

The fact of the relative infrequency of toxic sequelae, however, does not negative the reality of their existence. One can recall analogous relations in the use of other useful therapeutic agents. That of the newer arsenicals so commonly used in the treatment of syphilis and other similar infections are particularly apropos. The occurrence of aplastic anemia and related blood dyscrasias as well as cases of severe hepatic necroses in numerous instances, particularly after the use of neosalvarsan, can be regarded as indicating some type of peculiar susceptibility as contrasted to the great majority who have no such toxic manifestations.

Two practical lessons would appear obvious. First, the need of great caution and watchfulness in the administration of the drug by the physician, and second, the need of steps to minimize the widespread use of this powerful agent in the form of self-drugging through the agency of proprietaries and patent medicines.

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WILLIAM J. KERR, M. D. (University of California Medical School, San Francisco).—This paper on the subject of jaundice as an untoward effect following the administration of cinchophen is very timely. During the last four years a large number of cases have been reported in the literature where death resulted from the administration of cinchophen or compounds containing cinchophen. To date there have been upward of sixty such cases reported and, judging from discussions in various parts of the country, it may be assumed that there are many times this number of fatal cases as yet not reported in the literature. We have had three such cases in our Medical School during the last year, and there have been others where jaundice was probably on this basis.

The type of lesion which is usually seen in these patients represents a toxic cirrhosis with widespread necrosis of the hepatic cells. If the patient survives for a time there may be very active regeneration and then new tissue of the liver may be able to function, as far as carbohydrate metabolism is concerned; but new bile capillaries may not be connected with the bile ducts so that a secondary type of jaundice may result.

It is very difficult to detect those patients who would not be harmed by the administration of cinchophen. There has been some suggestion from our own experience that those patients who have had symptoms of chronic disease of the biliary tract or liver may be more susceptible to the drug. We have seen patients who developed marked evidence of cinchophen poisoning, resulting in death, from very small doses of cinchophen purchased at the corner drug store under various trade names. In one case it appeared that the patient had not taken more than thirty grains of cinchophen as a total dose. The widespread use of cinchophen and its compounds by the lay public as a result of extensive advertising in lay journals and newspapers offers a hazard to the public health which the medical profession and the state and government authorities should not tolerate. Certain restrictions are placed upon the sale of other dangerous drugs, and it would seem that it is high time that something should be done about the use of cinchophen. There is no doubt that cinchophen is a very valuable drug in controlling certain types of pain and is far superior to neocinchophen in this respect, but where the use of a drug is attended with so much risk it should be impossible for the layman to purchase this drug over the counter. Even in the hands of physicians who should be expected to know something about its use and its dangers there would, no doubt, be a certain number of fatalities. So far we have had no reports of serious damage to the liver from neocinchophen, but it should be more carefully studied with this possibility in mind. It seems to me that the California Medical Association, in conjunction with the State Board of Health and other state and national agencies, could do something about the control of the use of this drug.

## TYPHOID FEVER IN SAN FRANCISCO IN 1931 —APPARENTLY DUE TO SHELLFISH\*

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TYPHOID fever, although known to be a definitely preventable communicable disease, continues to occur, even in metropolitan areas, with a frequency altogether too high. Based on records of reported cases and deaths over a period of ten years, the disease in San Francisco has an expected yearly incidence of about thirty-five reported cases and eleven recorded deaths.

TABLE I INTERPRETATIONS

It is noteworthy that, in the series listed in Table 1, only in two instances, in 1928 and in 1931, are the numbers of reported cases in excess

TABLE 1.—Listing the Reported Cases and Deaths Over the Decade 1922-1931 Inclusive

Year	Typhoid Cases Reported	Deaths
1922	25	12
1923	36	17
1924	23	14
1925	39	12
1926	38	14
1927	40	10
1928	76	20
1929	34	6
1930	38	8
1931	68	9
Yearly average (excepting years 1928 and 1931)	35	11

of forty for the year. The increased incidence in 1928 was due to an outbreak which was traced to pasteurized milk contaminated by a bacillus carrier operating a faulty capping machine.† Since the increased incidence in 1931 was unusual in certain respects, the data given in Table 2 are presented.

TABLE 2 INTERPRETATIONS

During the past ten years, cases of typhoid fever have been reported in San Francisco in every month of the year, and, indeed, in only four separate and nonconsecutive months were there no cases recorded. The expected incidence might be described as of the low-level, year-round type. Weekly reports through July and August showed slight increase over the normal expectancy. During the month of September, however, there was a definite and marked elevation in the epidemic index. This rather sharp rise was of short duration, but cases continued to be reported, while with less frequency, it is true, nevertheless on through October, November, December, and even January.

