all hope and selfrespect and touch with an outside world that is changing faster and faster each generation. Because they are already cruelly hampered by incessant telepathic tormenting, therefore they must be lifelong prisoners along with the filthy, the obscene, the violent, the noisy and the pestering. The awful injustice of it all does not worry alienists, since their whole system, their whole philosophy is based on the fundamental injustice of treating human beings as irresponsible semi-automatons, the prey of their instincts and their delusions, and not as men and women, tremendously hampered, no doubt, by inherited passions, ignorance and false teaching, but still mainly capable of being influenced by rewards and punishments, and sometimes by reasoning.

Lectures in hygiene, physiology, psychology and logic should be given in all Asylums to all fairly quiet intelligent patients. On the contrary, the tendency is to treat thought as dangerous, doctors thus showing their obscurantist affinity to clergyman, to discourage all reading except the lightest and most frivolous books and magazines, and to assign to the patients, yokels and scholars alike, tasks of unskilled labour in field and garden and kitchen and corridor and laundry. "Laborare est orare" is not true. Prayer is foolish and wrong. Work is useful and beneficial. But unskilled work is not very useful nor very beneficial, neither to the person so employed nor to the world at large. Overstudy is injurious in itself, but much more so through what it bars out; fresh air, exercise, versatility, sociability. It is a question of the degree of badness, whether no company or bad company is worse for an individual. But in Asylums decent, wellbehaved folk are herded with the vilest of the vile. Instead of a dozen galleries or villas, there should be two-score or more in an Asylum of a thousand or more. Ill-behaviour only should condemn to the refractory wards, *viz:*—violence, filthiness, noisiness, pesteringness; not, as now, independence of character, selfdefence or self-protection against violence, insult, obscenity, pestering, noise and filth. Good conduct amounting to cure, and entitling to release, should not be cajoling, flattering and slavish obsequiousness to doctors, attendants and relatives. Asylums should be fewer and larger, and the Resident Superintendent should be a retired judge with a judge's salary, and none should be admitted or discharged except after a fair trial before a judge. Then merely hearing voices, changing one's religion, disagreeing with one's relatives, stigmatising any immoral smart set, comparing oneself to reformers of the past, temporary breakdowns, would no longer be held sufficient cause for sentencing to indefinite, in many cases lifelong, imprisonment.

Bacterial Change in Mental Disorder: Coliform Group.

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THE literature dealing with coliform intestinal bacteria in patients suffering from mental disorder is extremely scanty. Goodall, *Journal of Mental Science*, 1927, p. 368, writes: "As regards our knowledge of the intestinal tract as a source of infection I consider that the position is still very unsatisfactory. . . . For a few years prior to 1914 my colleagues and I at the Cardiff Mental Hospital Laboratory had carried out much tedious work on the bacteriology of the fæces in states of acute melancholia and mania. An extensive survey in 1914 of all the foreign literature of importance enabled me to state that extremely little work had been done in this direction." The same author, *ibid.*, 1923, p. 421, states: "In 1914 I stated that extremely little work had been done by way of bacteriological examination of the fæces in cases of mental

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disorder. That statement may also be made in respect of the years which have since elapsed. Barton White and I (1914) examined a considerable number of stools from freshly admitted cases of melancholia (18) and mania (10). The results showed that the number of total organisms per gramme of fæces (which means, of course, more especially *B. coli*) was above the average normal figure in a large proportion of the cases. *The B. coli were typical in as high a percentage of cases as obtains for normal stools.*" (The italics are mine.) In the paper here referred to (Goodall, 1914) the author shows that in 18 cases of melancholia 4% of the coliform bacteria isolated were atypical in that they did not ferment lactose, and in 10 cases of mania 6% were atypical in the same respect. Goodall compares these percentages with Houston's (1902–3) figures for the normal stools of healthy persons, which show 8% atypical, *i.e.*, not giving acid and gas in lactose. He therefore comes to the conclusion italicized above, but it should be noted that Houston's work of 1902–3 was planned to find the highest dilution of drinking-water in which typical *B. coli* could be found, and that his technique was adapted to this purpose. His figures are, therefore, not applicable to the present subject, since they are based on the examination of only 17 stools, and of only 6 bacteria from a second culture of each stool. Four out of the 8 atypical *B. coli* described by Houston and probably most of those described by Goodall were the same as the paracolon and mutabile bacteria with which the present paper deals.

W. Ford Robertson (1921) attributes infective disorders of the intestine chiefly to streptococci and *B. proteus*; he does not mention paracolon or mutabile. The latter statement also applies to Chalmers Watson's paper (1923).

