine. The day after, the animal was found dead in its cage. Post-mortem showed the peritoneum and the inner surface of the intestines tinged in spots with a red color. The small intestines were adherent for a considerable distance to the peritoneum. The cause of death was considered to be peritonitis without effusion. The result of this post-mortem is of much interest. The red spots consisted, as was determined by chemical analysis, of the azo-color, which is the basis of the azarin S. Consequently, in the peritoneal cavity the same splitting up of the azarin S had occurred which takes place when it is attached to textiles.

Administered by the stomach, the azarin S is harmless.

DISAZO-COLORS.

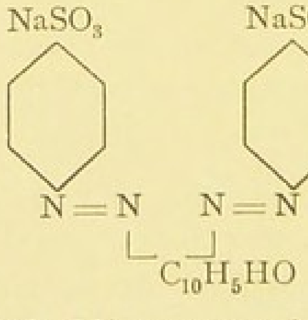
The following is a summary of the results obtained with the disazo-colors submitted to test by me, viz:—Fast brown G, woolblack, naphthol black P, Congo red, azo-blue, chrysamine R.

All these proved to be non-poisonous, except that naphthol black P had an injurious effect when administered subcutaneously.

PRIMARY DISAZO-COLORS.

Fast Brown G.

This color is produced by diazotizing two molecules of *p*-amidobenzenesulphonic acid and joining a molecule of *α*-naphthol. It has the constitution:—



It is sodium *α*-naphtholdisazo-*p*-azobenzenesulphonate. The specimen I employed was obtained from the Aniline Manufacturing Company of Berlin.

Typical Reactions.—A brown powder producing a red-brown solution in water, which gives with strong hydrochloric acid a violet precipitate, dissolving to a violet solution in hydrochloric acid, and in water to a brown solution. Sodium hydroxide and ammonium hydroxide produce a cherry-red liquid. Ammoniacal copper solution produces in concentrated solution a cherry-red precipitate easily soluble in water. The powder dissolves in concentrated sulphuric acid to a red-violet liquid which turns violet-yellow on boiling. The reddish-violet liquid, on being diluted with water, turns cherry-red.

Exp. 1.—Dog weighing 9630 grams, showing but little albumin in the urine, received on January 19th three grams by the tube. January 20th, urine contained but little albumin and was almost normal in color; addition of sodium hydroxide produced a bluish-red color; therefore, traces of the administered color were present. The urine, acidulated with acetic acid, dyed wool red-brown. January 21st, three grams given. January 22d, diarrhœa; urine red but not bloody; albumin slight; sodium hydroxide produces a bluish-red color, and the urine, acidulated with acetic acid, easily dyes yarn. January 23d, urine but little colored, becomes a weak bluish-red with sodium, hydroxide; two grams administered. January 24th, urine strongly red, little albumin. January 25th, urine normal in color, traces of albumin. January 26th to 29th, urine normal in color, traces of albumin. January 30th, urine almost free from albumin; five grams administered January 31st, marked diarrhœa; urine hardly colored, and gives with sodium hydroxide a weak fuchsin red, little albumin; weight, 8820 grams. February 3d, ten grams of the color administered. February 4th, severe diarrhœa; urine contained unchanged color; animal did not take food. February 5th, urine same as day before. February 7th, urine colorless; little albumin; diarrhœa; some food taken. February 12th, animal normal; albumin slight.

In a second experiment a dog weighing 5900 grams received during an entire month, daily, two grams of the color. After six days a slight diarrhœa was produced, which continued almost during the month. Appetite was diminished, and there was lost about one-fifth of the original weight.

According to these experiments this color in continuous, though slight, doses, or in larger doses, but less frequently, produces diarrhœa, anorexia, and emaciation.

Exp. 3.—A dog weighing 6730 grams, not showing any albuminuria, received on March 5th 0.1 gram of the color in 10 c. c. of lukewarm water subcutaneously. Urine was uncolored and contained little albumin. March 6th, no abscess; urine uncolored, no albumin; condition continued the same up to March 12th, when 0.1 gram was administered subcutaneously; March 13th, no abscess. March 14th, 0.1 gram subcutaneously; animal continued lively and took food. March 14th to 18th, no abscess; urine uncolored, no albumin. March 20th, animal lively; weight, 6450 grams. March 23d, no abscess; urine almost uncolored, and albumin slight; no change with sodium hydroxide or hydrochloric acid. March 26th, 0.1 gram subcutaneously. March 28th to April 10th, animal lively; no abscess.

