search Laboratories were used. Infrared spectra were obtained on a Perkin-Elmer model 21, double-beam instrument; a barium fluoride cell (0.052 mm) and a transmittance screen in the reference beam (*3*) were used. The spectrum of water has been published (*3*), and our spectrum for water corresponds to it.

A 20 percent (weight by volume) solution of CDMT was prepared and scanned as soon as possible after dilution to the mark, scanned again 5 minutes after dilution, and then scanned every 30 minutes thereafter for a total elapsed time of 6 hours. The scanning rate was approximately 30 sec/μ. Due to crowding of the curves during the run, only the initial and final curves are shown (Fig. 1), although the pen tracings during the experiment definitely showed progressive differences with time.

Examination of the spectra in Figs. 1 and 2 shows that CDMT has a slight resemblance to both cysteine hydrochloride and acetone. The spectrum of the solution of hydrolysis products (see Fig. 1, curve 2) closely resembles the spectrum obtained for a synthetic mixture prepared in the stoichiometric proportions expected for total hydrolysis (see Fig. 2, curve 3). The curve obtained (Fig. 1, curve 2) indicates that at the end of the 6-hour period the system is at equilibrium and that the point of equilibrium lies very close to total hydrolysis (*2*).

These data indicate that it is possible, by means of infrared spectrophotometric techniques, to follow the changes which small molecules undergo in aqueous solution if the concentrations of reactants and products are high enough and if their absorption spectra are sufficiently different. Similar experiments along these lines are being pursued.

DONALD M. KIRSCHENBAUM
FRANK S. PARKER
Department of Biochemistry, State University of New York, Downstate Medical Center, Brooklyn

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Further Studies on the Relation between Metals and Natural Pigments

In 1955, we published in *Science* an article entitled "Nature of pigments derived from tyrosine and tryptophan in animals" in which the relation between sorts of metals and natural pigments was discussed (*1*). Shortly thereafter, Goss and Green (*2*) published analytical results on the copper content of hair from different species which did not agree with our results. Since we felt that the difference in results might be due to differences in the respective ashing procedures, we exerted much effort to establish the most adequate ashing method. At the end of 1956, however, we discovered that one of our previous associates had been untrustworthy. We have therefore been obliged to reexamine the experimental results of our cooperative work.

Table 1. Amounts of iron, copper, and nickel in animal hair and tissues, in parts per million (dry material). The numbers in parentheses indicate the number of measurements.

Species and tissue	Hair color	
	Black	White
	Iron	
Rabbit, hair	30.2 ± 4.3 (11)	38.1 ± 5.3 (11)
Mouse, hair	81.0 (1)	56.0 (1)
Pig, hair	173.0 ± 9.8 (4)	68.7 ± 2.1 (4)
Guinea pig, hair*	25.3 ± 0.9 (6)	25.6 ± 2.6 (6)
Guinea pig, hair†	30.7 ± 2.5 (2)	31.1 ± 2.0 (2)
	Copper	
Rabbit, hair	17.4 ± 2.1 (11)	18.6 ± 2.4 (11)
Rabbit, liver, adult	32.2 ± 3.6 (6)	26.6 ± 4.0 (6)
Rabbit, kidney, adult	38.2 ± 7.3 (5)	30.5 ± 5.3 (5)
Rabbit, skin, adult, without hair	10.0 ± 1.5 (3)	9.2 ± 1.1 (3)
Mouse, hair	17.7 ± 2.3 (6)	11.3 ± 1.1 (5)
Mouse, liver, adult	19.4 ± 4.3 (5)	17.1 ± 6.9 (5)
Mouse, skin, just after birth	21.6 ± 3.2 (6)	12.1 ± 0.7 (5)
Mouse, skin, with hair, 10 days after birth	16.3 ± 3.2 (2)	6.3 ± 0.5 (2)
Mouse, skin, adult, without hair	15.3 ± 2.2 (5)	6.8 ± 1.8 (5)
Pig, hair	17.1 ± 1.9 (4)	17.6 ± 0.9 (4)
Guinea pig, hair*	23.0 ± 2.0 (3)	23.7 ± 2.0 (3)
Guinea pig, hair†	19.7 ± 9.2 (3)	15.2 ± 4.7 (3)
	Nickel	
Rabbit, hair	0.18 ± 0.08 (2)	1.70 ± 0.41 (2)
Guinea pig, hair†	trace (1)	trace (1)

* Samples obtained from different animals.
† Samples obtained from the same animal with piebald hair.

