planted sarcoma in CAF_1 mice, but in addition, a progressive decrease in Vit. B_6 content of the tumor during its growth with a simultaneous accumulation of kynurenin. In human subjects, Musajo *et al.*(7) isolated kynurenin and 3-hydroxykynurenin from the urine of patients with myeloid and lymphatic leukemia and Hodgkin's disease.

Summary. The amount of coenzymatically active Vit. B_6 was determined in plasma and leukocytes in patients with various diseases. Values for plasma and leukocytes varied widely in all groups examined. A statistically significant decrease of plasma B_6 was found only in patients with nutritional anemia and various forms of leukemia. However, the amount of pyridoxal phosphate was very low in individual patients with various other diseases. This may indicate a decreased intake of vitamin in some hospitalized patients or an increased need for it. B_6 values in leukocytes were consistently decreased in patients with various forms of leukemia. In contrast, cells from normal bone marrow and from tonsils showed significantly higher amounts of pyridoxal phosphate. The findings are discussed with reference to a specific disturbance in B_6 metabolism in some neoplastic conditions.

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Liver Ketogenesis (3). High Fat Feeding on Acetoacetate Production in Liver Slices, Utilization by Kidney Slices. (26178)

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Nath *et al.*(1-3) have reported that continued injection of acetoacetate to normal animals causes disturbances in carbohydrate metabolism and it has been postulated that gradual accumulation of acetoacetate in blood and tissues is one of the factors responsible for development of diabetes. Such accumulation may result either from overproduction of acetoacetate in the liver or its decreased utilization by the extra-hepatic tissues.

The authors(4) have reported that the hydrolyzed product of glucose cycloacetoacetate (GCA), a crystalline substance obtained by condensation of glucose with acetoacetate, prevents overproduction of acetoacetate by liver slices and increases its utilization by kidney slices when fed to rats along with a high carbohydrate diet. High fat diet has also been known to cause metabolic changes in rats, including diminished rate of lipogenesis (5), glycogenesis(6) and glucose utilization (7). Therefore, the effect of high fat feeding on liver ketogenesis and the influence of hydrolyzed GCA feeding with high fat diets is reported here. Desiccated thyroid and thiouracil were also mixed in the diet of 2 groups of animals to study their additional influence on liver ketogenesis and acetoacetate utilization by kidney slices.

Methods. In view of the relatively rapid response of young rats to thyroid and thiouracil feeding(8), male albino rats weighing 75-100 g and growing steadily on a standard diet were used. These rats were divided into 8

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groups of 6 rats each. Rats in Group I were maintained on high carbohydrate diet (Normal). All animals in other groups were fed high fat diet.

COMPOSITION OF DIETS

Constituents	Normal (%)	High fat (%)
Wheat flour	10	13
Sucrose	50	15
Casein	20	25
Ground-nut oil	9	34
Cod liver oil	1	1
Salt mixture	4	4
Yeast powder	4	6
Marmite	2	2

Rats in Group IIa were fed high fat diet for 19 weeks. Desiccated thyroid and thiouracil (.3% of diet by wt.) was mixed in the diet fed to rats in Groups III, VI and IV, VII respectively. Freshly hydrolyzed GCA (.8%) was fed along with diet to Groups V, VI and VII.

Tissue preparation and analytical methods. At the end of feeding period of 7 weeks (19 weeks in case of Group IIa), rats were sacrificed by stunning and decapitation. Liver and kidneys were removed immediately and placed in ice-cold saline. Tissue preparations were done as described by Umbreit *et al.*(9). Liver and kidney slices were then cut with razor blade, weighed in microbalance and suspended in conventional Warburg vessels containing 3 ml of Krebs' Ringer Phosphate buffer, pH 7.2. Vessels were gassed for one minute with oxygen, then incubated for 2 hr with constant shaking. At the end of incubation period, acetoacetate was estimated from the media according to the manometric method of Edson(10). Liver glycogen was estimated at the beginning, by the method of Good *et al.*(11), and blood sugar by that of Hagedorn and Jensen(12). GCA was prepared according to the method of West(13) as modified by Nath *et al.*(14). GCA was hydrolyzed with 2N HCl in boiling water bath for 12 min. and extracted with ether to remove resinous materials formed. Aqueous solution was adjusted to pH 7.2 by adding the requisite amount of 2N NaOH. Total fat content of liver was extracted thrice with hot alcohol-ether mixture (1:1). This extract was evaporated to dryness and remaining solids were reextracted with petroleum ether and evaporated in an air oven to dryness till constant weight is reached. From this the amount of fat was calculated per g of wet liver.