Repeated doses of .1 gram subcutaneously did not unfavorably affect the health of the animal.

SECONDARY DISAZO-COLORS.

Wool Black.

This color is produced by the action of diazotized amidoazobenzenedisulphonic acid on *p*-tolyl-β-amidonaphthalene, and has the following formula:—

$$C_6H_4(NaSO_3)N = NC_6H_3(NaSO_3)N = NC_{10}H_6(NH)(CH_3)C_6H_4.$$

It may be termed sodium *p*-tolyl-β-amidonaphthalene-azoamidoazobenzenedisulphonate. The specimen I used was from the Aniline Manufacturing Company of Berlin.

Typical Reactions.—Dark-blue powder producing bluish-violet in water, which gives with hydrochloric acid a reddish-violet precipitate soluble in water. Ammonium hydroxide gives a bluish-violet solution. With ammoniacal copper solution, a bluish-violet precipitate difficultly soluble in water. The powder dissolves in concentrated sulphuric acid to a blue solution which gives a brown precipitate on dilution with water: this is decomposed on boiling. By boiling with dilute sulphuric acid the wool-black, according to Witt, is decomposed to tolunaphtazin and amidoazobenzenedisulphonic acid. The color in acid bath dyes wool bluish black.

Exp. 1.—Dog weighing 29940 grams, showing a weak alkaline urine, with little albumin, received, December 28th, 5 grams of the color in peptone, by the tube. The urine remained normal color, was neutral, contained a little albumin, much sulphates, and produced with acids and alkalies, even on boiling with concentrated sulphuric and hydrochloric acids, no characteristic reaction. December 29th, 5 grams of the color administered. Animal remained lively; urine normal in color. December 30th, five grams of the color administered. Urine normal in color, animal lively; albumin and sulphates as before. Dec. 31st to Jan. 1st, urine uncolored. Jan. 2d, ten grams by the tube; urine intensely dark blue, in thick layers black; acidified, it colors wool bluish-black; it contained albumin, as was demonstrated after precipitation and filtration from the color. Jan. 4th, urine colorless, contained very little albumin. Ten grams administered. Jan. 5th, urine intensely dark blue; in thick layers, almost black. The color was separated from the urine by the addition of sodium acetate. Jan. 6th to 7th, animal took food; urine colorless, darkened from the surface downward on standing; reaction alkaline; albumin distinct, sulphates abundant. Jan. 7th to 12th, animal lively. Jan. 13th to 19th, albumin distinctly present; animal lively; appetite good. Jan. 20th, albumin slight.

Exp. 2.—Dog weighing 3520 grams, urine of which was colorless and free from albumin, received, Jan. 21st, .25 gram of the color in 10 c.c. of lukewarm water under the skin of the back. Jan. 22d, rectal temperature 39.5°; urine uncolored; no abscess; animal lively and took food. Jan. 23d, .25 gram administered; animal lively; no abscess. Jan. 24th, .25 gram administered. Urine uncolored; traces of albumin. Jan. 26th to 27th, urine uncolored, temperature normal. Jan. 28th, abscess on the right side of the back; 0.25 gram administered subcutaneously. Jan. 29th, urine colorless, little albumin. Jan. 30th, urine colorless, alkaline, little albumin; abscess reduced in extent.

Wool black is non-poisonous both by gastric and by subcutaneous administration.

Naphthol Black P.

This color is produced by the diazotizing β-amidonaphthalenedisulphonic acid G, and conjugation with α-amidonaphthalene. The α-azoamidonaphthalene-β-amidonaphthalenedisulphonic acid thus produced is diazotized again and united to β-naphtholdisulphonic acid (R-salt).

According to this synthesis the color has the following formula:—

$$C_{10}H_5(NaSO_3)N = NC_{10}H_6N = NC_{10}H_4(NaSO_3)_2HO.$$

and is the sodium amidoazonaphthalenedisulphonateazo-β-naphtholdisulphonate R. I am indebted to the firm of L. Cassella & Co., of Frank. o. M. for the specimens I used. Like wool black, it dyes wool bluish-black in acid bath.

Typical Reaction.—It appears in the form of a bluish-black powder dissolving to a dark blue-violet solution in water. The watery solution becomes a blue-violet by the action of hydrochloric acid, acetic acid, sodium hydroxide, and ammonium hydroxide. Ammoniacal copper solution produces a fuchsin-red liquid but no precipitate. Barium chloride and ferric chloride produce bluish-violet precipitates difficultly soluble in water. The powder dissolves in concentrated sulphuric acid to a dirty-green solution, which becomes blue on dilution with water.