During the past five years work has been carried out in this laboratory which has been intentionally confined to the coliform bacteria. It has been found that mental disease is frequently, though not constantly, associated with an increase of two groups of these bacteria in the intestine, namely, the paracolon and mutabile bacilli. In the present paper this association will be discussed under the following headings:

(1) Do paracolon-mutabile bacilli occur in a larger number of persons in a series of mental patients than in the general community?

(2) When they do occur, are they present in larger numbers (proportionally to the other coliform bacteria) in the insane than in the sane?

(3) Are they linked with any particular form of mental disorder?

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(4) In a given patient does the number of paracolon-mutabile bacilli present bear any relation to the severity of the illness? Is it greater in acute phases and less during intermissions and at convalescence?

(5) Are paracolon-mutabile bacilli more toxic than other coliforms?

(6) Do paracolon-mutabile bacilli produce agglutinins in the serum of their carriers?

Before we begin to discuss these points it will be well to define the two subgroups in question, and to see how they are related to the more common coliforms, such as *B. coli communis* (colon sub-group), and to those related bacteria which cause well-defined disease (paratyphoid and typhoid-dysentery groups).

Paracolon-mutabile differ from the former and agree with the latter in that they do not ferment lactose. They differ from the latter in that they are not agglutinated by any specific antiserum against food-poisoning (Gärtner or Aertrycke), paratyphoid, typhoid or dysentery "species," and if a special serum is prepared by injection of a strain of paracolon or mutabile, that serum will agglutinate only the strain used and has no effect on other strains of the same organism. In this absence of specific reaction they agree with *B. coli communis* and other members of the colon sub-group (Mackie, 1913).

B. coli mutabile (Neisser, Massini, 1906) is so named because in artificial culture it regularly gives off daughter-races which cannot be distinguished from colon. Paracolon also, although rarely, gives off mutabile or colon; and colon sometimes throws mutabile or paracolon. The three forms are in fact only variants of one species. (I have brought forward evidence to show that they are Mendelian variants, of which paracolon is the homozygous dominant, mutabile the heterozygote, and colon the homozygous recessive.) Variation to paracolon-mutabile takes place if colon is grown on carbolized media; the reverse variation from paracolon-mutabile to colon takes place in lactose media only. In fact the variation consists of this—that the bacterium adapts itself to its food supply, nevertheless it is not merely a functional change, but a heritable variation which is maintained even after prolonged growth on non-lactose media, and the unmodified mother-race persists alongside the modified daughter.

Although these facts have been observed in laboratory cultures only, there is every reason to suppose that similar changes take place in the bowel in response to unknown causes.

In the following classification of the coli-typhoid bacilli the coliforms are shown as a group equivalent to *Salmonella* or typhoid-dysentery. If, however, the members of these latter are good

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species, then the whole coliform group is equivalent to one species such as *B. typhosus*. I have therefore avoided the use of the term "species" altogether.

Classification of the Coli-Typhoid Bacilli.

Supergroup coli-typhoid.—Gram-negative, highly variable bacilli and cocco-bacilli growing freely on bile-salt media. Not liquefying gelatine.

Group A: Coliform.—Form acid and gas in glucose, maltose and mannite. Do not form agglutinins common to the "section." Not specifically pathogenic.

Subgroup I: Colon.—Form acid and gas in lactose.

Section (a) *B. acidi lactici.*
,, (b) *B. coli communis.*
,, (c) *B. coli communior*, *B. pneumoniæ*, Friedländer.
,, (d) *B. lactis aerogenes.*

Subgroup II: Mutabile.—Do not ferment lactose, but regularly form daughter-races which do so.

B. coli mutabile.

Subgroup III: Paracolon.—Do not ferment lactose and do not form lactose-fermenting daughter-races (except very rarely after prolonged stimulation).

B. paracoli.

Group B: Salmonella.—Form acid and gas in glucose, maltose and mannite. Form agglutinins common to the section. Specifically pathogenic.

Section (a) *B. paratyphosus A.*
,, (b) *B. paratyphosus B.*
,, (c) *B. paratyphosus C.*
,, (d) *B. Aertrycke.*
,, (e) *B. enteritidis*, Gärtner.
? *B. Morgani.*

Group C: Typhoid-Dysentery.—Form acid in glucose. Form agglutinins common to the section. Specifically pathogenic.

Section (a) *B. dysenteriæ*, Sonne.
,, (b) *B. dysenteriæ*, Flexner.
,, (c) *B. typhosus.*
,, (d) *B. dysenteriæ*, Shiga.

(1) Do paracolon and mutabile bacteria occur in a larger number of persons in a series of mental patients than in the general community?