Urine was tested qualitatively for sugar

TABLE I. Oxygen Uptake and Acetoacetate Produced by Liver and Kidney Slices. 6 rats in each group except Group IIa with 5 rats. Krebs' Ringer Phosphate Buffer pH 7.2, incubation temperature 37.5°C; oxygen as gas phase. (Avg values with stand. dev.)

	Oxygen uptake in μl/100 mg wet wt of tissue/2 hr					Acetoacetate (expressed as CO_2), * μl/100 mg wet wt/2 hr				
	Liver slices			Kidney slices		Liver slices			Kidney slices	
Group	No substrate	Butyrate .017 M	Acetate .08 M	No substrate	Aceto-acetate 300 μl	No substrate	Butyrate	Acetate	No substrate	300 μl aceto-acetate added as substrate
I	180 ± 14	273 ± 15	270 ± 14	550 ± 25	658 ± 30	15 ± 5	78 ± 8	54 ± 6	5 ± 3	68 ± 7
II	153 ± 12	222 ± 20	189 ± 12	540 ± 23	705 ± 32	38 ± 4	96 ± 8	68 ± 6	18 ± 3	145 ± 12
IIa	155 ± 10	229 ± 15	195 ± 11	515 ± 20	690 ± 30	46 ± 5	112 ± 8	76 ± 5	29 ± 5	103 ± 10
III	220 ± 18	329 ± 21	290 ± 19	600 ± 22	909 ± 41	43 ± 5	151 ± 13	77 ± 6	20 ± 5	117 ± 11
IV	126 ± 11	150 ± 13	136 ± 12	475 ± 30	600 ± 26	25 ± 6	58 ± 5	21 ± 5	25 ± 6	48 ± 6
V	185 ± 10	270 ± 11	209 ± 9	558 ± 32	704 ± 33	15 ± 4	52 ± 5	25 ± 4	11 ± 4	150 ± 11
VI	210 ± 15	300 ± 18	220 ± 14	—	800 ± 38	17 ± 4	80 ± 7	67 ± 6	—	140 ± 10
VII	180 ± 12	250 ± 15	220 ± 13	—	690 ± 35	12 ± 8	60 ± 5	33 ± 4	—	80 ± 8

* CO_2 in μl produced after decarboxylation of acetoacetate with aniline citrate.

TABLE II. Blood Sugar, Liver Glycogen, Liver Fat, % of Tissue Weights (Wet Wt) of Different Groups of Rats. 6 rats in each group except Group IIa with 5 rats.

Group	Blood sugar, mg/100 cc	Liver glycogen, g/100 g	Liver fat, g/100 g	Wet wt of tissues, g/100 g body wt	
				Liver	Kidneys
I	84 ± 3	2.45 ± .23	3.4 ± .2	3.5 ± .15	.8 ± .05
II	97 ± 2	1.94 ± .16	5.8 ± .3	5.2 ± .19	.92 ± .03
IIa*	100 ± 3	2.00 ± .12	6.96± .25	6.7 ± .29	1.00 ± .06
III	100 ± 3	.29 ± .1	4.8 ± .4	4.1 ± .11	.95 ± .04
IV	90 ± 2	.89 ± .2	5.1 ± .2	5.6 ± .21	.95 ± .05
V	89 ± 2	2.98 ± .17	3.8 ± .3	3.8 ± .16	.82 ± .02
VI	90 ± 3	.95 ± .15	4.6 ± .3	3.9 ± .12	.8 ± .02
VII	—	1.28 ± .16	5.0 ± .23	3.95± .2	.9 ± .03

* Rats fed high fat diet for 19 wk.

and ketone bodies weekly.

