ery, and none of the changes shown in Fig. 1 and by Bach and Seefelder (*3*) are apparent. Having examined full sets of horizontal sections through our sample of eyes, we suggest that Horsten and Winkelman's section was from the outer margin of the macular area. We therefore concur with Bach and Seefelder that the newborn infant's fovea is still very immature.

One notable feature in Fig. 1, B and C, is the prominent split in the inner nuclear layer near the fovea, at the vitread margin of a layer of larger and more densely stained cells. Bach and Seefelder (*3*) had described this split as the postnatal remnant of the "transient layer of Chievitz" between the amacrine cells ("inner horizontal cells") and the rest of the inner nuclear layer. Regardless of its nature, we find this split in the macular areas of all the human infant eyes we have examined, and it also can be seen near the fovea of the newborn macaque's retina (*5, 9*). The width of the split may depend on histological procedures; though present in all eyes from humans and monkeys, it is narrower in the eyes embedded in plastic.

The second major finding concerns the paucity of cones in the foveal region and their very immature appearance 8 days after birth (Fig. 1, C and D). Even though very young infants have considerable visual capacity (*1, 6*), we suggest that most of it is based on extrafoveal vision. This agrees with arguments from other considerations that vision in newborn infants is largely determined by peripheral regions of the retina (*10*). This could be the reason, for example, that color vision in young infants (*11*) shows some of the anomalies found in peripheral color vision in adults (*12*). When does the human fovea become adult in its morphology? Another eye from an 11-month-old female, which we have similarly processed, has slim, elongated foveal cones similar to those from adult eyes. We are attempting to obtain well-preserved retinas from intermediate ages to chart this maturation more precisely.

The peripheral retina of the newborn human infant is well developed, but the macular area is not; indeed, in the fovea the receptor layer is so poorly developed that it may barely be functional. This does not seem to be the case in the newborn macaque monkey (*5*); the macaque's fovea is immature at birth but its cones are far more mature than those of a newborn human. Even though the visual system of the macaque is often used as a model for the human system, our findings on the retinas of newborn human infants suggest that although newborn macaque monkeys may be models for somewhat older human infants, they may not be good models of newborn humans.

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Dietary Calcium in Human Hypertension

Abstract. *A pilot survey was made of the dietary calcium intake of normotensive and hypertensive individuals. Compared to 44 normotensive controls, 46 subjects with essential hypertension reported significantly less daily calcium ingestion (668 ± 55 milligrams compared to 886 ± 89 milligrams). The intake of other nutrients, including sodium and potassium, was very similar in the two groups. The hypertensives differed from the controls primarily in their consumption of nonfluid dairy products. The data suggest that inadequate calcium intake may be a previously unrecognized factor in the development of hypertension.*

Of the mineral elements in the human diet, sodium and potassium have received the greatest attention as being possible determinants in the pathogenesis of essential hypertension in humans (*1, 2*). Although the results of a number of dietary surveys have suggested a link between the dietary intake of these two cations and the development of hypertension, many other studies have shown no difference in the consumption of these two mineral elements among normotensive (NL) and hypertensive (HTN) individuals (*3, 4*). These seemingly disparate findings suggest that if sodium or potassium consumption in the diet influence blood pressure regulation, the effect may be mediated, in part, by other nutritional elements.

Calcium is an essential element in normal cellular physiology (*5*). Normal cardiovascular function is critically dependent on both extra- and intracellular calcium concentrations (*6*). Only recently, however, have abnormalities of extra- and intracellular calcium metabolism been identified in both human and experimental hypertension (*7–9*). Several of the reports (*7, 8*), as well as other studies (*10–12*), have suggested maintenance of an adequate or increased level of dietary calcium may protect the human or laboratory animal at risk. However, no studies appear to have been conducted on the dietary calcium intake of humans with essential hypertension. In this report we summarize our findings from a nutritional survey designed to compare calcium intake in humans with established hypertension with the intake reported in a normotensive population that was group matched for age, sex, and race. The data were also compared with nutritional data from the Health and Nutrition Examination Survey (HANES) of the National Center for Health Statistics (*13*).

The HTN population (diastolic blood pressure > 95 mmHg or mean arterial pressure > 105 mmHg) was composed of subjects recently identified as hypertensive in the Hypertension Clinic at the Oregon Health Sciences University (OHSU). The subjects were not receiv-

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ing medication for hypertension at the time of evaluation. Blood pressures were determined in the recumbent position according to the standard criteria of the American Heart Association, and were repeated on two separate occasions between 8:00 and 9:00 a.m. The HTN subjects were entered into the protocol if they met the blood pressure criteria, had not received nutritional counseling and, by standard history, physical, and laboratory examination (serum electrolytes, BUN and creatinine, urinalysis, complete blood count, chest x-ray, electrocardiogram) were diagnosed as having uncomplicated, essential hypertension. The NL control population was drawn from healthy volunteers at OHSU. A total of 44 NL and 46 HTN subjects participated in the survey.