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In a series of 199 patients in this hospital, 58, or 29%, carried paracolon or mutabile, or both (Table II). In a second series of 650 patients, 278, or 42%, contained these organisms (Table III).

TABLE I.—*Table of Sugar Reactions of the Supergroup Coli-Typhoid.*

	L	S	G	M	MN	D	LM	Gel	Ind	Phen
Coliform Group:										
B. acidi lactici	AG	o	AG	AG	AG	OV	AC	o	+	o
B. coli communis	AG	o	AG	AG	AG	AG	AC	o	+	o
B. coli communior	AG	AG	AG	AG	AG	AG	AC	o	+	o
B. lactis aerogenes	AG	AG	AG	AG	AG	OV	AC	o	o	+
B. coli mutabile a	V	OV	AG	AG	AG	OV	AC	o	+	o
,, ,, b	V	OV	AG	AG	AG	AG	AC	o	+	o
,, ,, c	V	AG	AG	AG	AG	AG	AC	o	+	o
,, ,, d	V	AG	AG	AG	AG	OV	AC	o	..	..
B. paracoli	o as *B. coli mutabile.*									
Salmonella Group:										
B. paratyphosus A / *B. paratyphosus B*	o	o	AG	AG	AG	AG	A	o	o	..
B. enteritidis, Gärt / *B. Aertrycke*	o	o	AG	AG	AG	AG	Ak	o	o	..
B. Morgani	o	o	AG	o	o	o	Ak	o	+	..
Typhoid-Dysentery:										
B. dysent., Sonne	V	V	A	A	A	o	V	o	..	..
B. dysent., Flexner	O	V	A	VA	A	O	Ak	o	o+	..
B. typhosus	o	o	A	A	A	V	Ak	o	o	..
B. dysent., Shiga	o	o	A	o	o	o	Ak	o	o	..
Various bacteria *in certæ sedis:*										
B. cloacæ	AG	AG	AG	AG	AG	o	AC	+	+	..
B. oxytocus perniciosus	AG	AG	AG	AG	AG	AG	AC	+	+	..
B. proteus vulgar.	o	AG	AG	AG	o	o	Pep	+	o	..
Zopfius zenkeri	o	o	AG	o	o	o	Ak	o	+	..

L, lactose; S, saccharose; G, glucose; M, maltose; MN, mannite; D, dulcite; LM, litmus milk; Gel, gelatine; Ind, indol; Phen, phenol. A, acid; G, gas; C, clot; V, varying by papilla-formation in which a non-fermenting race gives off a fermenting daughter-race; Ak, alkaline; o, *no change.*

TABLE II.—*Showing the Distribution of Paracolon-Mutabile in a Series of 272 Mental Patients and Convalescents.*

(*a*)	113 patients, acute, included carriers of paracolon-mutabile	36, or 31·8%.
	86 patients, chronic, included carriers of paracolon-mutabile	21, or 24·5%.
	73 convalescents included carriers of paracolon-mutabile	5, or 6·8%.
(*b*)	38 cases of acute mania, confusional insanity, or dementia præcox included carriers of paracolon-mutabile	19, or 50%.
	Same 38 cases included carriers of paracolon-mutabile above 20% of total coliforms	15, or 39·4%.

Similar statistics from healthy members of the general community are extremely scanty. Houston (1902–3, 1903–4) found paracolon or mutabile (non-lactose fermenting bacteria giving AG in glucose) in 1 out of 29 persons, or 3·5%. Morgan and Ledingham (1909) write: "During the investigation of fæces from series of normal persons, adult and infantile, one finds colourless or non-lactose colonies only in a small proportion of the cases. The predominant group, at least in normal stools, is that of the lactose fermenters."

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On the other hand they add—"Groups X, XII, XIV" (paracolon) "are common frequenters of normal and adult stools."

In this laboratory we have not as yet succeeded in getting sufficient observations on healthy persons, but such as we have show paracolon-mutabile in not more than 10%. Also these bacteria are entirely absent from persons in rude health. Persons of sedentary habit who take little exercise in the open air and suffer from obvious intestinal stasis are those who harbour paracolon-mutabile. A valuable set of figures for our present comparison

TABLE III.—*Showing the Distribution of Paracolon-Mutabile in a series of* 650 *Mental Patients.*

	Carriers.	Carriers of over 10 %.	Non-carriers.	Average % of P-M in total coliforms— among carriers.	among all cases.
650 patients	278 . 42·76%	114 . 17·53%	372 . 57·23%	15·48	6·684
119 acute adult	90 . 75·87%	42 . 35·29%	29 . 24·36%	17·54	13·265
430 chronic adult	133 . 30·93%	42 . 9·76%	297 . 69·07%	11·74	3·633
101 children	55 . 54·45%	33 . 32·67%	44 . 45·54%	21·89	12·162
Goodall's figures:					
10 acute manic	..	..	..	..	6
18 acute melancholic	..	..	..	..	4
Houston's:					
29 healthy	1 . 3·5	.. . ..	28 . 96·5%	.. . ..	.. . ..
17 healthy plated direct	0	..	17	..	0