Our main effort has been paid to the quantitative determination of Fe, Cu, and Ni involved in animal hair and tissue by wet ashing. Iron was determined by the *o*-phenanthroline method of Saywell and Cunningham (*3*), copper by the diethyldithiocarbamate method, and nickel by the dimethylglyoxime method (*4*). The revised results are summarized in Table 1.

Although in some cases our previous assumption that black hair contains more Fe and Cu and less Ni than white hair seems to be substantiated, this is not generally true. Presumably the metal content in animal hair and tissues varies according to the genetic background, as well as to the environmental condition, of the individual (*5*).

H. KIKKAWA, Z. OGITA,
K. ABE, K. DOI
Department of Genetics, Faculty of Medicine, Osaka University, Osaka, Japan

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Pain Sensitivity, Sensory Deprivation, and Susceptibility to Satiation

Abstract. The results reported bear out the hypotheses that (i) pain tolerance is positively related to satiability; (ii) sensory deprivation tolerance is negatively related to satiability. It is inferred that satiability may prove to be in part the mechanism of tolerance and intolerance, and that pain tolerance is inversely related to sensory deprivation tolerance.

Surgery of the brain's prefrontal areas can increase tolerance of pain without altering the perception threshold of pain. This operation of prefrontal lobotomy causes a constellation of changes in measurable aspects of personality (*1*). The fact that these changes are specifically present after lesions in this area of the brain and not in the four other areas studied, and that there are special types of personality that are most helped by surgery, suggests a relationship between personality and pain tolerance (*2*). The experiment discussed in this report examines this relationship further, with special emphasis on one variable in the constellation—perceptual satiation—and investigates the tolerance of pain and the tolerance of sensory deprivation as related to susceptibility to satiation.

In relation to an understanding of what underlies tolerance of pain and sensory deprivation, the measurement of satiation phenomena are of particular interest. Satiation was first described by Köhler, who showed that perceptual intensity diminishes after prolonged stimulation with a stronger stimulus (*3*). Thus, the fact that the size of an object which is touched with the hand appears to diminish after a period of stimulation by a larger object on the same hand is an example of satiation.

Michael Wertheimer (*4*) has demonstrated the existence of individual dif-

Table 1. Average amount of satiation of four groups of subjects differing in tolerance of pain and deprivation.

Satiation: loss in apparent size of test object (in mm)	Least tolerant				Most tolerant			
	Pain (7 subjects)		Deprivation (4 subjects)		Pain (6 subjects)		Deprivation (5 subjects)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
After 30 sec of stimulation	0.81	2.82	1.26	1.89	2.46	3.60	−0.03	1.92
After total of 90 sec stimulation	−0.42*	2.04	1.74	1.50	3.50*	4.02	−0.12	1.86
After total of 180 sec stimulation	−0.09*†	1.47	4.77†‡	2.22	4.95*	4.20	1.86‡	1.56
After total of 300 sec stimulation	0.96*†	2.31	4.68†‡	2.46	5.28*	4.80	2.04‡	1.41
After 15-minute rest period; no further stimulation	−0.42*†	1.23	2.55†	1.38	4.02*	3.30	1.83	2.67

Differences are significant between those (*) least and most tolerant of pain; (†) least tolerant of pain and deprivation; (‡) least and most tolerant of deprivation.

ferences in susceptibility to this kind of satiation and has shown that this susceptibility is general and independent of the particular department of sense. Visual susceptibility, for example, is correlated with tactual. Klein and Krech have shown that satiation is increased by certain types of brain injury (*5*).

Eysenck and Nichols have related susceptibility to satiation to the personality dimension called "introversion-extraversion": the more extraverted the personality, the greater his susceptibility to satiation (*6*). The effect of brain lesions is apparently selective; earlier work in England showed that four operations outside of the prefrontal region, which have no effects on sensitivity to pain, also have no effect on satiability and some other measures related to extraversion (*2, 7*).

The hypothesis which is thus suggested and to which the study under discussion brings some support is that the individual who tolerates pain best is also most susceptible to satiation. Satiation may indeed prove to be the mechanism of *tolerance* in that an intermittent bigger wave of pain causes subsequent pain to be perceived as less intense. If this is so, high satiability would be a handicap in a situation involving starvation of sensation, as in sensory monotony or deprivation. In such a situation of sensory starvation, susceptibility to satiation may be in part the mechanism of *intolerance* in that it would cause the limited stimulation available to be perceived as less intense. Our findings provide some support for the hypothesis that he who tolerates sensory deprivation least is most susceptible to satiation.