The week showing the maximum number of cases reported (twelve) was that ending September 19; it would be expected then that the dates of onset of a comparable maximum number

\* From the Department of Public Health, City and County of San Francisco.

† "Typhoid Fever Epidemic Occurring During the Summer of 1928." W. C. Hassler, M. D., J. A. P. H. A., February, 1930, 20:2, 137-146.

TABLE 2.—*Supplementary Report on Typhoid Fever Cases.  
For the period July 1, 1931— January 23, 1932 inclusive.*

Week Ending	Onset Date Total for Week	Normal Expectancy	Cases Reported		Trend	Epidemic Index %
			Local	Nonlocal		
June 13.....	1	....	....	....	.....	.....
July 4.....	4	0	0	0	Normal	.....
July 11.....	3	1	1	0	Normal	100
July 18.....	3	1	0	3	Low	.....
July 25.....	0	1	1	1	Normal	100
Aug. 1.....	0	1	0	0	Low	.....
Aug. 8.....	1	1	0	0	Low	.....
Aug. 15.....	4	1	2	0	High	200
Aug. 22.....	3	0	1	1	High	.....
Aug. 29.....	3	1	2	0	High	200
Sept. 5.....	10	1	2	0	High	200
Sept. 12.....	2	1	3	0	High	300
Sept. 19.....	2	1	12	0	High	1200
Sept. 26.....	2	1	4	1	High	400
Oct. 3.....	1	1	1	0	Normal	100
Oct. 10.....	0	1	0	0	Low	.....
Oct. 17.....	1	0	0	0	Normal	.....
Oct. 24.....	2	0	1	0	High	.....
Oct. 31.....	1	1	2	1	High	200
Nov. 7.....	2	1	0	0	Low	.....
Nov. 14.....	2	1	4	0	High	400
Nov. 21.....	0	1	3	0	High	300
Nov. 28.....	0	1	0	0	Low	.....
Dec. 5.....	3	1	1	0	Normal	100
Dec. 12.....	3	1	0	0	Low	.....
Dec. 19.....	0	1	1	0	Normal	100
Dec. 26.....	1	0	1	0	High	.....
Jan. 2.....	0	0	3	0	High	.....
Jan. 9.....	1	1	1	0	Normal	100
Jan. 16.....	1	1	0	1	Low	.....
Jan. 23.....	0	0	2	0	High	.....
	56		48	8		

of cases would antedate this by one to two weeks. The analysis of the cases showed that the week ending September 5 did see the onset of the disease in a larger group of individuals (ten) than any other similar period. Epidemiologic reasoning would conclude therefrom that the infection in this group occurred from two to three weeks previously, that is, during the middle of August or approximately one month before the cases were reported and investigated.

#### ANALYSIS OF ETIOLOGIC FACTORS

The analyses of individual cases in September revealed the interesting possibility that the source of infection in not a few cases might have been in raw shellfish, especially oysters and clams. On the basis of these epidemiologic findings there were initiated investigations into the sources of supply, methods of handling and conditions surrounding the sale and serving of raw shellfish in San Francisco. Concurrently, of course, the water and milk supplies were carefully checked, and in each reported case of typhoid fever a diligent search was made for bacillus carriers.

San Francisco, comprising an area of 46.7 square miles on the tip of the peninsula, with a population of 650,000, has a water supply mainly of surface origin, safeguarded by chlorination, and a milk supply of which 97.85 per cent is grade "A" pasteurized and the remaining 2.15 per cent is of certified and guaranteed grades. Sewage disposal is by direct outfall to San Francisco Bay, and all but a very small number of buildings, whose locations prohibit it, are connected with the sewage system.

At the time of the outbreak San Francisco was obtaining water from various sources: Crystal

Springs reservoir (San Mateo County), Municipal and Sunset wells (San Francisco), Calaveras reservoir, Sunol wells, and East Bay Municipal Water District (Alameda County). All these supplies, save the Municipal wells, were adequately chlorinated before distribution in San Francisco. (The Municipal well water, supplying an area small in extent, has since been chlorinated.) During the summer months, with dry weather and low levels in the reservoirs, it is expected that the amount of chlorin added must be increased to maintain the same factor of safety. During the summer of 1931, while the city's water supply was not entirely satisfactory, the variations found on bacteriologic examination were irregular and inconstant and not of sufficient import, it was believed, to account for cases of typhoid fever. This was borne out by the distribution of the reported cases over the city, there being no coincidence between the areas supplied by certain reservoirs and the areas in which the cases were located. It might be stated here that in at least three cases of nonlocal origin the source of infection was possibly in water drunk from an open stream or spring or irrigation ditch, and in one case of local origin the possibility presented is that of water from a source used for irrigation purposes only, in one of San Francisco's parks.