TABLE IIIB.—*Showing the Number of Carriers in Clinical Groups of the above Series.*

	Carriers.	Non-carriers.	Average % P-M to total coliform among carriers.
Acute adults:			
Dementia præcox	15	4	14·7
Typical manic-depressive insanity	7	2	28·2
Less defined mania and melancholia	58	21	17·6
Epilepsy	8	1	18
General paresis	2	1	1·8
Chronic adults:			
Dementia præcox	14	45	..
Typical manic-depressive insanity in interval	0	5	..
Less defined mania and melancholia	21	59	..
Epilepsy	13	47	..
General paresis	7	4	..
Secondary dementia	53	87	..
Post-encephalitic psychosis	5	12	..
Adult imbeciles	20	38	..
Children:			
Idiocy, imbecility, including epilepsy	55	44	..

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is derived from convalescents living under the same roof and under closely similar conditions with the patients. In a series of 73 such persons, only 5, or 6·8%, carried these bacteria (Table II).

We are therefore justified in assuming that carriers of paracolon-mutabile are at least four times more numerous among mental patients than in the general community.

(2) When paracolon and mutabile do occur are they present in higher proportion, relative to the total coliforms, in the insane than in the sane?

Table IIIB shows that nearly one-third of the manic-depressive cases carried a high proportion of paracolon-mutabile (28%).

Table III, column 4, shows the average percentage among carriers in the series of 650 patients.

The numbers dealt with by Houston are small and therefore can hardly be used for comparison. In fact the 27 specimens which were plated directly showed no paracolon-mutabile at all (1903–4). I believe that it is the experience of most bacteriologists that, in the general population, paracolon-mutabile occur in low percentage, and would be represented by only one or two white colonies on a lactose plate—say 1%. Reliable figures on a large scale are needed.

(3) Are paracolon and mutabile linked with any particular form of mental disorder?

Table IIIB shows that they are not, that carriers are fairly evenly distributed among the various clinical forms, although the average percentage of paracolon-mutabile to total coliforms is highest among the typical manic-depressive cases.

(4) In a given patient does the number of paracolon-mutabile demonstrable vary with the course of the illness? Is it greater during acute phases, and less during intermissions and at convalescence?

To answer this question two plans have been adopted: (*a*) To follow a number of patients through the course of their illness, charting the proportion of paracolon-mutabile found at regular intervals in comparison with the development of the symptoms; and for this purpose recurrent manic or confusional cases are most suitable. And (*b*) to compare series of acute with series of non-acute cases.

(*a*) Charts 1 to 5: The upper line in each instance represents the clinical state of the patient, rising with increase and falling with decrease of symptoms, the base being apparent sanity; the lower line represents the percentage of paracolon-mutabile in total coliforms.

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Charts 1 and 2 are of the same patient, F. O—, in two successive attacks of recurrent confusional insanity, and it will be seen that the two lines rise and fall together. In three subsequent attacks, however, paracolon-mutabile were found only in one or two platings out of many. In both the first and second attacks he was vaccinated against his own mutabile, but as the agglutinating power of his serum did not change, it is doubtful whether the treatment had any effect. This patient at the moment of writing is entering on still another attack and a paracolon has appeared in large numbers.