Exp. 1.—Dog weighing 26730 grams, the urine of which contained little albumin, received, March 3d, 3 grams by the tube. Urine remained almost uncolored, and showed but little albumin. No appreciable change was produced by either hydrochloric acid or sodium hydroxide. March 4th to 5th, 3 grams by the tube. Albumin distinct, urine uncolored. Fæces colored blue. March 5th to 6th, 5 grams, urine colored a weak, reddish-violet, becomes fuchsin-red with hydrochloric acid. March 6th to 8th, albumin slight; animal lively, took food freely. March 9th to 10th, urine dirty, bluish-red, colored orange-red with hydrochloric acid; bluish-red with sodium hydroxide; the acidified liquid dyes wool. March 12th, 10 grams administered. Animal took food; urine blue. March 13th, urine as before, little albumin. March 14th, 20 grams administered. Rather much albumin; animal lively; took food. March 15th, urine bluish, albumin distinct. March 19th, urine colorless, albumin slight. March 21st, weight, 26,620 grams.

A second dog weighing 4500 grams received during one month, daily, one gram of the color. It remained entirely well with good appetite.

Exp. 3.—Dog weighing 3200 grams, of which the urine was colorless and free from albumin, received, March 5th, 0.1 gram subcutaneously, dissolved in 10 c.c. of lukewarm water, introduced under the skin of the back on the right side. March 6th, urine scanty, uncolored, no albumin; no abscess. March 7th, 0.1 gram subcutaneously. Animal took but little food. March 8th, no abscess; urine uncolored, no albumin, took no food. March 9th, died during the preceding night. Weight, 2250 grams. Post-mortem showed no abscess, no induration at the point of injection; much unchanged color under the skin at the point of injection, which was free from microörganisms. Gelatin plates inoculated with the color taken from the point of injection remained sterile during nine days. The body was not yet rigid, but much emaciated. The mucous membranes were of normal color; the intestines were pale; mesenteric vessels were much injected. The liver, pancreas, kidneys, and lungs were strongly hyperæmic; no exudates were noted.

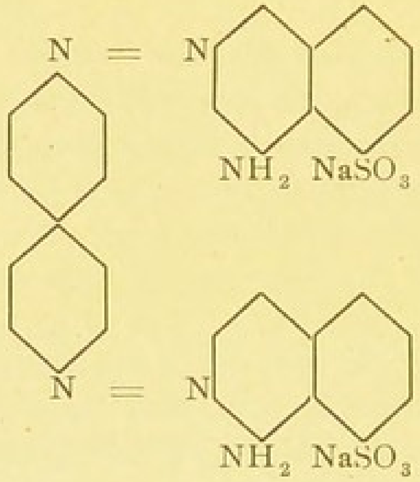
Exp. 4.—Dog weighing 3860 grams, which had been used for another experiment and very much emaciated, the urine being uncolored and containing a little albumin, received, March 12th, 0.1 gram subcutaneously in 10 c. c. of water. March 13th, no abscess; animal miserable; urine scanty, almost uncolored, no color change with sodium hydroxide, acetic acid, or hydrochloric acid; albumin distinct; .1 gram of the color subcutaneously. March 14th, 0.1 gram subcutaneously. Urine colorless; no abscess. March 16th, urine colorless; albumin very distinct; animal took food but was very miserable. March 19th, no abscess; animal very much emaciated; albumin distinct. March 21st, took food abundantly. Weight, 3887 grams. March 25th, animal very thin; took food, and was killed by hydrogen cyanide. Post-mortem. The subcutaneous cellular tissue beneath the point at which the injections were made was deep bluish-red, and the muscles showed the same color. The liver and other glands were strongly hyperæmic and hypertrophied, and the intestines were slightly bluish-red. The conjunctiva and mucous membrane of mouth were not colored.

This color is harmless when administered by the stomach, but poisonous subcutaneously.

DISAZO-COLORS OF THE CONGO GROUP.

Congo Red.

This color is obtained by diazotizing benzidine, and uniting the tetrazo-compound with two molecules of α-amidonaphthalenesulphonic acid. Its constitutional formula is, therefore, as follows :—



The commercial article is sodium benzidinedisazo-α-amidonaphthalenesulphonate-α-amidonaphthalenesulphónate. My specimen was obtained from the Aniline Manufacturing Company of Berlin.