Without prior warning the participants were asked to provide a complete oral recall of their dietary intake for the previous 24-hour period in accordance with a previously tested protocol (*14*). They were not told the purpose of the survey prior to providing the recall data. The recall protocol was applied to the NL's and HTN's in a random fashion without regard to the day of the week. The dietary recalls were then evaluated by means of a computer-facilitated dietary analysis program developed at the School of Dentistry of the OHSU.

The NL population included 16 males and 28 females; the HTN group included 19 males and 27 females. One NL male subject was excluded from the analysis because he reported a 24-hour calcium intake of 5123 mg. The mean age of the NL's was 39 years, while that of the HTN's was 42 years (not significant). The body weights of the subjects in the two groups were comparable. Total caloric intakes (mean ± standard error) of the HTN (1790 ± 108 kcal) and NL (1945 ± 107 kcal) subjects are shown in Fig. 1a and compared to the average U.S. intake (1971 kcal) reported in the HANES (*15*). Caloric intake did not differ among these three groups. The distribution of the primary food sources (Fig. 1b)—protein, carbohydrate, and fat—was also similar between the HTN and NL subjects in our study. Furthermore, with the exception of the carbohydrate consumption reported by the HTN's (189 ± 12 g; for HANES, 223 g), the distribution among all primary food sources for both our HTN and NL subjects was virtually identical to that noted in the HANES. Sodium consumption was also similar (Fig. 1c) among the three groups (*16*). Compared to the reported intake of sodium in the HANES (2229 mg; 97 meq), both the HTN (2564 ± 178 mg; 112 ± 8 meq) and the NL subjects (2508 ± 222 mg; 109 ± 10 meq) consumed similar quantities of sodium. Likewise, potassium intake (Fig. 1d) was similar for the two populations studied (HTN's, 1977 ± 134 mg, 51 ± 3 meq; NL's, 2001 ± 122 mg, 51 ± 3 meq) and equivalent to that reported in the HANES (2210 mg; 57 meq). As depicted in Fig. 1e, reported calcium consumption differed significantly (Mann-Whitney, $P < .05$) between the HTN's (668 ± 55 mg) and NL's (886 ± 89 mg). The dietary calcium intake of our NL subjects did not differ from the value reported in the HANES (857 mg), but the HANES value was greater than in our HTN subjects. As further evidence of the difference in the amount of calcium consumed by the HTN's, only 8 out of 46 HTN's reported consumption over 1 g of calcium per day, whereas 18 out of 44 NL's reported greater than 1 g ($P < .025$).

The sources of dietary calcium also differed between the two groups (Fig. 1f). The two groups consumed similar quantities of calcium from nondairy sources and from milk. However, dairy products other than milk provided 400 ± 78 mg of calcium to the diet of the NL's but only 148 ± 34 mg to the diet of the HTN's (median HTN, 21 mg as opposed to NL, 225 mg; Mann-Whitney, $P < .01$) (*17*).

Although sodium has been assigned a central role in the genesis of hypertension (*1*), the "sodium theory" remains controversial, in part because within most societies there is no demonstrable difference between the sodium intake of subjects with hypertension and subjects who remain normotensive. Although hypertension in some societies appears to be associated with the level of sodium in the diet, there are other cultures that have a remarkably low prevalence of hypertension in spite of high sodium intake (*3*). Rather than requiring a correlation between sodium intake and blood pressure, some investigators have speculated that there is a threshold of dietary sodium that unmasks the hypertensive state in those individuals genetically predisposed to the condition (*1*).

Our data indicate that individuals with hypertension may ingest less calcium than NL subjects. However, our survey was not designed to exclude possible differences between the two groups in other components of the diet or the possible influences of socioeconomic status. Further studies are needed to determine