Results and discussion. Oxygen consumption (Table I) is usually lower in high fat fed rats than in normal animals, and thiouracil feeding further depresses it. Hydrolyzed GCA feeding has been found to correct metabolism of high fat fed rats showing normal oxygen consumption and acetoacetate production. High fat feeding induces higher rate of fatty acid oxidation thereby producing more acetoacetate, which agrees with the results of Tepperman *et al.*(15). Thiouracil exerts a greater influence on high fat diet, and it appears from the results that a high fat diet suppresses the increased metabolic rate in hyperthyroid rats.

Although high fat feeding for a period of 7 weeks shows significant rise in acetoacetate utilization by kidney slices (Table I), when this diet is continued for a further period of 12 weeks, utilization of acetoacetate falls considerably. Production of acetoacetate by liver slices (Group II), however, is higher in high fat fed rats than in controls (Group I). Hydrolyzed GCA feeding has been found to decrease acetoacetate production and to increase its utilization in all groups *i.e.*, Groups V, VI, VII as compared to their respective controls (Table I).

Blood sugar values (Table II) indicate slight hyperglycemic effects in case of high fat diet and hyperthyroidism. Hypertrophy of liver and kidneys was found in these animals. Fat deposition in livers of high fat fed rats, as also observed by French *et al.* (16) is evident from the results in Table II. Liver glycogen in hyperthyroid rats is known to be very low(17) and when high fat fed rats are made hyperthyroid, the same low values are found. Liver glycogen in high fat fed rats is less than the control. Hydrolyzed GCA feeding increases liver glycogen of high fat fed, hyper- and hypothyroid rats. Glycogenic effect of hydrolyzed GCA has previously been reported by us(18). Thiouracil feeding with high fat diets augments hypothyroidism as previously shown by Kennelly *et al.*(19). It reduces ketogenesis and acetoacetate utilization by high fat fed rats (Group IV).

Urine from high fat (Group IIa) and thiouracil fed rats (Group IV) was found to contain traces of sugar and ketone bodies.

The results show the adaptation of animals in respect to fatty acid oxidation when maintained on high fat diet, and other effects of this diet on tissue metabolism.

Summary. High fat feeding increases blood sugar, liver fats and tissue weights (liver and kidneys). It increases acetoacetate production by liver slices and utilization by kidney slices, but this high rate of utilization is not maintained on prolonged feeding (19 weeks). High fat feeding augments hypothyroidism and suppresses hyperthyroidism to some extent. A beneficial effect of hydrolyzed GCA feeding with high fat diets to hyper- and hypothyroid rats is indicated.

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Effect of Mephentermine on Venomotor Tone, Blood Flow and Arterial Pressure in Forearm of Man.* (26179)

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Mephentermine sulfate§ is used effectively in treatment of hypotension(1-3), but there is confusion regarding the means by which the drug restores arterial pressure. A pressor amine may elevate arterial pressure by increasing arteriolar tone, increasing cardiac output or a combination of both(4). Welch *et al.* reported that mephentermine had little effect on peripheral arteriolar resistance in the dog but exerted its effect primarily on myocardial contractility(4). Several authors reported an increase in myocardial contractility after administration of mephentermine without reference to its action on the peripheral arterioles(5,6). Brofman *et al.*(3) found little change in cardiac output in man and dogs and attributed the elevation in arterial pressure to increased peripheral resistance. Aviado(7) reported vasodilation in the dog after intraarterial injection of mephentermine but Borden found vasoconstriction(8).

The effect of a pressor amine on cardiac output will depend not only on response of the myocardium, but also upon the changes induced in venous tone. Venous constriction with a shift of blood from the periphery would increase amount of blood available to the heart and help increase output. Data regarding the effects of mephentermine administration on venous tone in man are not available.

Because of these discrepancies, and since there may be a species difference, it seemed important to study the effect of mephentermine on forearm venous tone and blood flow in man.

Method. Normal male students were studied while lying supine. Room temperature was maintained at 79-81°F and every effort was made to keep the subjects comfortable. They remained in the recumbent position for at least 60 minutes before experiments were begun. Arterial pressure was measured intermittently with a cuff on the right arm. Venous pressure was measured in the antecubital vein of the dependent right arm with a strain gauge. The data were ana-

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