To measure satiation we have used an adaptation of the method of Köhler for kinesthetic figural aftereffect—a method which was later employed by Klein and Krech (*5*), by Eysenck (*6*), and by one of us (A.P.) at the Institute of Psychiatry in London. The subject is blindfolded and feels with the thumb and forefinger of one hand the width of a test object (38.1 mm), a standard block of smooth unpainted wood. With his other hand, also with the thumb and forefinger, he feels a long tapered bar of similar unpainted wood until he finds the place where the bar seems just as wide as the test block. This is the position of subjective equality. The measurements are always made four times in succession.

The subject is then given a wider test block (63.5 mm) to rub with finger and thumb at a constant rate (at the time intervals shown in Table 1). The purpose of this rubbing of a wider block is to induce satiation if it is to occur. The series of periods of rubbing to induce satiation is followed by a series of intervals of rest, with measurement of the test object after each interval. The apparent decrease in size, the measure of satiation, is expressed in millimeters.

For these same subjects we also have measures for pain thresholds, determined in earlier experiments by U. Neisser, formerly of Harvard Psychological Laboratories (*8*). An adaptation of the Hardy-Wolff-Goodell dolorimeter was used (*9*). This instrument concentrates radiant heat upon the skin and makes determinable the temperature at which the subject first feels pricking pain and also the temperature at which he can no longer endure the pain. For this second measurement the subject was instructed to endure the pain as long as he possibly could. The difference between these two thresholds constitutes a measure of algesic tolerance for the individual subject, a new measure which may be called "pain tolerance."

Tolerance of sensory deprivation was measured in the nine subjects who, during the past 9 months, had volunteered to remain in a tank-type respirator under conditions which resemble those of the original experiment on deprivation in H. O. Hebb's laboratory in Montreal (*10*). The deprivation investigations were carried out at Boston City Hospital by Liederman, Mendelson, Wexler, Kubansky, and Solomon (*11*). The time the volunteer remained in the respirator is the measure of tolerance used.

The subjects were 28 adult male students, 19 in the pain group, 9 in the deprivation group. Their ages ranged from 20 to 26.

Table 1 gives a comparison of results for those least and most tolerant of these two forms of stress. We divided the 19 subjects into three groups according to their tolerances for pain; (below 5.5°C, 5.5°C to 8.5°C, and above 8.5°C). The 9 sensory-deprivation subjects were divided into two groups, those that remained less and those that remained more than 6 hours in the respirator. The mean amount of satiation—measured by loss in the apparent size of the object—in those who are most tolerant of pain is significantly greater than in those who are least tolerant of pain. The differences are statistically significant after 60 seconds, 180 seconds, and 300 seconds, respectively, of stimulation. On the other hand, the loss in apparent size of the object for those who are most tolerant of deprivation is significantly smaller than for those who are least tolerant (*12*). The differences between these two groups are statistically significant after 180 seconds, and 300 seconds, respectively, of stimulation.

In addition, the loss in the apparent size of the object for those who are least tolerant of pain is significantly smaller than for those who are least tolerant of deprivation. After 180 seconds of stimulation, this difference is significant at the .005 level of probability, and it is significant at this level also a quarter of an hour after the cessation of stimulation (*13*).

ASENATH PETRIE
WALTER COLLINS
PHILIP SOLOMON
Harvard Medical School,
Boston City Hospital, and
Boston Sanatorium,
Boston, Massachusetts

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Occurrence of Lithocholic Acid in Feces of Healthy Men

Abstract. Crystalline lithocholic (3α-hydroxycholanic) acid was isolated from a pooled sample of feces from healthy men for the first time. This acid, which occurs in small amounts in human bile, was obtained by alcohol extraction, followed by solvent partition and chromatography. Under these conditions most of the acid was recovered in the form of its methyl ester.

Of the cholanic acids isolated from human bile, chenodeoxycholic (3α,7α-dihydroxycholanic) acid and cholic (3α,7α,12α-trihydroxycholanic) acid are the most abundant. Deoxycholic (3α,12α-dihydroxycholanic) acid was found in smaller amounts, but lithocholic (3α-hydroxycholanic) acid only rarely and in very small amounts (*1*). Little isolation work has been reported on the bile acids of human feces, but they are known to contain cholic (*2*) and deoxycholic acid (*3*). The occurrence of lithocholic acid in human feces has not yet been described. This bile acid was first found in gallstones of cattle by Hans Fischer in 1911 (*4*) incidental to his work on bilirubin. In the course of an extensive investigation of the lipid fraction of human feces (*5*), we have isolated lithocholic acid in pure form.