Typical Reaction.—It is a red powder, producing with water a blue solution in which hydrochloric and acetic acids produce blue precipitates scarcely soluble in hot water. Sodium hydroxide produces in concentrated solution a reddish-brown color but slightly soluble in water. Ammoniacal copper solution produces a gelatinous red precipitate, soluble in excess of water with a red color. The powder dissolves in concentrated sulphuric acid to a blue solution, which on dilution with water gives a blue precipitate. It colors cotton and wool without a mordant.

Exp. 1.—Dog weighing 7300 grams, showing very slight albuminuria, received, December 18th, two grams of the Congo red dissolved in peptone administered by the tube. Animal lively; urine entirely normal in color. December 19th, two grams of the color administered. Urine pale, feebly alkaline, traces of albumin, no sugar. December 20th, two grams of the color administered. Urine a weak red color, no change on addition of acids, becomes yellow with sodium hydroxide; little albumin. December 21st, three grams of the color. Animal lively; urine somewhat reddish; cotton could not be colored with the urine without previous preparation, and the dyed stuff turned red on treatment with acids; little albumin. December 23d to 26th, animal lively; urine weak reddish in color and gives a reddish sediment, probably Congo red. December 27th, five grams in peptone. Animal lively; urine almost uncolored, feebly alkaline; some albumin. December 28th, ten grams of Congo red; but little albumin in the urine; cotton dyed easily. December 30th, ten grams. Animal took but little food, but was otherwise comfortable; urine but little colored, feebly alkaline, little albumin, sulphates present; weight, 6980 grams; lost, therefore, 320 grams in sixteen days. December 31st, animal lively; experiment discontinued. January 15th, animal in good condition.

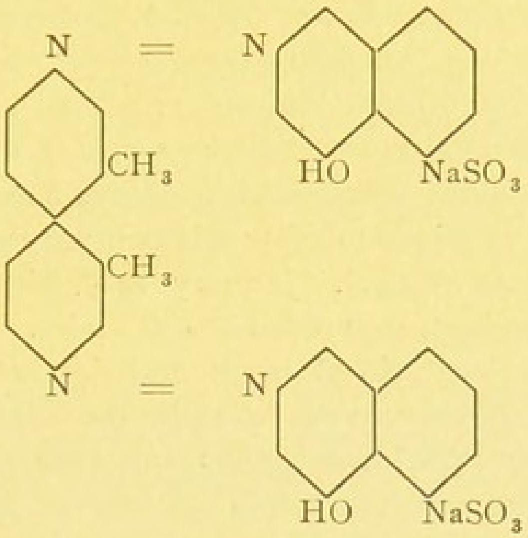
A second dog weighing 4300 grams received during one month daily one gram of Congo red with the tube. It remained entirely well.

Exp. 3.—Dog weighing 4970 grams, showing traces of albumin in urine, received, January 5th, 1889, .25 gram of Congo red dissolved in 10 c.c. of water introduced under the skin on the right side of the back. January 6th, urine scarcely colored, almost free from albumin. January 7th, .25 gram injected similarly; urine uncolored, alkaline, but little albumin; animal seemed weak. January 8th, took but little food; urine uncolored; no abscess. January 9th, urine uncolored, and but little food taken; .25 gram introduced under the skin of the back on the left side. Abscess appeared on the abdomen to the right of the mesial line. January 10th, but little food taken; urine uncolored; .25 gram administered subcutaneously under the skin of the left side of the back. Large abscess to the left of the linea alba, January 11th, animal very weak. Urine almost uncolored and contained little albumin. A large abscess on the right side of the abdomen was opened and about 15 c.c. of a blood-red liquid was discharged in which fatty globules could be seen by the naked eye. The liquid coagulated in about ten minutes, and after suitable dilution showed the oxyhæmoglobin bands, though very weakly. Acids made the liquids intensely blue, and it, therefore, consisted in large part of unchanged non-absorbed color. Microscope showed fatty globules, red blood corpuscles, some of which were normally formed and some shriveled. Pus cells were also present, but microbes colored by Gramm's method were not found. January 12th, animal very weak and melancholy. Weight, 4300 grams, therefore lost 670 grams in eight days. January 13th to 14th, the abscess which opened on January 11th spontaneously discharged a red liquid which contained much Congo red, as was indicated by the bluing by acids. The opened abscess on the left side seemed to have been absorbed. Rectal temperature 39.5° ; .25 gram administered. January 16th, animal very miserable, did not eat ; rectal temperature 39.5° ; the opened abscess seemed about to close. January 18th, rectal temperature 39.2° ; animal was uncomfortable, ate but little. January 22d, took some food ; cross and miserable ; rectal temperature 40.5°. January 24th, weak and cross ; took food. January 29th, one abscess opened spontaneously and discharged unchanged color mingled with some pus. Animal took food but was very weak. February 5th, animal again lively, took food. The abscess over the abdomen was doubtless a hypostatic abscess from the material introduced at the point of injection.

