- * Bernard, Claude: *Leçons sur la Diabète et la Glycogénèse Animale*, Paris, 1877.
- † Bierich, R.: *Klin. Woch.*, 1924, iii, 221.
- ‡ Bierich, R., and A. Rosenholm: *Biochem. Zeit.*, 1924, clii, 193.
- § Bokelmann, O.: *Arch. f. Gynäk.*, 1926, cxx, 726.
- || Chipman, W.: *Lab. Rep. Roy. Coll. Physic. Edin.*, 1903, viii.
- ¶ Clausen, S. W.: *Journ. Biol. Chem.*, 1922, lli, 263.
- ‡ Driessen, L. F.: *Arch. f. Gynäk.*, 1907, lxxxii, 278.
- § Kerridge, P. T.: *Journ. Sci. Inst.*, 1925-26, iii, 404.
- || Lewis, W. C. M.: *Journ. Cancer Research*, 1927, xi, 16.
- ‡ Lochhead, J., and W. Cramer: *Proc. Roy. Soc. Med.*, 1908, lxxx, 263.
- § Lochhead, J.: *Marshall's Physiology of Reproduction*, Second Edition, London, 1922, 513.
- ¶ Looser, A.: *Zentralbl. f. Gynäk.*, 1926, i, 1819.
- ‡ Mendel, B., and I. Goldscheider: *Klin. Woch.*, 1925, iv, 1502.
- § Mendeléeff, P.: *Compt. Rend. Soc. Biol.*, 1923, lxxxviii, 146, 291.
- || Meyerhof, O.: *Pflüger's Archiv*, 1920, clxxxv, 11, and 1921, clxxxviii, 114.
- ¶ Murphy, J. B., and J. A. Hawkins: *Journ. Gen. Physiol.*, 1925, viii, 115.
- ‡ Negelein, E.: *Biochem. Zeit.*, 1925, clxv, 122.
- § Pemberton, H. S., and L. Cunningham: *Lancet*, 1925, ii, 1222.
- || Slemmons, J. M.: *The Nutrition of the Fetus*, 1919.
- ‡ Warburg, O.: *Biochem. Zeit.*, 1923, cxlii, 317 (and many other papers). Reviewed by R. K. Cannon, *Cancer Review*, 1927, ii, 289.
- § Warburg, O.: *Biochem. Zeit.*, 1927, clxxxiv, 484.
- || Warburg, O., and F. Kubowitz: *Biochem. Zeit.*, 1927, clxxxix, 245.
- ‡ Williams, Whitridge: *Obstetrics*, 1923, 173.

HEREDITARY ICTERUS, OR FAMILIAL ACHOLURIC JAUNDICE.

BY

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THE following is a description of a family, some members of which show very distinctly an icteric tinge in the skin and conjunctivae. The title "hereditary icterus" would seem to be more accurate than the alternative "familial acholuric jaundice," for there was no splenic enlargement, and the jaundice does not affect either the duration or enjoyment of life.

Attention was first directed to a girl (IV 1), aged 10 years, about seven years ago. She was brought to me by her mother on account of jaundice. At the time this was thought to be an attack of catarrhal jaundice. There had been some slight malaise, but no prominent symptoms. On a subsequent occasion three years later she was seen on account of the same condition. In May, 1927, she was brought again for examination on account of jaundice and for an opinion as to her fitness for entry to a training college. She had now grown into a well made, strongly built young woman, full of vigour and with a zest for games. The skin and conjunctivae showed a distinct icteric tinge. The faeces were normal and the urine was free from bile. There was no enlargement of the spleen, and all the other organs were normal. Her mother informed me that when her daughter was bathing in the sea the parts of the body not covered by the bathing dress (neck, shoulders, and legs) became intensely red. It may be conjectured that this showed an abnormal sensitiveness of the skin to exposure to sunlight. A diagnosis of haemolytic jaundice was made, and a consultation was arranged with Dr. T. H. Oliver of Manchester. He saw her on June 2nd, agreed with the diagnosis, and arranged to have the blood examined at the clinical laboratory of the Manchester Royal Infirmary.

As I was aware that the girl's father (III 2), aged 49, also had a yellow tinge in his skin and conjunctivae, Dr. Oliver agreed to see him and arrange for a blood examination. After examination on June 16th Dr. Oliver decided that the father had the same condition as the daughter, but in a lesser degree. The father has a sister, aged 50, who has a yellow skin. She had an operation for gall stones some years ago, but no information is obtainable as to whether stones were found or not. She still has the yellow tinge in her skin.

The father informed me that he had a brother (III 4) living in another town who was quite pale and free from yellowness in the skin. I arranged to examine both brothers together in the daylight and so make a comparison. This was striking; the one was indeed a yellow man, while the other was a pale-face. Owing to the kindness and interest of Dr. Oliver, the pale brother's blood was examined at the Manchester Royal Infirmary. The results of the three blood examinations are given in detail. On making further inquiry into the history of the family, the father of my first patient informed me that his father,

who died in 1909, aged 64, had a yellow skin, but that his mother was pale and clear-skinned. He also remembers that his father's mother was yellow-skinned (she died in 1897, aged 78), and that his paternal grand-uncle was yellow-skinned. He died aged 81. My informant cannot remember his father's father.