CHART 1.—*Patient F. O—. Recurrent Confusional Insanity.*

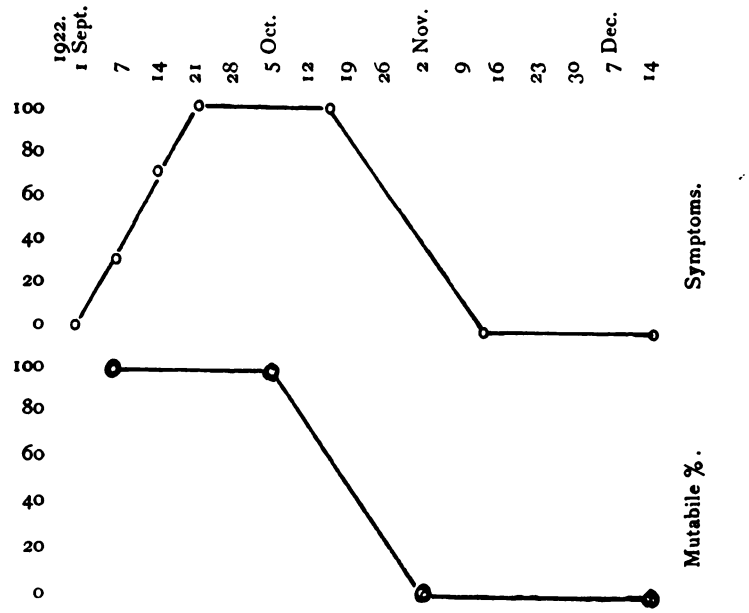


Chart 3: Confusional attack in a man with history of prolonged alcoholism and numerous previous attacks. Precipitating cause in this case also alcohol. Mutabile in the stools. *B. fæcalis alkaligenes* was also found, but is not included in the lower-line figures.

Chart 4: Recurrent confusional insanity in a mental defective. Paracolon in the stools. There was so much secondary dementia between the attacks that the upper line is never brought below the 40 level.

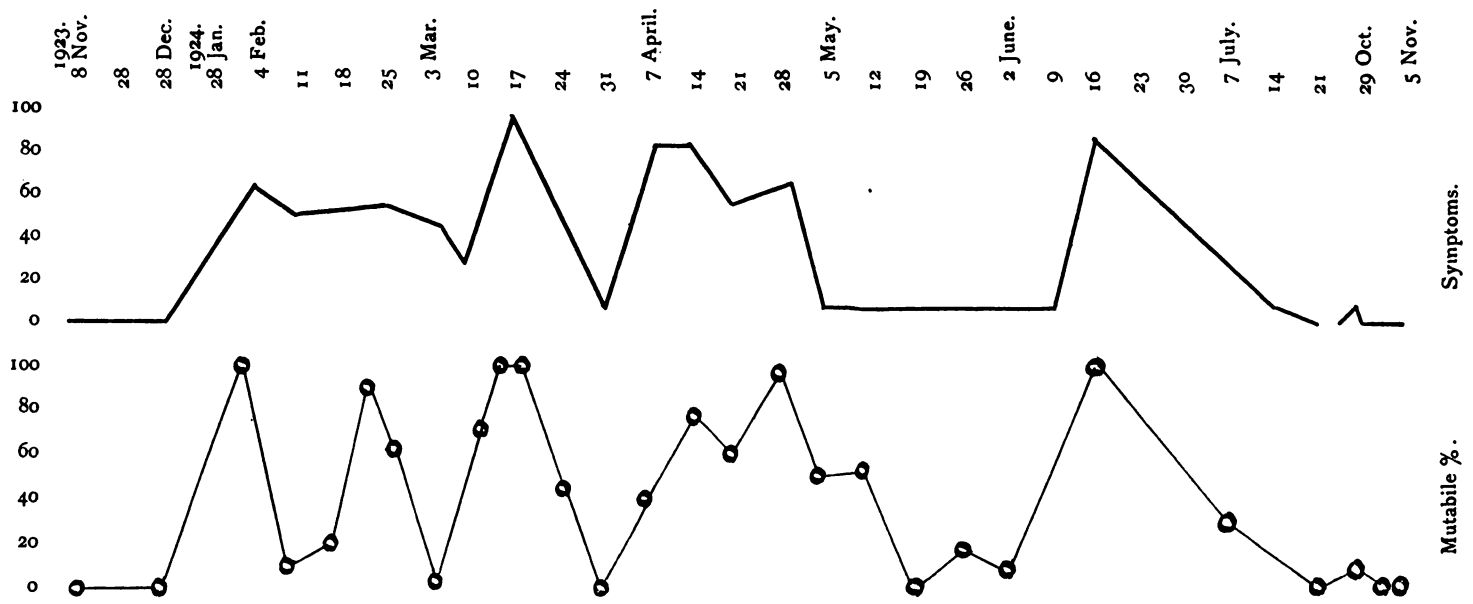
Chart 5: Semi-chronic mania with exacerbations. Mutabile and paracolon in the stools.

The above four patients are the only cases that have been fully worked out so far, but in order to avoid one-sided evidence it is well

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CHART 2.—*Patient F. O—. Recurrent Confusional Insanity.*