According to experiments 1 and 2, Congo red is, after long-continued administration by the stomach, harmless. The disturbances which ensued on subcutaneous injection were probably dependent upon an invasion of putrefactive bacilli and had no direct relation to the color.

Azo-blue.

This color is produced by diazotizing one molecule of orthotoluidine and joining the tetrazo-compound so formed to two molecules of α-naphtholmonosulphonic acid (N. W.). The constitutional formula is as follows:—



and the color is, therefore, sodium tolidinedisazo-α-naphtholmonosulphonate (N. W.) α-naphtholmonosulphonate (N. W.). The specimen used was obtained from the Aniline Manufacturing Company of Berlin. The color dyes cotton, in alkaline bath, grayish violet.

Typical Reactions.—It is a bluish-black powder tolerably easily soluble in water to a red-violet liquid. The watery solution produces with hydrochloric acid a reddish-violet precipitate easily soluble in water and alcohol. Sodium hydroxide produces a cherry-red liquid. Concentrated sulphuric acid produces in the solution a blue precipitate that is soluble in excess of acid to an indigo-blue liquid. The powder dissolves in concentrated sulphuric acid to an indigo-blue liquid which becomes turbid on the addition of water from the separation of a violet precipitate. The precipitate is soluble in water to a violet solution. The solution of the color in concentrated sulphuric acid is decomposed by boiling, becoming brown. Ammoniacal copper solution produces a cherry-red precipitate that is difficultly soluble in water.

Exp. 1.—Dog weighing 8450 grams, urine of which was pale and contained but little albumin, received, January 8th, two grams dissolved in peptone administered by the tube. January 29th, animal was lively, took food; urine was uncolored. Sodium hydroxide produced a transient green color; albumin doubtful. January 10th, two grams by the tube. Urine uncolored, but had a violet sheen; strongly alkaline; little albumin. Sodium hydroxide and ammonium hydroxide produced a transient greenish tint. No characteristic reaction with ferric chloride. January 11th, five grams by the tube; urine colorless; little albumin. Boiling with concentrated sulphuric acid, but not with dilute acetic acid, produces a distinct bluish black and dark color. It yields to ether a bluish red substance. The distillate was free from phenol. January 12th, eight grams administered. Urine abundant, somewhat bluish violet. Animal lively.

Urine contained but little albumin, and did not produce alkaline copper solution. January 13th to 14th, no administration. Urine colorless. January 15th, urine colorless. Five grams of the color. January 16th, urine colorless, little albumin. January 18th, urine colorless, little albumin. Five grams administered. January 20th, urine colorless, little albumin. Weight, 8490 grams.

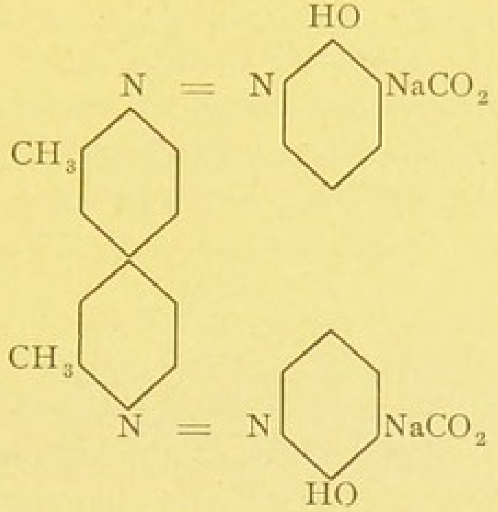
Exp. 2.—Another dog weighing 4700 grams received during one month one and a half grams daily by means of the tube. Animal remained well, with good appetite. A slight amount of albumin made its appearance in the urine.