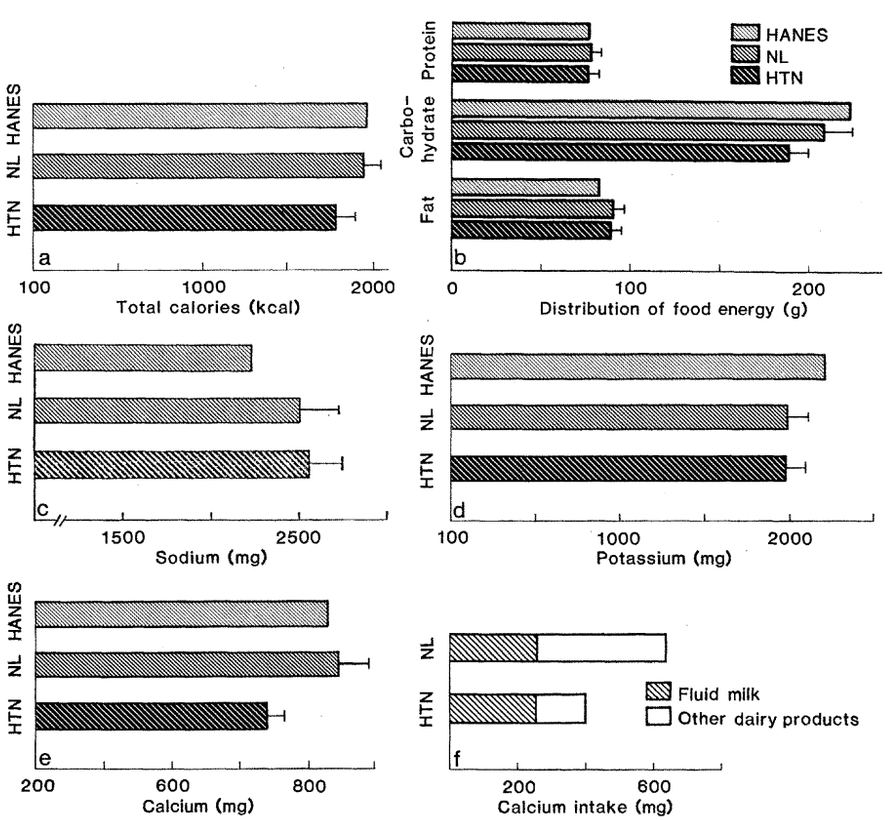

Fig. 1. Results of a pilot survey of the dietary calcium intake of 46 subjects with essential hypertension and 44 normotensive control subjects. The results are compared with the HANES data (*13*). (a) Reported dietary intake of total calories; (b) distribution of food energy; (c) sodium intake; (d) potassium intake; (e) calcium intake; (f) distribution of dairy calcium intake between fluid milk and other dairy product sources.

the relation of our findings to magnesium balance, energy metabolism, sodium and potassium handling by vascular and renal tissue, and the contribution of essential vitamins to cardiovascular physiology. It is also possible that the condition of hypertension predisposes individuals to decrease their calcium intake.

There is evidence that humans with essential hypertension, as well as laboratory animals used as models of hypertension, have associated abnormalities of calcium metabolism (*7–9, 18*). Data from a number of epidemiologic studies indicate an inverse correlation between the calcium content of drinking water and the mean arterial blood pressure or prevalence of hypertension in humans living in specified geographical regions (*19*). In laboratory animals, increased calcium intake lowers blood pressure in normotensive animals and attenuates the development of hypertension in hypertensive models (*8, 11, 12*); the earlier a calcium supplement is introduced, the greater the long-term reduction in blood pressure (*11*).

Our results are interesting for several reasons. First, the HTN patients and NL volunteers reported typical values for the other nutritional components of their diet. Second, although the calcium intake of the HTN's was significantly lower than that of the NL's, the HTN's intake was still within the lower limits recommended for Americans. If, as the data suggest, HTN subjects require a normal or even increased amount of dietary calcium, the calcium intakes reported by the HTN's in our survey may be inadequate. Third, in contrast to the values for sodium or potassium intake, we found a significant difference in calcium intake when the study population was segregated on the basis of the presence or absence of high blood pressure. Overall these data suggest a link between decreased calcium intake and excessive dietary sodium in the pathogenesis of human hypertension. For example, increased sodium intake is associated with enhanced sodium excretion by the kidney and consequent calciuresis (*20*). At the cellular level, modification of calcium homeostasis in vascular tissue may alter intracellular concentrations of Na^+ and K^+ as well as transmembrane fluxes (*21*).

Calcium intake is decreasing in the United States (*22*), and dietary calcium is already well below acceptable levels among some segments [black and elderly subjects (*23*)] of the society who are at greater risk of developing high blood pressure. The results of our survey should also sound a note of caution as several of the dietary restrictions (for example, low cholesterol, low sodium) now recommended to persons with hypertension could potentially result in concurrent, inadvertent, additional reduction in calcium intake.

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16. The HANES and our survey estimated the sodium content of the food. The reported values, therefore, do not account for sodium added by individuals.
17. There was no correlation between age and reported calcium or sodium intake in either the NL's or the HTN's when all subjects were considered; however, within the female subset (NL and HTN), calcium intake declined with age ($P < .05$).
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23. The HANES documented insufficient levels of calcium intake (< 650 mg/day) in blacks and in individuals over 65 years of age.
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Intrathecal Interferon for Multiple Sclerosis

Jacobs *et al.* (*1*) reported a clinical trial in which intrathecal interferon reduced exacerbations in patients with multiple sclerosis. However, the methods these authors used and certain errors in their report raise questions about their findings.

Although Jacobs *et al.* described their study as "a randomized controlled study," the number of years on study was longer for every patient in the treated group than for any patient in the control group (*2*). The reason for this was not explained.

The authors reported a statistically significant difference ($P < .05$) in the rates of exacerbation in the treated and control groups during the study, but, according to the data in their table 1, the probability was .104 (two-tailed *t*-test). A further difficulty is that the non-normality of the rates makes the *t*-test inappropriate; with the more appropriate Mann-Whitney *U* test (*3*), $P = .12$.

Jacobs *et al.* did not describe the procedure for retrospectively determining the number of exacerbations before the study or the duration of disease. The treated patients reported a significantly higher prestudy rate of exacerbations than controls (which is unlikely in a truly randomized study). Since a spuriously high rate in the treated group would overstate the efficacy of the treatment,

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