been caused by a direct stimulating ic acid comparable to that observed in ny volunteers. This effect may also be ible for the increased feeling of well-being ted in patients receiving deep X-ray treatment en they are given folic acid.[17]

Whether the gastrointestinal disturbances are mediated through a similar central pathway or resulted from a direct effect on the gut remains conjectural. But it is of interest that folic acid seems to be concentrated in saliva,[18] a fact which may explain the bad or bitter taste complained of by some of our volunteers.

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Requests for reprints should be addressed to R. H.

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ENZYME INHIBITION BY LEAD UNDER NORMAL URBAN CONDITIONS

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Summary A close negative correlation was found between the concentration of lead in blood and the activity of erythrocyte δ-aminolævulinic acid dehydrogenase in 26 healthy individuals, never exposed occupationally to lead. The results indicate that present levels of environmental contamination with lead can produce a measurable biochemical alteration in man.

INTRODUCTION

LEAD is absorbed into the human organism by respiratory and digestive routes and is distributed to organs and tissues by the bloodstream.[1] Metabolism is complex—some lead being excreted and some deposited; the rest forms a metabolically active pool reflected by the blood-level of lead.[1-4] As a result of growing industrial use and the introduction of alkyl lead compounds as petrol additives, exposure to lead is substantially above[5-9] the background of absorption from food and drinking-water. Epidemiological and experimental data point to a logarithmic correlation between the concentration of lead in the air and that in the blood of exposed individuals or populations,[7-8] suggesting that, in man, lead can accumulate as a result of increasing environmental contamination.

Any effect of the absorbed lead on health will depend on the degree of accumulation. The generally accepted "safe" upper limit for the concentration of lead in the blood of persons exposed industrially is some 70–80 μg. per 100 ml.,[1-4] and mean values for occupationally unexposed populations are usually between 15 and 25 μg. per 100 ml.[3,7,10] These levels are considered by most workers to be without any biological effects.

Inhibition of haem synthesis is one manifestation of lead toxicity; and measurements of intermediate products of this metabolic chain—e.g., coproporphyrin and δ-aminolævulinic acid (A.L.A.) in urine—have long been used as quantitative tests of the response of the organism to surplus lead,[3,11] and have thus formed one basis for the evaluation of what is harmful and what is not. The finding that erythrocyte A.L.A. dehydrogenase activity is specifically inhibited by lead has provided a new, specific, and sensitive method for the detection of early lead effect.[11-13] We have used this test to see if measurable biological effects due to present levels of urban exposure to lead can be found in man.

MATERIAL AND METHODS

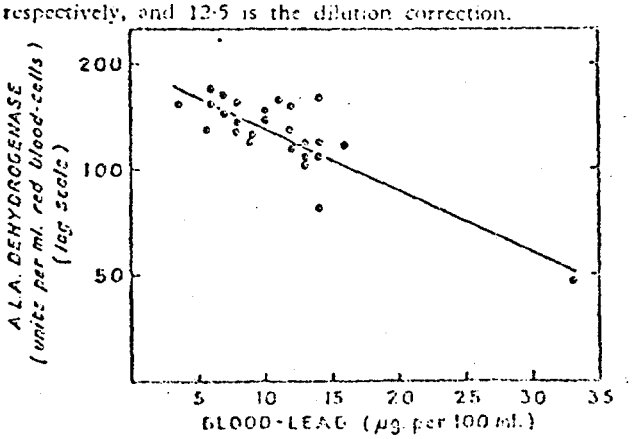
Blood-lead levels and erythrocyte A.L.A. dehydrogenase activity were measured in 26 healthy medical students (16 males, 10 females) with no present or previous occupational exposure to the metal. The concentration of lead in whole blood was measured after wet ashing using a dithizone method.[14] The standard deviation of duplicate measurements was 1·3 μg. per 100 ml. A blind control of the lead estimation gave the following result (the concentration in the blank sample recorded as 9 μg. per 100 ml.):

Added	*Measured*
μg. per 100 ml.	
15	12
50	49
100	101

A.L.A. dehydrogenase was measured from fresh heparinised whole blood according to Bonsignore's method.[15] The results were corrected for hæmatocrit value, and the enzymatic activity was calculated from the formula:

$$1000 \times 12{\cdot}5\ (A_{60}-A_0)/\text{hæmatocrit (\%)}$$

A_t and A_0 are the absorbencies at 60 and 0 minutes, respectively, and 12·5 is the dilution correction.