Exp. 3.—Dog weighing 4600 grams, showing normal urine, received, January 29th, .20 gram in 10 c. c. of water subcutaneously on the left side of the back. January 30th, abscess appeared at the left side; .20 gram given in 10 c. c. of water subcutaneously on the right side of the back. January 31st, abscess on the left side opened, and discharged a violet gelatinous mass with only a small amount of blood. The color was the unchanged azo-blue. The pus contained numerous pus corpuscles and large quantities of putrefactive bacilli. The urine was unchanged in color and contained a little albumin. Weight, 4580 grams. February 3d, dog ate and was more lively. February 7th, .20 gram under the skin of the abdomen with a carefully sterilized syringe after thorough disinfection of the parts injected. February 10th, no abscess; animal lively. February 15th, no abscess. February 24th, animal lively, no abscess.

Azo-blue is harmless, both when administered by the stomach and subcutaneously. Disturbances produced by the subcutaneous method were ascribable to the introduction of putrefactive bacilli.

Chrysamin R.

This color is produced by diazotizing one molecule of *o*-tolidine in conjugation with two molecules of salicylic acid. The constitutional formula is as follows :—



The color is, therefore, sodium orthotolidinedisazosalicylate-salicylate. The sample was obtained from the Aniline Manufacturing Company of Berlin.

Typical Reactions.—It was a brownish yellow powder, and produced a brown solution in water. This solution gave with hydrochloric acid a gelatinous, brown precipitate which was difficultly soluble in water, more easily in alcohol, to a brown color. Acetic acid gives a brown flocculent precipitate. Sodium hydroxide gives a gelatinous, reddish brown precipitate soluble in water to a red-brown color. Ammonium hydroxide gives a red-brown solution. Ammoniacal copper solution gives a gelatinous, red-brown precipitate difficultly soluble in water. The powder dissolves in concentrated sulphuric acid to a red-violet liquid which on dilution with water deposits a brownish flocculi. Colors cotton, in alkaline bath, yellow.

Exp. 1.—Dog weighing 9230 grams, showing normally colored urine, alkaline, very little albumin, and plenty of sulphates, received, on January 3d, five grams of chrysamin in peptone by the tube. Urine was alkaline yellowish, dyeing of cotton easily performed ; very little albumin. January 4th, five grams of the color administered. January 5th, urine yellowish, became red by sodium hydroxide; diarrhœa; animal took food. January 6th to 7th, animal lively; slight diarrhœa; urine almost uncolored, albumin slight, sulphates abundant, alkaline. January 7th, one gram of the color. Urine slightly colored, contained distinct amount of albumin. January 8th, urine slightly colored, some albumin. January 9th, one gram administered. Animal lively. January 10th, two grams administered. Animal lively; wandered about freely the whole day. January 11th, two grams administered. Animal lively. January 12th, three grams of the color. January 13th, animal lively, took food. January 14th, weight, 9600 grams; therefore, a gain of 370 grams in 12 days. January 15th, lively. Three grams of the color administered. January 16th to 20th, albumin slight, animal lively, took food.

In a second experiment, an animal weighing 11,300 grams took in the course of 10 days three doses of seven grams each of the color by means of the tube. Urine was yellowish in color, and contained very little albumin. Animal remained lively even 14 days after the administration.

Exp. 3.—A dog weighing 3680 grams, urine of which was uncolored and contained traces of albumin, received, January 10th, .25 gram of the color in 10 c. c. of lukewarm water subcutaneously. Urine was neutral, somewhat yellowish, albumin slight. January 11th, animal took no food; no abscess; dyeing of cotton did not succeed; .25 gram injected. January 12th, animal weak, no abscess; urine very slightly colored; albumin slight; .25 gram was injected. January 13th, albumin slight. January 14th, animal melancholy; no injection; two abscesses on the back; 40° rectal temperature. January 15th, .25 gram subcutaneously. Urine weakly yellow; albumin distinct; does not color cotton. January 16th, no injection, animal cross; temperature 39.5°; took little food. One of the abscesses of the back opened spontaneously and discharged a yellow liquid (chrysamin). January 17th, animal cross; rectal temperature 39.5°; abscess as above. January 18th, abscess discharged but little color. January 19th to 21st, temperature 39.5°; cross; had taken little food. There seemed to be a new abscess forming. January 22d, ate but little.

The abscesses, which were opened with a knife, discharged about 20 c. c. of a gelatinous mass exhibiting the color of injected dye, and in which the unchanged material itself was found. Bacteria were not with perfect certainty recognizable in the discharged liquid, and those which are colored by Gramm's method were completely absent. Many fatty globules, only traces of albumin. Weight, 3210 grams.