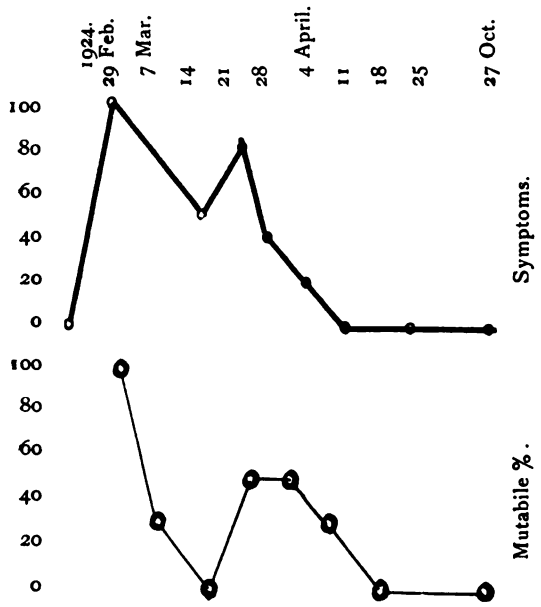


to recall that out of the series of 38 acute cases (manic, confusional, dementia præcox) to which they belong only one-half carried paracolon-mutabile, 3 carried *B. fæcalis alkaligenes* or *B. coli anaërogenes*, and 13 were without demonstrable change in their coliforms.

Tables III and IIIB show that paracolon-mutabile are nearly twice as common in acute as in chronic cases.

We may consider here the question whether increase of paracolon-mutabile is due entirely to the following causes: (i) Constipation,

CHART 3.—*Patient T. B—. Recurrent Alcoholic Confusion.*



(ii) confinement and want of exercise. Acute mental illness is (as Goodall and other writers emphasize) nearly always accompanied by constipation, therefore in the charts shown, the increase of paracolon-mutabile at the beginning of the illness undoubtedly coincides with this condition. Nevertheless paracolon-mutabile continue after the constipation has been removed, and they are often entirely absent from highly constipated stools. There is some evidence that confinement and want of exercise in the open air tend to increase paracolon-mutabile both in the sane and the insane. But, of the latter, persons who are constantly employed out of doors may still carry paracolon-mutabile in great numbers. In Chart 2 the sharp rise of the two lines on June 16 followed a game of cricket during a hot summer day.

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CHART 4.—*Patient J. W—. Recurrent Confusional Insanity in a Mental Defective.*

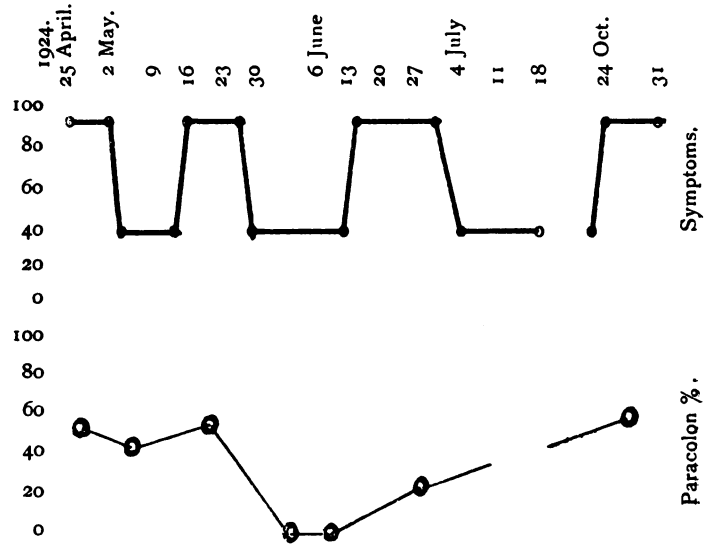
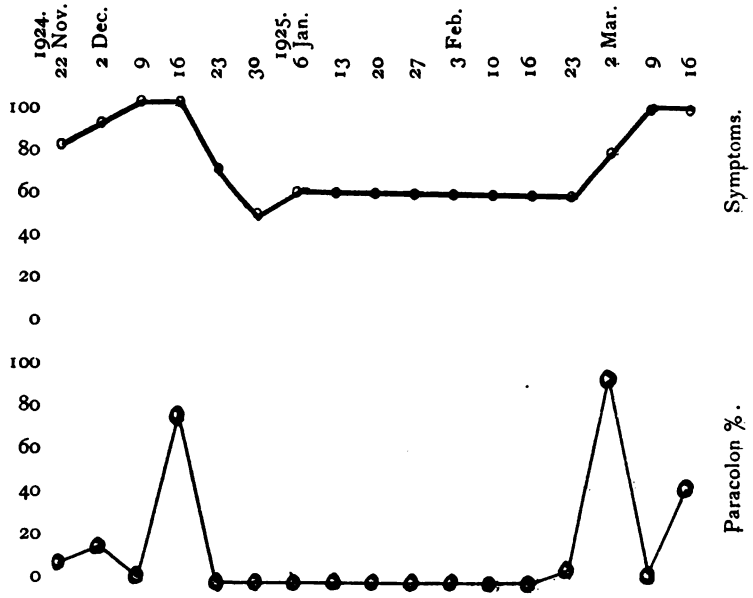


CHART 5.—*Patient F. M. G—. Chronic Mania with Exacerbations.*



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(5) Are paracolon and mutabile more toxic than colon?