A pedigree chart based on this information and on the facts observed can be constructed as follows (the members of the family who had yellow skins are indicated by an asterisk):

depression (the jaundiced outlook), but in the cases here described the temperament is placid, pleasant, and cheerful, in spite of the high blood content of bilirubin.

I am greatly obliged to Dr. T. H. Oliver of Manchester for his kindly help and assistance, and Drs. W. M. Roberts, G. F. Langford, and G. S. Smith for the laboratory work.

REFERENCE.
1 *C. R. Soc. de Biol.*, Paris, 1905, p. 937.

OBSERVATIONS ON THE COMBINED ACTION OF COLLOIDAL LEAD AND RADIATION ON TUMOURS.*

BY

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THERE is evidence that the inoculation of colloidal lead into the circulation gives rise to thrombosis of the blood vessels of tumours.¹ Radiation also causes interference with the blood supply and thrombosis apart from its direct destructive

Similarly, three-quarters of the lethal dose of radiation—that is, fifteen minutes—never caused the tumour to disappear, though a temporary slowing of the rate of growth occurs, as seen by comparing Charts 1 and 3.

Combining these two treatments two sets of experiments were carried out. In one set the lead inoculation was given first and the radiation after varying intervals of time. In the other set the radiation preceded the inoculation of lead. When the radiation was given first mice were grafted with small pieces of T/63 into both flanks. When one of these had grown to 5 by 5 or 6 by 4 mm. superficial area it was radiated for fifteen minutes. After intervals of 1, 2, 3, 4, and 5 days 0.06 c.cm. of lead per gram of weight (mouse) was inoculated into the tail vein. The tumour on the other side served as a control.

In the experiments when lead colloid was given first mice were grafted as before. The lead was inoculated when one of the tumours measured 5 by 5 mm. or less, and the radium applied within a few hours, or later, when the tumour had grown to 5 by 5 mm. Long intervals between lead and radiation were difficult to arrange, because it was not possible to know precisely how long a small nodule

CHART 1.—Showing the normal rate of growth of T/63, measurements being made three times a week. (As also in all subsequent charts.)

CHART 2.—Showing the rate of growth in animals which have had 0.06 c.cm. of lead colloid per gram of mouse inoculated into the tail vein at the time of the first measurement.

CHART 3.—Showing the rate of growth of tumours exposed to fifteen minutes' radiation at the time of the first measurement.

action on tumour cells.^{2,3} Experiments have therefore been carried out to see whether, by combining these two therapeutic measures, tumours can be made to disappear by such doses that the toxic effects of lead on the patient would be avoided, and likewise the destructive action of radiation on normal tissues and its other harmful effects.

EXPERIMENTAL DETAILS.

The mouse tumour T/63 was used. This tumour having once grown to a measurable size has never been observed to regress. Its disappearance is, therefore, certain evidence that it is the experimental conditions which are adversely affecting the tumour, and not concomitant immunity. The colloidal lead, containing 0.5 per cent. of lead, was supplied by British Colloids, Ltd. Radiation was obtained from a radium applicator of 110 mg. RaBr, 4H₂O, having an area of 2 by 2 cm. and screened with 0.15 mm. of silver. Preliminary observations showed that 0.08 c.cm. of lead colloid per gram of weight (mouse) was approximately the lethal dose. Previous work had shown that twenty minutes *in vivo* exposure to a T/63 tumour measuring 5 by 5 mm. was just sufficient to cause it to disappear. It was decided to work with three-quarters of these doses in each case. For lead an inoculation of 0.06 for each gram of mouse weight never caused death. It did, however, affect the general health of the animal, as shown by a decrease in weight beginning on the third or fourth day, with recovery on about the tenth day; the decrease amounted to about 10 per cent. There was also a slight slowing of the rate of growth of the tumour, as seen by comparing Charts 1 and 2.

* A paper read at the British Institute of Radiology on January 19th.

would take to grow to 5 by 5 mm. after lead treatment. The results of all these experiments are given in the following table. Each + or - represents a treated tumour.

Table of Results.

Radium Exposure before Lead Inoculation.

Days' Interval.	Tumours Grew.	Tumours Disappeared.
5	++	
4	+++++	
3	+++++	
2	++++++	
1	++	

Lead Inoculation before Radium Exposure.

Days' Interval.	Tumours Grew.	Tumours Disappeared.
0	+++	
1	+++	
2	+++++	
3	++++++	-----
4	+++++	---
5	+	
7	+++	
12	+	

The table shows that when the radiation precedes the lead treatment up to an interval of 5 days, no disappear-