Chrysamin is harmless when taken into the stomach. The abscess produced by subcutaneous administration may be referable to putrefactive organisms, although these were not definitely recognized.

CONCLUSIONS.

Of the 23 azo-colors subjected to examination only two, metanil yellow and orange II, produce such effects when administered by the stomach that we can consider them poisonous. With dogs, the lethal dose is less than one gram per kilo of the body weight of orange II, and only .53 gram per kilo of metanil yellow. Of the remaining colors some produce vomiting (*e.g.*, Bismarck brown), and others diarrhœa (fast brown, chrysamin R), and many develop a slight albuminuria. The phenomena produced by subcutaneous administration are not all susceptible of the same interpretation. The abscesses were in some cases (for instance, azo-blue) referable to the invasion of microörganisms. Naphthol black P., however, is plainly poisonous when introduced into the subcutaneous cellular tissue. A striking fact is how long, in some cases, the aqueous solution of the color remains unabsorbed in the subcutaneous cellular tissue. Congo red, for instance, in Experiment 3 could be recognized in considerable amount seven days after the injection. Similar observations were made with chrysamin.

The investigations of the color prepared from the *m*-nitraniline and *β*-naphthol, *p*-nitraniline and Schæffer's salt, *p*-nitraniline and naphthionic acid (archil-substitute), showed that the introduction of a nitro-group into an azo-color does not necessarily produce a poisonous body, this being contrary to what the experiments with the nitro-colors proper has led us to anticipate. This harmlessness of the nitro-group in the azo-colors is not, however, due to the presence of the sulphonic acid group,—the detoxicating influence of which was recognized in connection with the nitro-group. For instance, *m*-nitrazotin, prepared from *m*-nitraniline and *β*-naphthol, contains no sulphonic group and yet is non-poisonous, in spite of the nitro-group present. Further, in spite of the presence of the sulphonic groups, colors may be poisonous, as is shown with orange II, prepared from *p*-amidobenzenesulphonic acid and *β*-naphthol, and metanil yellow, prepared from *m*-amidobenzenesulphonic acid and diphenylamine. The poisonous qualities of orange II and metanil yellow are not referable with certainty to their constitution, since two other colors of known constitution, closely analogous to them have been shown to be non-poisonous. For instance, the poisonous metanil yellow corresponds to the non-poisonous diphenylamine orange. The difference between the two is in the relation between the sulphonic group and the azo-group. In diphenylamine orange, these groups stand to each other in the para-position ; in metanil yellow, in the meta-position. The correctness of these formulæ is shown by the fact that the metanil yellow is obtained by the diazotizing of *m*-amidobenzenesulphonic acid, while diphenylamine orange is obtained by diazotizing *p*-amidobenzenesulphonic acid. Further, orange II, which is poisonous, corresponds to another color, orange I, which is not poisonous. These bodies differ only in the position of the hydroxyl in the naphthalene residue. In orange II the hydroxyl has the *β*-position ; in orange I, the *α*-position. This is shown by the methods of preparing the colors, one being made from *α*- and the other from *β*-naphthol. Other azo-colors which contain the *β*-naphthol residue, for instance, Soudan I, new coccin, fast red B, xylidine red, and azarin S, are entirely non-poisonous.

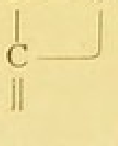
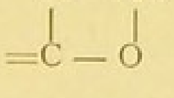
The urine obtained from the animals fed or treated subcutaneously with the azo-colors was generally colored and contained the unchanged color only when considerable quantities of the material had been administered. A portion of the color administered was found in the fæces, and especially when the color was insoluble. Generally the complex color molecule is split up in the animal organism into uncolored derivatives. When animals to which azo-colors have been administered have excreted a urine of normal color, I have never been able to obtain any coloring materials analogous to the azo-body used.

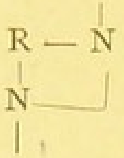
APPENDIX.

Formation of Dyestuffs.—The conditions under which an uncolored body, or one not capable of coloring fibres, becomes converted into a dyestuff are explained by the following theoretical suggestions of O. N. Witt.

Witt assumes the presence of certain characteristic groups—chromophorous groups—in all dyestuffs, which, by introduction into colorless bodies, give rise to the basis structure of dyestuffs—chromogenous groups. When these chromogenous groups are joined to salt-forming groups, such as hydroxyl or amidogen, dyestuffs are formed.