Following the occurrence in 1928, in which a bacillus carrier operating a faulty capping machine in a local pasteurizing plant was responsible for a milk-borne outbreak of typhoid fever involving some sixty-two patients, with twelve deaths, milk handlers have been examined by the Department of Public Health, in an effort to uncover new carriers. The milk supply is regularly carefully checked before, during and after pasteur-

ization. Irregularities had been remarkably few, and, here again, they were inconstant in their occurrence. The distribution of cases also was not that of milk routes, and there was the added factor that too many different plants were involved.

The investigation into the possibilities of carriers within the household, particularly with the occurrence of multiple cases, revealed several heretofore unknown carriers of *Bacillus typhosus*. Continued observation of these carriers and immunization of other members of the family not yet affected is, of course, to be carried out.

#### SHELLFISH INDUSTRY STUDIES

By far the most interesting points were found in the investigation into conditions within and surrounding the shellfish industry. The investigation comprised three studies: the oysters offered for sale at the counter, either in cocktails or to be taken home; the oyster shucker and conditions surrounding the handling of the bivalve after its removal from the bed and especially from the time it is removed from the shell until it is offered for sale; and the oyster beds supplying the San Francisco market. The methods used in these studies included bacteriologic examination of specimens as well as rigid inspection of the premises and methods of handling the shellfish.

Samples of oysters and clams were obtained on the open market from establishments serving cocktails at the counter, as early as September 10. Laboratory studies, based on the methods approved by the American Public Health Association and the United States Public Health Service, showed contamination to an extent considerably higher than regulations permit. In several instances the score was five hundred, indicating pollution of sufficient degree to cause growth of *Bacillus coli* in all tubes of all dilutions used. The examination of oysters and clams removed directly from the beds to the laboratory showed that there was contamination of the bivalves in the beds in several instances. In other cases, the specimens removed from the beds were within the accepted standards, but the shucked product, as offered for sale on the market, showed a higher contamination. Conditions surrounding the shucking and preparation of oysters for the retailer, in certain instances at least, were found to be such that this change of score could well be accounted for. Washings from jars used to transfer the shucked oysters from the wholesaler to the retailer were found to show high bacterial counts. It was also found that, while the unopened jars of quantities of oysters (100 to 200 per jar) were kept on ice, it was not infrequent that the stock immediately offered for sale was not properly chilled by being kept in a container surrounded by ice. The possibilities of contamination of the oyster at the time of shucking are great, not alone from the shells, utensils, and water, but, perhaps greatest, from the shucker himself, particularly should he be a bacillus carrier and unclean in his

personal hygiene. The examination of oyster shuckers, including physical examination and bacteriologic cultures of the bodily discharges, is now carried out.

#### TYPHOID FEVER INCIDENCE IN SAN FRANCISCO IN 1931

It is intended in this brief discussion to call attention to the fact that typhoid fever in San Francisco during 1931 occurred with a frequency considerably above the expected incidence. Of some fifty-six cases with four deaths, forty-two were of local origin, and fourteen of nonlocal origin, epidemiologically. Of the total group, twenty-four, or 38 per cent, were in the age groups ten to twenty and twenty to thirty years, and males predominated over females in the ratio three to two. The use of raw shellfish was admitted by twenty of those affected, and this constituted the most frequent source of infection determined.

Investigations showed that the distribution of cases possibly did not implicate the water or milk supplies, and these conclusions were borne out by laboratory studies. A small number of cases were undoubtedly traceable to three carriers of *Bacillus typhosus* who were undiscovered before the 1931 series of cases.

The most fruitful studies, in uncovering real and potential sources of infection, were those made on oysters and clams. The studies made by the San Francisco Department of Public Health were confined, of course, to the city and county of San Francisco, with the exception of certain oyster and clam beds in adjacent counties in which the coöperation of the state and local departments of public health was afforded. While San Francisco Bay beds presented the most serious problem, as far as pollution and contamination are concerned, other oysters shipped into the city were not entirely satisfactory in certain instances, thus showing that San Francisco Bay beds are not the only offenders, and, too, that the shucking and handling of the bivalves probably play important rôles in the contamination of the product offered for sale. Through the activities of the Department many of these irregularities have been corrected, and a recurrence through the same channels is not expected. Certain beds in San Francisco Bay have been closed to the industry. It should be emphasized that there has been shown, on the part of the dealers in San Francisco, an excellent spirit of coöperation in their agreement to buy oysters and clams only from known reliable and approved sources.