To answer this question accurate dosage is necessary. Either paracolon, mutabile or colon will kill a mouse by septicæmia if a large dose (1000–5000 million) is injected hypodermically, and the organism can then be recovered from the liver, spleen or heart-blood. If, however, the dose is reduced to 0·01 or 0·02 c.c. of a 24-hour bouillon culture, then certain strains of para-colon and mutabile appear to be more toxic than colon. This dose, even if it does not kill, may cause obvious illness. Of course it is not easy to be sure whether a mouse is ill or not, but the following tests seem to be beyond cavil and they have been adopted in these experiments: (i) The mice lie for hours on the top of their cotton-wool bedding hunched up, and with coats staring and moist, while the control animals are nested. (ii) With the same appearance they eat no food for 24 to 48 hours, while the controls eat all the food given them.

TABLE IV.—*Classification of* 435 *Colonies, White on Lactose McConkey Plates, and giving AG in Glucose Peptone Water; from Patients in Cheddleton Mental Hospital, none of whom were Suffering from Acute Bodily Illness.*

(1) Paracolon	189, or 43·4%.
(2) Mutabile	187, or 42·9%.
(3) Like mutabile, but give A/Lact. within 24 hours in first subculture	6, or 1·3%.
(4) Like (3), but give AG/Lact.	31, or 7·1%.
(5) *Proteus vulgaris*	2, or 0·4%.
(6) *Zopfius zenkeri*	3, or 0·6%.
(7) *B. Morgani*	17, or 3·9%.

I believe that Groups 3 and 4 are either paracolon or mutabile which have undergone variation to lactose fermenters in the first subculture under the shock of recent isolation. They were all emphatically white on the primary lactose plates. The following observation confirms this view: Two lactose plates spread from fæces of the patient G. T— grew colonies 94% red and 6% white. Three white colonies were pricked out on to a second lactose plate; the daughter-colonies came up red. The same three white colonies gave AG in glucose peptone water. The red daughter-colonies were then sown into lactose peptone water and gave A, no G in 24 hours. These lactose peptone water cultures were then spread on lactose McConkey plates, and two quite distinct sets of colonies appeared, *viz.*, red and white. The white colonies on the primary plate were, I believe, mutabile or paracolon on the point of variation, although the facts may also be explained if we suppose that all three white colonies on the primary plate were impure. Either way—and this is the important point for the present argument—the white colonies which went red on subculture contained paracolon or mutabile. After including Groups 3 and 4 in the paracolon-mutabile figures, only groups 5, 6 and 7, representing 5% of the total, remain as a possible source of error.

Statistical.—The plate percentage of paracolon-mutabile in total coliforms is struck as explained above. The average percentage for any one person is got by adding the percentages from his successive plates and dividing by the number of plates. The percentages in Table III, column 4, are got by adding the average personal percentages of all carriers in the group and dividing by the number of carriers, and for column 5, by dividing by the number of all patients in the group.

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Table V summarizes the results of six experiments, and it will be seen that, out of 60 mice dosed with paracolon or mutabile, 3 died and 27 were obviously ill (50% positive); while 30 dosed with similar quantities of colon (*B. coli communis* and *B. lactis aerogenes*) remained well (100% negative).

It may therefore be said that paracolon and mutabile are undoubtedly more toxic than either *B. coli communis* or *B. lactis aerogenes*, but that they are nevertheless not highly virulent.

TABLE V.—*Summary of Experiments: Injection of Paracolon-Mutabile and of Colon into Mice.*

Injection (hypodermic) of 0·01 c.c. of 24-hour bouillon culture.

Paracolon-Mutabile.				Colon.		
Died.	Ill.	Not affected.		Died.	Ill.	Not affected.
0	6	0	.	0	0	3
1	5	0	.	0	0	3
2	4	6	.	0	0	6
0	6	9	.	0	0	6
—	—	—		—	—	—
3	21	15	.	0	0	18
Injection of 0·02 c.c.						
0	0	15	.	0	0	6
0	3	0	.	0	0	3
0	3	0	.	0	0	3
—	—	—	.	—	—	—
3	27	30	.	0	0	30

Methods, Bacteriological and Statistical.—The method adopted in this laboratory to estimate the distribution of paracolon-mutabile is as follows: A suspension of the fæces is made in sterile salt solution, the concentration being judged by eye. A few drops of this are spread on a pair of lactose McConkey plates (the primary plates), which are then incubated 24 hours. If white, non-lactose-fermenting coliform colonies are present, both the white and the red colonies are counted, and the percentage of each to the total coliform is struck. One or more colonies is then tested by Gram's stain, and complete sugar and gelatine reactions. If the sugar reactions are those of *Salmonella*, the bacterium is put up against the appropriate Oxford standard sera to exclude this group. Mutabile is distinguished from paracolon by late fermentation in lactose peptone water or by observation of red papillæ on a lactose plate.