Relation between blood-lead and activity of erythrocyte A.L.A. dehydrogenase of 26 persons never occupationally exposed to lead.

RESULTS

There was a strong negative correlation between the concentration of lead in the blood and the logarithm of A.L.A. dehydrogenase activity (see figure):

$$y = 2{\cdot}307 - 0{\cdot}018x; r = -0{\cdot}83$$

The results indicate that an inhibition of A.L.A. dehydrogenase that is proportional to the concentration of lead in the blood can be shown even for people representing "normal" urban exposure to lead. There is no lead level on the regression line below which it can be stated that no inhibition occurs.

We later extended our observations to 142 workers, representing various degrees of occupational exposure, with blood-lead values ranging from 11 to 94 µg. per 100 ml. The regression line was almost identical.

$$y = 2{\cdot}274 - 0{\cdot}018x, r = -0{\cdot}90$$

These observations confirm the results presented above and clearly show the interrelationship between the concentration of lead in the blood and the activity of A.L.A. dehydrogenase.

DISCUSSION

So far as we know, there have been no earlier reports indicating that present environmental contamination with lead has any biological effect on man. Our finding is an example of how the border between "effect" and "no effect" can be shifted by the introduction of more sensitive methods. Indeed, inhibition of A.L.A. dehydrogenase was found at such low lead concentrations that one may ask whether there is any lead dose small enough to have no effect at all. The same may be true for other poisons; but a lack of sensitive methods for measuring toxic effects leaves this question open.

The effect of environmental contamination with lead on health has been subject to speculation [1-3]. The finding that A.L.A. dehydrogenase is partly inhibited in the "normal" urban population cannot be considered as proof of an effect on the health, since its significance is unknown as yet, but it demonstrates that even the comparatively low exposure to lead, prevailing today, interferes with metabolism. This interference may or may not be harmful. Without taking any standpoint on this question, it may be assumed from the Goldsmith-Hexter regression [8] that this and other possible effects will become more pronounced if contamination becomes heavier in the future.

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Requests for reprints should be addressed to S. H.

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DISSECTING-MICROSCOPY OF RECTAL MUCOSA

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Summary Under the dissecting microscope the normal appearance of the rectal mucosa is a honeycomb pattern of units formed by a vascular network. Under oblique light, pits (presumably crypts of Lieberkühn) can be seen in the centre of these units. This vascular pattern is clearly disturbed in biopsy specimens from patients with ulcerative colitis, and in many cases no pits can be seen.

INTRODUCTION

THE dissecting-microscope appearances of the normal and abnormal jejunal mucosa are well known, and the findings are of considerable value in the diagnosis of small-bowel disease. To our knowledge, this technique has not been used to investigate the large-bowel mucosa.

We describe here the dissecting-microscope appearances of the normal rectal mucosa and the changes found in ulcerative colitis.

MATERIALS AND METHODS

Fifty rectal-biopsy specimens were taken at routine sigmoidoscopy at least 5 cm. or higher from the anal verge. Four of these were too damaged for evaluation. The specimen was immediately placed in a petri dish containing formalin, examined without delay, and photographed within 15 minutes. Within 20–30 minutes the specimen usually became white and features necessary for examination by this method.

RESULTS

Normal Rectal Mucosa

The striking feature is a "honeycomb" pattern of the mucosal surface. Each "unit" of the honeycomb is formed by a fine, fairly complex network of vessels which merge with each other at the corners of the unit producing a uniform and regular architecture (fig. 1).

Fig. 1—Narrow vascular channels dividing mucosa into "mucosal units". Reduced to about ⅓ of [illegible]