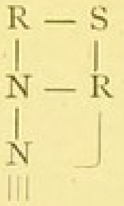
The following are examples of chromophorous groups :—

$— NO_2$	characteristic for	nitro-colors.
$— NO$	"	" nitroso-colors.
$— N = N —$	"	" azo-colors.
 $\begin{array}{l} R — N \\ \vert \\ C \\ \Vert \end{array}$	"	" rosaniline colors.
 $\begin{array}{l} R — O \\ \vert \\ C \\ \Vert \end{array}$	"	" rosolic acid colors.
 $\begin{array}{l} R — CO \\ \vert \quad\;\; \vert \\ =C — O \end{array}$	"	" phthalein colors (eosin, etc.).
 $\begin{array}{l} CO \\ \vert\,\vert \\ CO \end{array}$	"	" anthraquinone colors (alizarin).



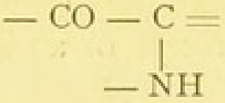
characteristic for indamines.

" " indophenols.



" " methyl blue, etc.

$N \equiv N$ (azine group) characteristic for azines, safranine, etc.



$$-CO-\underset{\displaystyle -NH}{\underset{|}{C}}=$$

" " indigo.

Azobenzene, $C_6H_5 - N = N - C_6H_5$, contains the chromophorous group $- N = N -$, and is a chromogen, but not a dye, because it has no affinity for fibres. By introduction of NH_2, or HO, we obtain respectively amidoazobenzene and hydroxyazobenzene, both of which are dyes. Salt-forming groups, which develop the coloring power of bodies, are called "auxochromous" groups.

Representing by R, Rx, Ry, Rz various hydrocarbon radicles, we may express the principal types of azo-compounds as follows:—

Monazo-colors:—

$$R - N = N - Rx\ HO$$

$$R - N = N - Ry \begin{matrix} HO \\ HSO_3 \end{matrix}$$

$$R - N = N - Rx\ NH_2$$

$$R - N = N - Rx \begin{matrix} OH \\ HSO_3 \end{matrix}$$

Primary diazo-colors:—

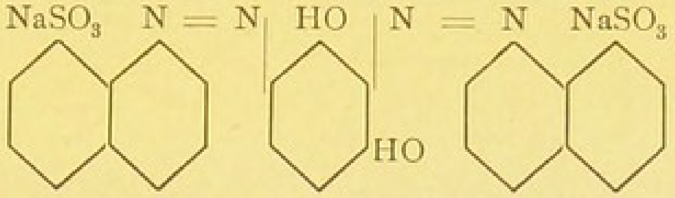
$$\left.\begin{array}{l} R - N = N \\ R - N = N \end{array}\right\} Rx\ HO$$

$$\left.\begin{array}{l} R - N = N \\ Ry - N = N \end{array}\right\} Rx\ HO$$

$$\left.\begin{array}{l} R - N = N \\ Ry - N = N \end{array}\right\} Rx\ NH_2$$

$$\left.\begin{array}{l} R - N = N \\ Rx - N = N \end{array}\right\} Ry\ NH_2$$

Fast brown, for instance, is—



Secondary diazo-colors: —

Note to page 100.—It is to be noted that diazo-compounds are produced when nitrous acid acts on the salts of primary amines of the benzene series at low temperatures:—

$$\underset{\text{Aniline hydrochloride.}}{C_6H_5 - NH_2HCl} + HNO_3 = \underset{\text{Diazobenzene chloride.}}{C_6H_5 - N = N - Cl} + 2H_2O$$

If primary diamines are employed under the same conditions, tetrazo-compounds are formed:—

$$\underset{\text{Diamidodiphenyl hydrochlor'de.}}{\begin{array}{l} C_6H_4 - NH_2HCl \\ | \\ C_6H_4 - NH_2HCl \end{array}} + 2HNO_3 = \underset{\text{Tetrazodiphenyl chloride.}}{\begin{array}{l} C_6H_4 - N = N - Cl \\ | \\ C_6H_4 - N = N - Cl \end{array}} + 4H_2O$$

The nitrous acid can be applied in the condition of vapor (obtained by the action of nitric acid upon arsenious oxide or starch), led into the cooled mixture of the amine and water, until saturation is reached and the diazo-compound separated by the addition of alcohol and ether. It is usual, however, to employ solutions of sodium or potassium nitrite of known strength, which are added to the well-cooled solution of the amine salt. Sufficient hydrochloric acid must be present to liberate the equivalent amount of nitrous acid.

INDEX.

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