This is the full examination, but in the large number of cases dealt with it was not possible to carry it out in all. Therefore in some of the first series and in most of the second an abbreviated scheme was adopted, as follows: When white colonies are present on the primary plates, six of them are picked off into glucose peptone water, and if they give AG they are accepted as paracolon or mutabile. They might, of course, also belong to any of the following groups: *Salmonella*, *B. Morgani*, *Proteus vulgaris*, *Zopfius zenkeri*. But I consider that I was justified in classing them as paracolon-mutabile in 95% of cases from experience in this laboratory of the particular kind of patient. In the first place no cases of acute bodily illness are included in the series. *Salmonella* and *B. Morgani* are thus excluded except for chronic "carriers." In the second place a series of 430 white coliform colonies from lactose McConkey plates, which gave AG in glucose peptone water, proved on full examination to belong to the classes set out in Table IV. The 430 colonies were taken from about 200 separate plates, and should, therefore, give a reliable view of the bacteria found in our patients.

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(6) Do paracolon-mutabile bacilli produce agglutinins in the serum of their carriers?

The serum of 12 carriers who were acutely ill was tested against their autogenous bacteria, but only two reacted, and then only in low dilution, namely 1/50. The same 12 sera were tested against Oxford standard bacterial emulsions. Nine were completely negative. The 3 which reacted gave the following results:

F. O— agglutinated *B. enteritidis*, Gärtner, 1/50; autogenous mutabile 1/50.

F. M. G— agglutinated *B. enteritidis*, Gärtner, 1/400; *B. typhosus* 1/300; autogenous paracolon 1/50.

F. S— agglutinated *B. typhosus* 1/40; *B. paratyphosus A* 1/200; *B. paratyphosus B* 1/65.

No history of typhoid fever or food-poisoning could be obtained in any of the three cases.

Summary.

The facts brought to light by this work may be summarized as follows:

Paracolon or mutabile are to be found in 30 to 40% of mental patients, and in 17% of these patients the bacteria in question make up from 10 to 100% of the coliform flora. Carriers of paracolon-mutabile are at least four times more common among the insane than in the general community. Paracolon-mutabile occur in all forms of insanity, but more frequently and abundantly in acute illness than in chronic. In some recurrent cases which have been closely studied they are absent or few in number during intervals, increase rapidly at the onset of an attack, fluctuate with the symptoms, and disappear at convalescence; nevertheless in one and the same patient they may be present in large numbers in one attack and absent in the next.

Paracolon-mutabile are more toxic to mice than colon.

Discussion of the factors which cause the increase of paracolon-mutabile.—The increase of these organisms is probably due to some change of environment in the bowel—a change which acts either by causing massive variation from colon to paracolon-mutabile, or by favouring overgrowth of small numbers of the latter bacteria which may already be present. The change of environment postulated may take origin either in the secretions of the host or in those of some other intestinal micro-organism. Here we have practically no data to go on; indeed the only observations bearing on the matter are the following: Several authors (*e.g.*, Massini, Baerthlein) state that the colon derived from mutabile will revert to mutabile if it is grown on media containing phenol, and Tissier,

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1923, states that *B. lactis aerogenes* and *B. aminophilus* form phenol from tyrosine in the intestinal digestion of proteins.

Turning now to the practical question *whether paracolon and mutabile take any part in producing mental disease.*

It is clear that the association which seems established between mental disease and increase of these organisms may be one of three: (1) A constitutional basis of mental disease may alter the secretions of the patient and so call out the bacterial change. (2) The increase of paracolon-mutabile may be one of many causes capable of upsetting an unstable nervous system, and we have seen that paracolon-mutabile are actually more toxic than normal colon. (3) A substance, such, for example, as phenol, if formed in the intestine may give rise to an increase of paracolon-mutabile, and after absorption cause the mental illness, and here we should recall the work of Metchnikoff, 1910, who showed that phenol combined with sulphuric and glycuronic acid is lethal to guinea-pigs, and produces arterio-sclerosis if given over long periods in sub-lethal doses. Wladytchko also found proliferation of neuroglia and neuronophagy in the brain of a guinea-pig which had been treated in this manner.

It is possible that all three modes come into play in a series of vicious circles.

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