The isolation procedure involves a separation scheme similar to the one used by Dobriner *et al.* (*6*) for the isolation of steroids from urine. Fifty kilograms of fresh stool from about 20 healthy men was homogenized in ethanol containing 1 mole of hydrochloric acid per liter at 50°C for 7 hours, filtered, and concentrated in a vacuum. The concentrate was dissolved in 15-percent ethanol and extracted with chloroform. Acidic material was separated from the chloroform solution by extraction with 2*N* sodium hydroxide, and the neutral material was partitioned between 80-percent ethanol and petroleum ether. The material in the alcohol phase was separated into a ketonic and a nonketonic fraction by use of Girard's reagent, and the nonketonic fraction was separated into an alcoholic and a nonalcoholic fraction via the hemiphthalates.

The acidic fraction was subjected to a counter-current distribution in an *n*-heptane/97.5-percent aqueous acetic acid system (*7*), and a fraction of the aqueous phase was chromatographed on Celite, the solvent system of Matschiner *et al.* (*8*) being used. The fraction eluted with petroleum ether crystallized from aqueous ethanol and gave an infrared spectrum (*9*) which indicated the presence of lithocholic acid. Upon recrystallization from aqueous ethanol and again from aqueous acetic acid crystals of mp 176° to 181°C (*10*) [reported, 185° to 186° (*11*)] were obtained, which gave an infrared spectrum identical with that of authentic lithocholic acid. In another experiment the chromatographic fraction containing lithocholic acid was treated with diazomethane for conversion into the methyl ester. The latter was purified by chromatography on silica gel by the method of Wootton (*12*) and yielded a fraction which on recrystallization from aqueous methanol afforded crystals melting at 79° to 84°C (labile form). Methyl lithocholate, prepared, chromatographed, and crystallized as above, melted at 82° to 85°C [reported, 90° to 93°C (*13*)] and gave an infrared spectrum identical with that of the methyl ester of the isolated specimen. Alkaline hydrolysis of this material, followed by recrystallizations from aqueous ethanol and aqueous acetic acid, afforded crystals of mp 182° to 185°C. This substance showed no depression of the melting point upon admixture with authentic lithocholic acid and had the same infrared spectrum as the authentic acid.

The major portion of the lithocholic acid was isolated from the neutral fraction. When the neutral nonketonic alcohols were acetylated and chromatographed on alumina, by the method of Reichstein (*14*), the methyl ester of 3α-acetoxycholanic acid was obtained. The compound, rechromatographed and recrystallized from ether-petroleum ether, crystallized in oblong leaflets, mp 132° to 134°C [reported, 134° (*15*)]. The substance showed no depression of the melting point upon admixture of authentic methyl 3α-acetoxycholanate and gave the same infrared spectrum as the authentic ester. The analysis (*16*) showed C, 75.16; H, 10.47 (calcd. for $C_{27}H_{44}O_4$: C, 74.95; H, 10.25) and $[\alpha]_D^{20} + 48.6°$ in acetone (reported, $[\alpha]_D^{15} + 48.4 \pm 3°$ (*15*)). Saponification of this acetate with sodium methoxide gave the methyl ester of lithocholic acid, which crystallized from aqueous acetone in needles, mp 81° to 86°C (labile form) and showed no depression of the melting point upon admixture with authentic methyl lithocholate. The infrared spectrum of the product was identical with that of the authentic material and analysis showed C, 76.89; H, 10.68 (calcd. for $C_{25}H_{42}O_3$: C, 76.87; H, 10.84) and $[\alpha]_D^{20} + 30.9°$ in acetone (reported, $[\alpha]_D^{13} + 32.8 \pm 2°$ (*15*)).

While the methods employed do not permit an accurate quantitative determination of the amount of lithocholic acid present in human feces, it is estimated that they contain approximately 3 g/100 kg of wet weight, a concentration which is in the order of that in ox bile (*17*). Our methods give no indication of the form in which lithocholic acid is excreted, and further work will be required to account for the isolation of its methyl ester.

ERICH MOSETTIG, ERICH HEFTMANN, YOSHIO SATO, EKKEHARD WEISS*
National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland

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