#### THE PREVENTION OF TYPHOID FEVER IN CIVIL LIFE

In the control of typhoid fever preventive medicine and public health have accomplished only a part of that which is possible. The methods which have been so successful in reducing the morbidity and mortality rates in the armed forces of the greater nations are available for application to the civil population. The continual occurrence of this

preventable disease, not only in sporadic cases but in outbreaks as well, challenges the public health official to overcome the barriers of indifference, ignorance and inadequate legislation. The enviable record of the United States Army, in which the incidence of typhoid fever is so low, and was so low during the World War that it is considered to be of minor importance, can be attained in civil groups, but only when there can be had the complete coöperation and earnest effort of the privately practicing physician, the public health minded laboratory worker, the sanitary engineer, and the health officer. There must be utilized, in addition to good concurrent epidemiology, health education, vaccination, modern sanitation, systematic search for and supervision over the bacillus carrier and rigid inspection and control over food establishments, particularly those serving or selling food to be eaten uncooked or without further preparation. The gap between what can be done and that which is actually accomplished in public health is wide, and we can go only as far as public opinion wants that we should go, but the goal is not unachievable.

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### LEUKODERMA—ITS TREATMENT\*

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THE treatment of leukoderma or vitiligo requires not only a deposition of pigment in the areas of depigmentation, but it also requires a redistribution of pigment from hyperpigmented borders, so that the result will be an even distribution of the normal amount of cutaneous coloring. The effect of an added general coloring to a patient's skin, suffering from vitiligo, would result in a difference of color scale, as an artist would term it, with the depigmented areas a darker color, but relatively the same unless the coloring used be pitch-black. This point can be demonstrated by painting the area of a vitiligo skin with a transparent brown stain. The white areas will color brown, but the tan of the borders of lesions will be little short of black. Knowing well that the white areas are as white as they will ever be, it is possible to lessen the conspicuousness of this contrast with the surrounding skin color by bleaching the dark skin to match the white with dermatologic bleach. On the other hand, it is more difficult to tint the white areas to match the surrounding, somewhat more normal looking skin. Diluted butternut stain, such as is used for dyeing hair, is used by some patients. Others use grease paints of suitable tints, or special powders, to disguise their leukoderma.

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### INTRACTABLE NATURE OF LEUKODERMA

All methods of establishing a complete cure of leukoderma to date have been relatively unsatisfactory. Local methods are those most frequently employed to produce pigmentation in areas lacking color. Bouchi dana (*psoralia corylifolia*) in ointment form is that most used in India. A 10 per cent alcoholic solution of oil of bergamot, applied to depigmented areas, followed by raying of the parts by ultra-violet rays, as advocated by Berlocq, has met with favor in America. These treatments produce dilatation or congestion of the deep venous plexus of the skin which in some ways favor pigmentation.

The full effect of the action of certain rays upon cells or tissues, capable of becoming pigmented, is not perfectly understood. We know that ultra-violet rays, x-rays, radium rays, and complex sun's rays have the power of stimulating pigmentation, but this usually follows definite erythema of the parts. Light has a soothing effect on the nerves, but if the nerves of the skin be anesthetized and an exposure of it be made to ultra-violet rays, we are informed that no inflammatory reaction will take place, as might ordinarily be expected. Another point worth taking into consideration at this juncture is the chemical alteration in the tissues. This can be induced by the injection or the administration of such drugs as hematoporphyrin, sulphon methane, and acridin, which will cause the skin to burn from rays of the sun much more readily than it otherwise would; that is, these drugs induce photosensitivity. It is but reasonable to suppose that the reverse of photosensitivity can be induced by other drugs if we but knew them.

### CHEMISTRY OF PIGMENT

The chemistry of pigment has been investigated by an examination of the pigment in hair, which does not apparently owe its coloring matter to any of the chemical constituents of blood. Hellmick believes, "pigment is a direct product of the epidermal cells, and is not a hematogenous substance which has been conveyed to the epidermis by chromatophores, and that the nuclear substance is probably the mother substance of this pigment." Hooker has demonstrated the development of pigment in cells of the epidermis of frogs (*ryma pipiens*). The elaboration of pigment was observed in some of the epidermal cells, at first appearing as a mass of brown granules in the immediate vicinity of the nucleus. The pigment gradually spreads throughout the entire cell. After the elaboration of a considerable amount of pigment, these cells either actively or passively migrated to a position below the nonpigment-bearing cells.

It has been suggested that if the essential pathologic change lies within the restricted areas of the skin, it would be logical to endeavor to induce a change in the chemistry of the cell, possibly by proper doses of roentgen rays. There is no doubt in my mind but that a certain amount of pigment